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

Phosphorothioic triamide, *N*-propyl-

Assessment statement (CA10053)

17 October 2025

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AICIS assessment (CA10053)

Chemical in this assessment

Name	CAS registry number
Phosphorothioic triamide, *N*-propyl-	916809-14-8

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 Focus type.

Defined scope of assessment

The chemical has been assessed:

- as imported into Australia at up to 15 tonnes/year
- as imported at 10% concentration
- for local reformulation into finished end use fertiliser products at up to 0.02% concentration for use by professional workers/farmers, and consumers
- for end use application at a maximum rate of 46 g/hectare

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 as a solid formulation with the assessed chemical at 10% concentration in intermediate bulk containers (IBC) for local reformulation into finished end use fertiliser products.

While the reformulation will not take place at the applicant's Australian facilities, other local suppliers will formulate the end use products by incorporating the assessed chemical with urea fertiliser at their own facilities.

The reformulated end use fertiliser products will contain the assessed chemical at up to 0.02% concentration and will be used as a fertiliser by professional workers/farmers and consumers. The fertiliser will be applied either in granular form or by spray application, directly under the soil surface, predominantly as a pre-planting application. The application rate of the assessed chemical as provided by the applicant will be 46 g/hectare.

Human health

Summary of health hazards

The submitted toxicological data are for the assessed chemical from a reaction mass of the assessed chemical and an analogue chemical (Phosphorothioic triamide, *N*-butyl-, CAS No. 94317-64-3) at 1:3 ratio (see **Supporting information**). The data provided indicate that the assessed chemical is:

- of low acute oral and dermal toxicity (LD50 > 2,000 mg/kg bw in rats)
- not a skin sensitiser
- not genotoxic

The toxicological information also indicates that the assessed chemical is:

- a slight skin and eye irritant

In a 28-days repeated dose oral toxicity study in rats, a no observed adverse effect level (NOAEL) of 200 ppm (18.10/19.80 mg/kg bw/day in males/females) was determined for the test substance (a reaction mass containing the assessed chemical and an analogue chemical at approximately 1:3 ratio), based on reduced body weights in rats at higher doses.

In a prenatal developmental toxicity study, a NOAEL of 100 mg/kg bw/day was determined for systemic toxicity based on signs of maternal toxicity and ossification delays in pups at the highest tested dose of 300 mg/kg bw/day (see **Supporting information**). Postnatal ossification in pups was not evaluated in this study to check if the ossification delays were due to maternal toxicity. The assessed chemical is not classified as a developmental toxicant.

In a two-generation reproductive toxicity study performed on the analogue chemical, the NOAEL for effects on fertility in males was established as 200 ppm (21 mg/kg bw/day), based on decreased sperm motility and epididymal lesions in F1 generation males at 800 ppm (84 mg/kg bw/day) and above. The NOAEL for effects on fertility in females was established as 800 ppm (84 mg/kg bw/day), based on delayed or non-recovery of oestrus cyclicity post-pregnancy for F1 generation females at 3,200 ppm. Therefore, based on the above reproductive effects, the assessed chemical is classified as a Category 2 reproductive toxicant (H361f: Suspected of damaging fertility), according to GHS criteria.

No acute inhalation toxicity data was provided for the assessed or the analogue chemical.

Hazard classifications relevant for worker health and safety

Based on the data provided by the applicant, 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
Reproductive Toxicity	Category 2	H361f: Suspected of damaging fertility

Summary of health risk

Public

Potential consumer exposure to the assessed chemical at up to 0.02% concentration may occur through the use of fertiliser products in home gardens either in granular form or in liquid form via spray application. However, the use of products containing the assessed chemical by the consumers is expected to be limited with use of small volumes/quantities of fertilisers.

While the principal route of exposure will be dermal, ocular and inhalation exposures are also possible. However, considering the infrequent use, low use concentration of the assessed chemical (at up to 0.02%), low vapour pressure (1.2 x 10^{-7} kPa at 20 °C), and the particle size distribution (particles larger than 10 µm), exposure to consumers is expected to be limited. The exposure will be further reduced with the use of gloves.

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

Workers

Potential exposure of workers to the assessed chemical at 10% concentration may occur during formulation operations (see **Supporting information section**) and to professional workers/farmers at up to 0.02% concentration during application of finished end use fertiliser products either in granular form or in liquid form via spray application. The principal route of exposure will be dermal, while ocular and inhalation exposures are also possible. Considering the particle size distribution of the assessed chemical (particles larger than 10 µm) and outdoor application to the ground/soil, inhalation exposure to particles or spay mist will be limited.

