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

Alkanes, $C_{8–18}$-branched and linear

Assessment statement (CA09590)

22 March 2023

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AICIS assessment statement

Chemical in this assessment

Name	CAS registry number
Alkanes, $C_{8–18}$-branched and linear	2252265-89-5

Reason for the assessment

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

Certificate Application type

Very low to low risk

According to information submitted by the applicant and criteria in the Industrial Chemicals (General) Rules 2019 and the Industrial Chemicals Categorisation Guidelines, this introduction is in the **reported** category. The reason is that this introduction has **low** indicative risk for **human health** because it is in:

- human health exposure band 4
- human health hazard band A

The introduction of this chemical has **low** indicative risk for the **environment** because it is in:

- environment exposure band 4
- environment hazard band A

Defined scope of assessment

The chemical has been assessed for use as an aviation (jet) fuel that is imported into Australia in a neat form. The importation volume is up to 80,000 tonnes per year.

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 up to 100% concentration for use as an aviation fuel (without any additional blending) at various airports around Australia.

It will be imported by sea and transferred directly from various ports by pipeline into storage tanks at the ports. It will then be transferred by pipeline to fuel tankers for transport to airports by road. Trained workers will connect and disconnect hoses and pumping equipment and conduct refueling operations on aircraft.

Human health

Summary of health hazards

Based on the data submitted, the assessed chemical is toxic by aspiration, warranting hazard classification (see below).

The submitted toxicology data on an analogue chemical (see **Supporting information**) indicate that the assessed chemical:

- is of low acute oral, dermal and inhalation toxicity
- is slightly irritating to skin and eyes
- is not a skin sensitiser
- is not considered to be genotoxic
- is of low dermal absorption
- is not likely to cause systemic toxicity following repeated oral exposure (up to 1000 mg/kg bw/day in rats)
- is not likely to cause adverse effects in reproductive organs, embryotoxicity or teratogenicity following repeated oral exposure (up to 1000 mg/kg bw/day in rats).

While the assessed chemical is of low acute inhalation toxicity, considering the presence of alkanes of chain length < C10 (12%) in the assessed chemical, inhalation of vapours of the assessed chemical may cause some adverse health effects, as reported in an acute inhalation toxicity study in mice (see **Supporting information**).

The assessed chemical is a Flammable Liquid (Cat 3) based on its flash point of ≥ 23 °C and ≤ 60 °C (UNECE 2017). As the assessed chemical has a kinematic viscosity of ≤ 20.5 mm^2/s at 40 °C, classification for Aspiration Toxicity (Cat 1) is warranted according to the GHS criteria (UNECE 2017) (see **Supporting information**).

Hazard classifications relevant for worker health and safety

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 follows. This does not consider classification of environmental hazards.

Health hazards	Hazard category	Hazard statement
Aspiration toxicity	Asp. Tox. 1	H304: May be fatal if swallowed and enters airways
Physical hazards	**Hazard category**	**Hazard statement**
Flammable liquid	Flam. Liquid 3	H226: Flammable liquid and vapour

Summary of health risk

Public

When introduced and used in the proposed manner as aviation fuel, it is unlikely that the public will be exposed to the assessed chemical.

This assessment does not identify any risks to public health that would require specific risk management measures when the assessed chemical is introduced and used in accordance with the terms of the assessment certificate.

Workers

Potential exposure of workers to the assessed chemical at a concentration of 100% may occur during connecting/disconnecting hoses to the trucks, the storage vessels, and aircraft during transfer/storage/use of the aviation fuel containing the assessed chemical. While the exposure to the assessed chemical will be mainly dermal, ocular and inhalation exposure may also occur.

Control measures to minimise inhalation exposure may be needed if aerosols or mists are formed during work activities (see **Means for managing risk**).

Environment

Summary of environmental hazard characteristics

According to domestic environmental hazard thresholds and based on the available data the chemical is:

- Not Persistent (not P)
- Not Bioaccu mulative (not B)
- Not Toxic (not T)

Environmental hazard classification

The chemical satisfies the criteria for classification according to the *Globally Harmonized System of Classification and Labelling of Chemicals* (GHS) (UNECE 2017) as Chronic Category 3 (H412) based on the chronic toxicity data for invertebrates for an analogue of the assessed chemical. Considerations were also made for the degradation of the assessed chemical.

Environmental Hazard	Hazard Category	Hazard Statement
Hazardous to the aquatic environment (long-term)	Aquatic Chronic 3	H412: Harmful to aquatic life with long lasting effects

Summary of environmental risk

No significant release of the assessed chemical is expected to occur as a result of its use as an aviation fuel. The assessed chemical will be combusted during its use.