The applicant has further indicated that the professional workers/farmers may wear appropriate body protection such as a chemical protection suit, gloves and suitable eye protection such as face masks or safety glasses to reduce exposure during application of fertilisers.

Given the risks of critical health effects of the assessed chemical (developmental toxicity), control measures to minimise exposure are needed to manage the risk to workers during reformulation activities (see **Means for managing risk section**).

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

Based on the ecotoxicological information available for the assessed chemical, it is not expected to be harmful to aquatic life. Therefore, the assessed chemical is not formally

classified under the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS) for acute and chronic aquatic toxicities (UNECE, 2017).

Summary of environmental risk

The fertiliser product containing the assessed chemical will be applied to agricultural soil directly. The product containing the assessed chemical is expected to primarily remain in soil after being applied to soil. A small fraction of the assessed chemical is likely to enter aquatic compartments due to run-off after the application.

The assessed chemical is not readily degradable in water and is persistent in the aquatic compartment. However, a study indicated that the assessed chemical is not persistent in the soil compartment. The assessed chemical does not have potential for bioaccumulation and not expected to cause toxic effects in aquatic or terrestrial organisms.

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. The available ecotoxicity information shows that the assessed chemical is not expected to be harmful to aquatic or terrestrial organisms. 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 soil compartment and the low hazard in the aquatic compartment, the environmental risk from the introduction of the assessed chemical can be managed.

Means for managing risk

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:

- 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 dust, mists and aerosols

- Use of personal protective equipment (PPE)
  - Impervious gloves

    - Protective glasses
    - Protective clothing
    - Respiratory protection where local ventilation may be inadequate

- 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.

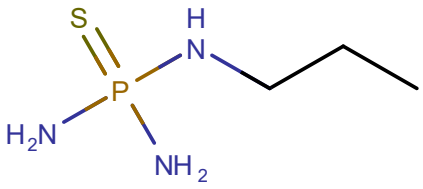
Note:

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	916809-14-8
CAS name	Phosphorothioic triamide, *N*-propyl-
Molecular formula	$C_3H_{12}N_3PS$
Associated names	*N*-Propylphosphorothioic triamide
Molecular weight (g/mol)	153.19
SMILES (canonical)	S=P(N)(N)NCCC
Structural formula	



Relevant physical and chemical properties

Physical form	White crystalline solid
Melting point	91 °C
Relative Density	1,253 kg/m^3 at 20 °C
Vapour pressure	1.2 x 10^{-7} kPa at 20 °C, 2.8 x 10^{-7} kPa at 25 °C, 1.6 x 10^{-5} kPa at 50 °C
Water solubility	51.5 g/L at 20°C, pH 7.5
Particle Size	Inhalable fraction (< 100 µm): 1.23 % Respirable fraction (< 10 µm): 0.00%
Ionisable in the environment	No
log K_{oc}	< 1.25
log K_{ow}	< 0.3 at 24 °C

Human exposure

Workers

Reformulation

The assessed chemical at 10% concentration in IBC will be transported from the applicant's facilities to the local customers' facilities for local reformulation into finished end use fertiliser products. The reformulation process involves treating urea fertiliser with the assessed chemical using either a batch mixer, rotating drum mixer or continuous mixer. These processes will be handled by the industrial fertiliser producers.

In a typical reformulation process, the assessed chemical in IBC is placed on a balance and connected to a gear pump. With a controller, the pump flow can be regulated to match the desired application rate. A coarse nozzle is used to avoid formation of aerosols. The treated urea is then filled into big bags or 50 kg bags or handled as free-flowing bulk material immediately after application.

The applicant has further stated that all the reformulation processes are carried out indoor under well-maintained adequate local exhaust ventilation, like a receiving or capturing hood at points of potential emission. Worker exposure is further reduced with use of PPE such as long-sleeved clothing and/or coveralls, impermeable gloves (nitrile/chloroprene/butyl rubber), and protective boots.

Health hazard information

The test substance used in the following studies is a reaction mass containing the assessed chemical and the analogue chemical at approximately 1:3 ratio. Therefore, the reaction mass is considered representing the neat assessed chemical to derive hazard information.

The granulometric data for the assessed chemical (NPPT) indicated that 98.77% of the particles are larger than 100 µm, with only 1.23% of the total volume being less than 100 µm in size. As there are no particles smaller than 10 µm, the inhalation risks to the assessed chemical during use situations are expected to be limited.

Acute toxicity

Oral

In an acute oral toxicity study (OECD TG 423), the test substance was administered to two groups of female Wistar Crl:WI (Han) rats (3 rats/group) at 2,000 mg/kg bw in olive oil by oral gavage. Clinically, impaired general state, dyspnoea, reduced faeces, staggering gait, salivation, exsiccosis and piloerection were observed. These findings were observed up to day 8 following administration. All treated animals showed expected mean bodyweight gains during the study. All animals survived until the end of the study period (day 14), and no abnormalities were observed at necropsy. The acute oral median lethal dose (LD50) value for the test substance was determined to be > 2,000 mg/kg bw. Therefore, the assessed chemical is of low acute oral toxicity.

Dermal

In an acute dermal toxicity study (OECD TG 402), the test substance in olive oil was applied at a single dose of 2,000 mg/kg bw to the clipped skin (dorsal and dorso-lateral parts of the trunk) of Wistar Crl:WI (Han) rats (n=5/sex) by a semi-occlusive dressing for 24 hours. The animals were observed for 14 days following application. All animals survived until the end of the study period (day 14) and no clinical signs/skin effects were observed. The mean body weight of the animals increased within the normal range during the study period. No apparent abnormalities were observed at necropsy in any animal. Under the conditions of this study, the acute dermal LD50 of the test substance was determined to be > 2,000 mg/kg bw in rats. Therefore, the assessed chemical is of low acute dermal toxicity.

Corrosion/Irritation

Skin irritation

In a skin irritation study (OECD TG 404), 0.5 g of the undiluted test substance was applied under semi-occlusive conditions to the intact skin of 3 New Zealand White male rabbits for 4 hours. Animals were observed for 72 hours after removal of the patch. A slight erythema was observed in all animals at 1 hour after removal of the patch. The cutaneous reactions were reversible in all animals within 24 hours after removal of the patch, with the average score for irritation was calculated to be 0.0 for erythema/oedema at up to 72 hours. Therefore, under the conditions of this study, the assessed chemical is a slight skin irritant.

Eye irritation

In an eye irritation study (OECD TG 405), 0.1 mL of the undiluted test substance was instilled into the conjunctival sac of one eye of each of 3 New Zealand White rabbits. The other eye remained untreated and served as control. The ocular reactions were assessed approximately at 1, 24, 48 and 72 hours after application and on day 7.

Slight corneal opacity, moderate iritis, moderate conjunctival redness, slight to marked conjunctival chemosis and slight to severe discharge were observed in the animals during the study. Contracted pupil and redness in the white part of the eye were reported. The ocular reactions were reversible in all animals within 7 days after application. Calculated mean scores for each animal over 24, 48 and 72 hours were 0.9 for corneal opacity, 0.4 for iris lesions, 2.0 for redness of the conjunctiva and 1.2 for chemosis. Even though the score of 2.0 for redness of the conjunctiva were observed in all three animals at three time points, as the ocular reactions were reversible in all animals within 7 days after application, the test substance is considered as slightly irritating to the eye. Therefore, the assessed chemical is slightly irritant to the eyes.

Sensitisation

Skin sensitisation

The skin sensitisation potential of the test substance was tested in a local lymph node assay (LLNA) in mice (OECD TG 429). Three groups of 5 female mice (CBA/J) received topical application of 25 µL of the test substance at 3%, 10% and 50% concentration in methyl ethyl ketone to the dorsal surface of both ears for 3 consecutive days. The control group of five female mice was treated with 25 µL per ear of the vehicle alone. Three days after the last injection, the mice were then injected intravenously with 20 µCi of ^{3}H-thymidine in 250 µL of sterile saline into a tail vein. There were no signs of systemic toxicity and body weights were

comparable to controls. The stimulation indices (SI) for ^{3}H-thymidine incorporation as compared to the vehicle control were: 1.00 for 0% (vehicle); 0.93, for 3% concentration; 1.11 for 10% concentration; and 1.09 for 50% concentration, respectively.

The test substance did not induce a biologically relevant response (increase above the cut off stimulation index of 3) at all concentrations applied and there was no relevant increase in lymph node weights. Although the test substance was tested at up to 50% concentration, there is no dose response or increase in the SI with increased concentrations tested. Therefore, the assessed chemical is not expected to be a skin sensitiser.