Most of the constituents of the assessed chemical are not expected to persist in the environment, bioaccumulate or cause toxic effects in aquatic organisms. Some constituents of the assessed chemical may be persistent, but this hazard is expected to be mitigated by negligible release of the chemical.

The hazards of the assessed chemical are not expected to differ significantly from other existing substances available for use as jet fuels in Australia. Additionally, the introduction of this chemical is not expected to increase the total use volume of jet fuels as it will be supplied to a demand-driven market. Introduction of this chemical is therefore not expected to significantly increase the environmental risks associated with the use of jet fuels in Australia.

It is expected that the environmental risk from the introduction of the assessed chemical can be managed within existing frameworks.

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**).

Advice to Industry

- The following control measures could be implemented to manage the risk arising from exposure to the use of the assessed chemical:
    - Use of engineering controls such as
        - Enclosed and automated processes where possible
        - Adequate workplace ventilation to avoid accumulation of vapours, mists, or aerosols
    - Use of safe work practices to
        - Avoid inhalation of mists or aerosols
    - Use of personal protective equipment (PPE)
        - 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, 2012) or relevant State or Territory Code of Practice.
- A copy of the Safety Data Sheet (SDS) should be easily accessible to workers.

Environment

Recommendation to Department of Climate Change, Energy, the Environment and Water

The chemical may be scheduled under the Industrial Chemicals Environmental Management (Register) Act 2021. Information from this assessment statement will be considered as part of

any scheduling process. This may include information on chemical identity, environmental hazard characteristics, GHS classification and environmental risk.

Conclusions

The conclusions of this assessment are based on the information described in this statement.

Considering the means of managing risks, the Executive Director is satisfied that when the assessed chemical is introduced and used in accordance with the terms of the assessment certificate the human health and environment risks can be managed. This is provided that:

- all requirements are met under environmental, workplace health and safety and poisons legislation as adopted by the relevant state or territory.
- the means of managing the risks identified during this assessment are implemented.

Note: Obligations to report additional information about hazards under section 100 of the *Industrial Chemicals Act 2019* apply.

Supporting information

Chemical identity

Chemical name	Alkanes, $C_{8–18}$-branched and linear
CAS No.	2252265-89-5
Synonyms	Renewable hydrocarbons (kerosene type fraction)
Molecular weight (g/mol)	142 – 240
Chemical description	Unknown variable composition or biological (UVCB) substance

The assessed chemical is obtained by the hydrodeoxygenation and catalytic hydroisomerisation of vegetable oils and/or animal fats. It is a complex combination of hydrocarbons consisting predominantly of branched and linear paraffins having carbon numbers in the range of C8 to C18 and boiling in the range of approximately 125 – 275 °C.

Relevant physical and chemical properties

Physical form	Colourless liquid
Melting point	< -20 °C
Boiling point	125 – 275 °C
Flash point	48 °C
Vapour pressure	43 Pa at 25 °C
Water solubility	≤ 3.59 mg/L (calc.)
Ionisable in the environment?	No
log K_{ow}	> 6.23
log K_{oc}	> 5.62
Kinematic viscosity	2.25 mm^2/s at 40 °C

Human exposure

Workers

Worker exposure during storage and transportation is expected to be low, as loading and unloading will consist of connecting/disconnecting hoses to the trucks and storage vessels for

transfer of the aviation fuel containing the assessed chemical. Spillage during transfer of aviation fuel is prevented by the use of a special air backflush system, however dermal exposure resulting from drips and spills may occur during the connecting/disconnecting of transfer hoses. The applicant has stated that only trained service personnel will be involved in the transfer process and worker exposure is expected to be limited through the use of enclosed systems and PPE such as protective clothing, safety glasses and impervious gloves.

Public

The aviation fuel containing the assessed chemical is not available to the general public and will only be used in the aviation industry. Therefore, exposure of the general public to the assessed chemical is not expected.

Health hazard information

The applicant has not submitted data for the toxicological endpoints for the assessed chemical. The applicant has, however, submitted toxicological data for a suitable analogue chemical, which were appropriate for read across to the assessed chemical.

Toxicokinetics

Based on the physicochemical properties of the assessed chemical (log K_{ow} greater than 6.23 and water solubility of the predominant iso-alkanes of less than 1.5 x 10^{-5} g/L), dermal absorption is expected to be low. These properties also suggest that uptake of the assessed chemical by lung may occur following inhalation of vapour or respirable aerosol (if formed) and uptake of the substance across the gastrointestinal tract is possible. The predicted uptake was found to be approximately 60% of the total chemical present as determined by in silico modelling (Albro and Fishbein 1970).