Repeat dose toxicity

Oral

In a repeated dose oral toxicity study (OECD TG 407), the test substance was administered to Wistar rats (n = 5/sex/dose) via drinking water at dose levels of 0, 200, 1,000 and 5,000 ppm for 28 days. These dose levels were equal to 18.1/19.8 mg/kg bw/day for male/female at 200 ppm, 86.0/98.2 mg/kg bw/day for male/female at 1,000 ppm, and 377.1/419.5 mg/kg bw/day for male/female at 5,000 ppm. There were no deaths during the study and there were no treatment-related changes in clinical examinations, food consumption, functional performance battery tests and motor activity measurement. In addition, no treatment-related changes were noticed in the clinical chemistry, haematological, urinalyses, and at necropsy and histopathological examination.At 1,000 ppm, water consumption was decreased in both sexes towards the end of the administration period with a maximum decrease of 15/13.8% in males/females, respectively, on day 28. The body weight was statistically significantly decreased in male animals on day 21 and 28 (-6.5% on both days).

At 5,000 ppm, water consumption was also decreased in both sexes at up to 34.7/38% in male/female animals, respectively, on day 28. The mean body weight was statistically significantly decreased in both sexes from day 7 till the end of the study, up to 14.3% on day 28 in male animals and 9.9% on day 14 and 9.1% on day 28 in female animals.

Under the conditions of this study, the study author established a NOAEL of 200 ppm (18.1/19.8 mg/kg bw/day in males/females) for the test substance in this study, based on presence of signs of adverse general systemic toxicity (decreased water consumption and reduced body weight) at higher doses. Therefore, a NOAEL of 200 ppm (18.1/19.8 mg/kg bw/day in males/females) is determined for the assessed chemical. As there were no adverse effects reported in animals at 1,000 ppm (86-98 mg/kg bw/day) except for mean body weight reductions of < 10% in males, the assessed chemical was not classified for repeated dose toxicity.

Genotoxicity

The test substance was not mutagenic in a bacterial reverse mutation assay, when tested in *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and *Escherichia coli* strain WP2 uvrA, with and without metabolic activation (OECD TG 471). No precipitation of the test substance was found. A weak bacteriotoxic effect was infrequently noted depending on the strain and test conditions at 5,000 µg/plate. No relevant increase in the number of his+ or trp+ revertants was observed in the standard plate test (20 – 5,000 µg/plate) or in the preincubation test (312.50 – 5,000 µg/plate) either with or without S9 mix.

The test substance did not induce the formation of micronuclei in an *in vitro* micronucleus test in Chinese hamster V79 cells (OECD TG 487). Two independent experiments were conducted: 4-hour exposure with 24 hours harvest time at up to 5,800 µg/mL with and without S9-mix

(experiment 1); 24-hours exposure at up to 2,000 µg/mL in the absence of S9-mix, and 4-hours exposure at up to 3,000 µg/mL with S9-mix, both with a 24 hours harvest time (experiment 2). The test substance did not show any biologically relevant increase in the number of cells containing micronuclei either without S9 mix or after adding a S9 mix in the two experiments carried out independently of each other. Therefore, under the conditions of the study, the test substance is not considered to have a chromosome-damaging (clastogenic) effect nor induce numerical chromosomal aberrations (aneugenic activity).

The test substance was also assessed for its potential to induce gene mutations at the hypoxanthine-guanine phosphoribosyl transferase (HPRT) locus in Chinese Hamster Ovary (CHO) cells with or without metabolic activation (S9-mix) (OECD TG 476). Five independent experiments were carried out. The results indicated that the test substance did not cause any biologically relevant increase in the mutant frequencies either with/without S9 mix in five experiments performed independently of each other. Therefore, under the conditions of this study, the assessed chemical was not mutagenic in CHO cells.

Overall, the assessed chemical is not genotoxic.

Development toxicity

In a prenatal developmental toxicity study (OECD TG 414), the test substance was administered to mated female Wistar (Han) rats (n = 22/dose group) at doses of 0, 30, 100 and 300 mg/kg bw/day via oral gavage from Days 6 to 19 post-coitum. Rats of the control group received the vehicle alone (1% (w/w) carboxymethyl cellulose suspension in water). On Gestation Days (GD) 20, all surviving dams were subjected to macroscopic post-mortem examination.

Treatment at 300 mg/kg bw/day resulted in statistically significantly lower food consumption compared to controls from Days 6-9 and 15-20.

A statistically significantly lower mean body weight and mean body weight gain were noted in the females of the highest treatment group (300 mg/kg bw/day), as compared to controls, from Days 16/17 post-coitum onwards. This effect increased progressively until the end of the observation period (Day 20 post-coitum). In line with this, significantly decreased mean body weight was reported for females of the highest treatment group, compared to controls, after correction for uterus weight as determined at necropsy.

No maternal toxicity was observed at 30 and 100 mg/kg bw/day. At 300 mg/kg bw/day, maternal findings included one unscheduled death (killed in extremis), treatment-related clinical signs such as lethargy, piloerection, hunched posture, uncoordinated movements, abnormal gait, pale faeces, pale and/or lean appearance), reduced body weight/body weight gain with reduced food consumption. While these clinical findings were noted in 7 out of 21 females on one or more days during the third week of treatment, the other 13 out of 21 females showed no clinical signs. No gross findings were noted or considered related to the treatment at necropsy in all treatment groups.

There were no treatment-related effects on viability, litter size, sex ratio, the number of corpora lutea, implantation sites, viable or dead foetuses, early or late resorptions, or pre- and post-implantation loss at up to the highest tested dose (300 mg/kg bw/day). Reduced mean foetal body weights were observed in both male (statistically significant) and female (not statistically significant) pups at the highest dose. The reduced mean foetal body weight could be due to the considerable maternal toxicity observed in the highest tested dose group.

There were no test substance-related effects on foetal external morphology, foetal visceral morphology, and foetal skeletal malformations at up to the highest tested dose (300 mg/kg bw/day). However, several skeletal variations were noted at higher incidences in the 300 mg/kg bw/day group pups, indicative of a developmental delay. These included a reduced ossification of the skull (16.4%/litter), unossified sternebra number/s 5 and/or 6 (18.8%/litter), unossified hyoid (6.9%/litter), bipartite ossification of vertebral centra (2.0%/litter) and entire sternum unossified (2.1%/litter). The incidence of ossified cervical centrum no. 1 was decreased (20.9%/ litter) at highest tested dose (300 mg/kg bw/day), compared to the concurrent control value (37.2%/ litter).

Although retardation of ossifications in pups could be due to maternal toxicity at the highest tested dose, some of the delayed ossifications could be due to treatment related developmental toxicity in this strain of rats (Chahoud & Paumgartten, 2005). However, other publications (Carney & Kimmel, 2007; Hofmann et al. 2016; DeSesso & Scialli, 2018) state that delayed or reduced ossification observed in rodent developmental toxicity studies should generally be regarded as a transient, reversible developmental variation rather than as an adverse effect or malformation, particularly when such findings occur in the context of maternal toxicity and/or reduced foetal weight. As postnatal ossification in pups was not evaluated in this study to rule out maternal toxicity as a reason for reduced ossification, the assessed chemical cannot be classified as a developmental toxicant.

In a two-generation reproductive toxicity study (OECD TG 416) (NICNAS, 2011), the analogue chemical was administered in the diet to four groups (n = 32/sex) of CD strain of Sprague-Dawley origin rats at 0, 200, 800 or 3,200 ppm. Treatment of F0 males and females commenced 10 weeks prior to pairing. For F1 males and females, offspring not selected for continuation of the study were sacrificed on day 35 postnatal day (PND). Treatment of selected F1 animals (n = 32/sex) commenced at PND 28, then 10 weeks from weaning prior to pairing until termination (when litters were weaned). After 10-week pre-mating treatment, 1 male and 1 female from the same treatment group were paired in a cage for up to 3 oestrus periods or up to 2 weeks without partner exchange and no pairing of siblings. The actual amount of analogue chemical intake varied at different stages (pre-mating, gestation and lactation) of the experiment. The mean intakes of analogue chemical in the F0 generation were 21, 84 and 334 mg/kg bw/day and in the F1 generation were 23, 90 and 362 mg/kg bw/day.

There were no treatment-related mortalities seen in both F0 and F1 generations.

Treatment with the analogue chemical neither affected the mating performance in F0 animals nor produced adverse reproductive effects in F0 females. Histopathological examination of the epididymis showed that all high-dose F0 males had epithelial fatty vacuolation in the corpus. Other changes included epididymal fat granulomas, reduced sperm content, luminal germ cells and corpus interstitial inflammatory infiltrate. Sperm evaluation revealed that the percentage of normal morphology, progressively motile, straight-line velocity and curvilinear velocity were significantly lower ($p < 0.01$) in the epididymis of the high-dose males.

Examination of male reproductive organs revealed that F1 high-dose males had significantly lower seminal vesicle absolute weight, and higher epididymis and testis relative weights. Sperm evaluation from epididymis samples showed that percentage of motile sperm was significantly lower ($p < 0.01$) in F1 mid- and high-dose males. Percentage of progressively mobile sperm ($p < 0.05$) and percentage of rapid sperm ($p < 0.01$) were significantly lower in high-dose males. From histopathological results, the epithelial cells lining the epididymal duct exhibited macro and micro vesiculation resembling fat vacuoles in all high-dose males and in 13 out of 31 mid-dose males, compared to nil in both the controls and the low-dose males.

For the F1 females, high-dose females had significantly lower ovarian and oviduct weight ($p < 0.05$). Histopathological investigations of high-dose females reported a clear increase in the number of animals exhibiting atrophic and mucified vaginal epithelium and histological indications of anoestrus (animals not returned to normal oestrus cycle).

There were no other significant differences between test substance-treated animals and the controls in reproductive performance.

Mean implantation count and total and live litter size on day 1 in high-dose F1 females were both slightly lower compared with the control group, and the difference attained statistical significance for live litter size. Other litter parameters were not affected by treatment. Bodyweight of male and female offspring on PND 1 and PND 14 were also not adversely affected but decreased thereafter compared to controls (10%, 7% and 5% for high-, mid- and low-dose males and 12%, 7% and 5% for high-, mid- and low-dose females at PND 14-35).

Mean implantation count and total and live litter size on PND 1 were slightly lower at high-dose than in controls (with no effect at mid- and low-dose) in the F2 generation. Bodyweight and bodyweight gains for both male and female offspring on PND 14 were also not adversely affected. Thereafter, high-dose male and female offspring had lower weight gain than controls (10% and 7% respectively) at PND 14-35 although a dose response was not seen. There was no effect on the timing of developmental milestones. Adverse effects on reproductive organs were observed in both male and female rats, that could affect fertility.

The NOAEL for effects on fertility in males was established as 200 ppm (21 mg/kg bw/day) based on decreased sperm motility and epididymal lesions in F1 generation at 800 ppm (84 mg/kg bw/day) and above. The NOAEL for effects on fertility in females was established as 800 ppm (84 mg/kg bw/day), based on delayed or non-recovery of oestrus cyclicity post-pregnancy for F1 generation females at 3,200 ppm. Therefore, based on the above reproductive effects the assessed chemical is classified as a Category 2 reproductive toxicant (H361f: Suspected of damaging fertility), according to GHS criteria.

The NOAEL for developmental toxicity was not determined in this study. The decreased bodyweight gain in pups was considered to be due to maternal toxicity.

Environmental exposure

The assessed chemical will be imported into Australia and reformulated locally into finished fertiliser products. The reformulation of the assessed chemical will occur in a closed system with engineering controls including well-maintained local exhaust ventilation to capture any potential emission, minimising the release of the assessed chemical from the reformulation processes.

The finished fertiliser product will be transported and stored following the standard operations. As such, significant release of the product containing the assessed chemical to the environment is not expected during transportation and storage.

Fertiliser products containing the assessed chemical will be used by professional workers/farmers, applying the assessed chemical directly to soil in a granular form, liquid form or via spray application. The assessed chemical is expected to primarily remain in the soil compartment after being applied in agricultural soils, with a small amount of the assessed chemical entering aquatic compartments due to the run-off.

Environmental fate

Partitioning

The assessed chemical is readily soluble in water (water solubility = 51.5 g/L) with a low potential to partition from water to organic phase (log K_{ow} < 0.3). The assessed chemical is expected to remain in water compartment when entering water environments.

The assessed chemical is expected to have high mobility when released to soils based on the measured adsorption/desorption coefficient (log K_{oc} < 1.15 – 1.8).

The assessed chemical is slightly volatile (vapour pressure = 2.8 × 10^{-4} Pa at 25 °C) and is not expected to partition into the air compartment.

Degradation

The assessed chemical is considered persistent based on its measured biodegradation in water. However, the assessed chemical is not persistent in soil based on the measured half-life of the analogue chemical in soil.

A ready biodegradation screening test conducted according to OECD TG 301A on a mixture of the assessed chemical and analogue chemical, showed 12% degradation of the test substance in 28 days. Therefore, the assessed chemical is considered not readily biodegradable.

A provided literature study showed the half-lives of the analogue chemical in soil were $t_{1/2}$ = 0.68 days at pH 4.9 and $t_{1/2}$ = 3.18 days at pH 6.9, respectively (Hendrickson et al 1993), indicating that the assessed chemical is not persistent in soil.

The hydrolysis test conducted according to OECD TG 111 on a mixture of the assessed chemical and analogue chemical indicated that the assessed chemical is not stable in acidic environments ($t_{1/2}$ = 5.7 hours at 25 °C, pH 4). However, it may be hydrolytically stable in neutral and alkaline environments ($t_{1/2}$ = 79 days 25 °C, pH 7).

Bioaccumulation

Based on its log K_{OW} value, the assessed chemical does not have the potential to bioaccumulate.

No experimental bioaccumulation information was provided for the assessed chemical. However, the experimental partition coefficient of the assessed chemical (log K_{ow} < 0.3) is below the domestic bioaccumulation threshold of log K_{ow} = 4.2 (DCCEEW, 2022).

Predicted environmental concentration (PEC)

Soil compartment

The application specified that the maximum application dose for the assessed chemical is 46 g/hectare.

Soil bulk densities for loamy soils typically range from 1.1 to 1.4 g/cm³ (NRCS USDA) and a typical depth for applying fertiliser during soil tillage ranges from 5 to 20 cm (Strip-Till Farmer).

Assuming the soil bulk density of 1.3 g/cm^3 and a soil depth 5 cm, the mass of 1 hectare soil will equal to 6.5 ×10^5 kg (= 10,000 m^2 × 0.05 m × 1.3 g/cm^3 = 10,000 m^2 × 0.05 m × 1.3 × 10^3 kg/m^3). The PEC_{soil} of the assessed chemical in soil is approximately 0.071 mg/kg of soil (= 4.6 × 10^4 mg/6.5 ×10^5 kg).

Water compartment

The assessed chemical is likely to enter aquatic environments from run-off when applying to topsoil in agriculture applications. Assuming a 100 mm rainfall event with 20% of that water running off, resulting in 200 m^3 run-off water per hectare (= 100 mm × 1 hectare × 20% = 0.1 m × 10,000 m^2 × 20%). The run-off water is calculated to carry 5% of the assessed chemical for the worst-case edge-of-field scenario. This does not consider the uptake by plants, and degradation of the assessed chemical. The PEC_{runoff} from a run-off is approximately 11.5 µg/L (= 46 g/ha × 0.05 ÷ 200 m^3 run-off water/ha).

Environmental effects

Effects on aquatic Life

The test substance in the following ecotoxicological studies refers to a reaction mass containing the assessed chemical and analogue chemical at approximately 1:3 ratio.

Acute toxicity

The following measured median lethal concentration (LC50) and median effective concentration (EC50) values for model organisms were provided for the test substance.

Taxon	Endpoint	Method
Fish	Test substance: 96 h LC50 > 120 mg/L	*Danio rerio* (Zebra fish) Mortality OECD TG 203 Static conditions Nominal concentration
Invertebrate	Test substance: 48 h EC50 > 120 mg/L	*Daphnia magna* (Water flea) Immobility OECD TG 202 Static conditions Nominal concentration
Freshwater algae	Test substance: 72 h ErC50 > 120 mg/L	*Desmodesmus subspicatus* (Green algae) Growth inhibition OECD TG 201 Static conditions Nominal concentration

Chronic toxicity

The following measured no effect concentration (NOEC) value for algae was provided for the test substance.

Taxon	Endpoint	Method
Freshwater algae	Test substance: 72 h NOErC = 120 mg/L	*Desmodesmus subspicatus* (Green algae) Growth inhibition OECD TG 201 Static conditions Nominal concentration

Effects on terrestrial Life

The following studies of toxic effects of the test substance and analogue chemical on terrestrial life were provided.

Taxon	Endpoint	Method
Earthworms	Test substance: 14 d LC50 > 1,000 mg /kg dry weight soil	*Eisenia fetida* (Earthworm) OECD TG 207 Mortality Artificial soil Nominal concentration
Terrestrial arthropods	Test substance: 28 d $NOEC_{reproduction}$ = 10 mg/kg dry weight soil	*Folsomina candida* (Soil Arthropod) OECD TG 232 mortality and reproduction Artificial soil Nominal concentration
Terrestrial Plants	Analogue chemical: 21 d EC10 = 10 mg/kg soil.	Seeds from *Triticum aestivum L.* (wheat), *Sorghum bicolor L.*(sorghum), Potential phytotoxicity Buckney and Sparta soils Nominal concentration
Soil microorganisms	Analogue chemical: 21 d NOEC = 10 mg/kg soil	Effects on nitrification of organic nitrogen by soil microorganisms Harps, Canisteo and Storden soils Nominal concentration

In the supplied terrestrial plant toxicity study detailed above, the harmful effect observed was caused by inhibition of urease in a urea rich environment leading to a toxic build-up of urea in the organism rather than direct toxicity from the analogue chemical.

Predicted no-effect concentration (PNEC)

The assessed chemical is not harmful to aquatic life based on the measured results as summarised above. Therefore, a predicted no-effect concentration (PNEC) is not calculated for the water compartment.

A PNEC = 10 mg/kg of dry weight soil was calculated for the assessed chemical in the soil compartment. This value was derived using the endpoint value for soil arthropod (28 d NOEC = 10 mg/kg of dry weight soil). An assessment factor of 10 was applied to this endpoint as chronic toxicity data were available for three trophic levels of terrestrial species (EPHC, 2009). The endpoint for soil arthropod was selected, over the endpoints of soil plant and soil microorganisms, for the PNEC calculation as the arthropod study was conducted according to the OECD guidelines and the test results were reliable.

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 low measured log K_{ow}, the assessed chemical is categorised as Not bioaccumulative.

Toxicity

Not Toxic (Not T). Based on available ecotoxicity values above 1 mg/L, 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 soil:

Compartment	PEC	PNEC	RQ
Soil	0.071 mg/kg soil	1 mg/kg soil	0.071

For the soil compartment, an RQ less than 1 indicates that introduction of the assessed chemical, in line with the terms outlined in this assessment certificate, is not expected to pose a significant risk to the environment. Additionally, the available aquatic ecotoxicity information shows that the assessed chemical is not expected to be harmful to aquatic organisms. Therefore, the risk from the assessed chemical can be managed, based on consideration of the environmental hazard characteristics and estimated releases.

References

Bakand S, Hayes A, Dechsakulthorn F (2012), Nanoparticles: a review of particle toxicology following inhalation exposure, *Inhalation Toxicology,* 24(2):125-35.

Carney EW, Kimmel CA (2007): Review Article. Interpretation of Skeletal Variations for Human Risk Assessment: Delayed Ossification and Wavy Ribs. Birth Defects Research (80), 473-496.

Chahoud I and Paumgartten F.J.R (2005), Relationships between fetal body weight of Wistar rats at term and the extent of skeletal ossification. Braz J Med Biol Res, April 2005, Volume 38(04) 565-575. https://www.scielo.br/j/bjmbr/a/rZP6h36JPFcBGJtFMD5Fz7D/?lang=en.

DCCEEW (2022) Australian Environmental Criteria for Persistent, Bioaccumulative and/or Toxic Chemicals, DCCEEW, accessed 24 July 2025.

DeSesso JM, Scialli AR (2018): Bone Development in Laboratory Mammals Used in Developmental Toxicity Studies. Birth Defects Research, 1-31.

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.

Hendrickson L L, Douglass E A (1993), Metabolism of the urease inhibitor N-(n-butyl) thiophosphoric triamide (NBPT) in soils, *Soil Liiol. Biochem.,* 25(11):1613-1618.

Hofmann A, Busen R, Schneider S, van Ravenzwaay B (2016): Postnatal fate of prenatal-induced fetal alterations in laboratory animals. Reproductive Toxicology (61), 177-185.

NRCS USDA (Natural Resources Conservation Service, US Department of Agriculture), Bulk Density - Soil Health Guide_0.pdf, Accessed 24 July 2025.

Strip-Till Farmer, 21 Strip-Till Fertility Tips for Feeding Plants the Right Diet, 21 Strip-Till Fertility Tips for Feeding Plants the Right Diet, Accessed 25 July 2025.

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 07 August 2025.

SWA (Safe Work Australia) (2023), Code of Practice: Managing Risks of Hazardous Chemicals in the Workplace, Safe Work Australia, Accessed 07 August 2025.