Acute toxicity

Oral

In an acute oral toxicity study (OECD TG 423), 2 groups of fasted female Sprague-Dawley CD rats (3/group) were administered an analogue chemical via oral gavage at a dose of 2000 mg/kg bw. No deaths or signs of systemic toxicity were observed. There were no macroscopic findings in any treated animals. The median lethal dose (LD50) was determined to be greater than 2000 mg/kg bw. Based on the results of this study, the assessed chemical is likely to be of low acute oral toxicity.

Dermal

In an acute dermal toxicity study (OECD TG 402), the analogue chemical was applied at a single dose of 2000 mg/kg bw evenly on the intact skin of 10 Sprague-Dawley CD rats (5/sex) and covered with a semi-occlusive dressing for 24 hours. No deaths or signs of systemic toxicity were observed. No skin irritation was noted in males, however all females showed evidence of drying/defatting of the skin at the application site. The LD50 was determined to be greater than 2000 mg/kg bw. Based on the results of this study, the assessed chemical is likely to be of low acute dermal toxicity.

Inhalation

In an acute inhalation toxicity study similar to OECD TG 403 (Nilsen et al. 1988), male CF-1 mice (n = 4/dose) were exposed (whole body) to n-C9 to n-C13 alkanes in the form of a vapour for 8 hours at the following concentrations (maximum achievable vapour concentrations in air): n-C13 (41 ppm), n-C12 (142 ppm), n-C11 (442 ppm), n-C10 (1369 ppm), and n-C9 (5280, 4438, 3560 and 2414 ppm). The animals were observed for 14 days following inhalation exposure. The four exposures to n-nonane (n-C9) showed a strong dose response relationship with respect to mortality with 0/10, 1/10, 4/10, 9/10 at 2414, 3560, 4438 and 5280 ppm, respectively. Gross ataxia, general and focal seizure and spasms were observed in animals exposed to n-C9 in the range from 3560 to 5289 ppm. No mortality was recorded for the other test substances after exposure to the maximum achievable vapour concentration in air.

The length of time to the appearance of specific symptoms or death was inversely proportional to the concentration of n-nonane in the inhaled air. The authors have reported an LC50 value for n-nonane of 4467 ppm (23.4 mg/l). Based on this data, the assessed chemical is likely to be of low acute inhalation toxicity. It is also noted that, as the study was conducted in mice only and the exposure duration was 8 hours and not 4 hours as required under OECD TG 403, the assessed chemical is not considered for classification according to GHS Criteria (UNECE 2017).

Corrosion/Irritation

Skin irritation

The data from an analogue chemical was provided for skin irritation potential in rabbits (OECD TG 404). The test substance (0.5 mL) was applied undiluted to an area of clipped dorsal skin, covered with a semi-occlusive dressing for 4 hrs and reactions at the test site recorded at 1, 24, 48 and 72 hr after patch removal. Well defined erythema (grade 2) and very slight oedema (grade 1) were present at 1 hr following patch removal, decreasing to very slight erythema (grade 1; no oedema) at 24 hr, resolving in two animals by 48 hr and in the third by 72 hr. Under the conditions of the study, the test substance was determined to be a mild skin irritant in rabbits. Based on the results of this study, the assessed chemical is likely to be a mild skin irritant.

Eye irritation

The data from an analogue chemical was provided for eye irritation potential (OECD TG 405). Treatment of 3 female New Zealand White rabbits with 0.1 mL undiluted test substance to the lower conjunctival sac of one eye resulted in no effects on the cornea or iris in any animal at any time point during the study. Mild conjunctival redness, chemosis and discharge (all grade 1) were present in all treated eyes at the 1 hr time point but were generally fully resolved by 24 hr except in one eye, which was fully resolved by 48 hr. Under the conditions of the study, the test substance was determined to be a slight eye irritant in rabbits. Based on the results of this study, the assessed chemical is likely to be a slight eye irritant.

Sensitisation

Skin sensitisation

The skin sensitisation potential of an analogue chemical was tested using a guinea pig maximisation test (GPMT) (OECD TG 406). Following preliminary tests, an intradermal induction concentration of 25% and topical induction concentration of 100% were used, with a

single topical application at 12.5% and 25% concentrations used for challenge after 10 days rest period following induction.

Only slight to moderate erythema was present in 3/20 animals at 24 hours after challenge with 25% concentration, with slight erythema remaining in 1/20 animals at the 48-hour time point. These reactions were fully resolved by 72 hours. No erythema or oedema was recorded in any test animal challenged with 12.5% concentration. There were no deaths or signs of systemic toxicity, and body weight gains in the treatment group were comparable to controls. Based on these results, the test substance is not considered to be a skin sensitiser under the conditions of the study.

A further test of the skin sensitisation potential of the analogue chemical was conducted using a local lymph node assay (LLNA) (OECD TG 429). Three groups of five female mice (CBA/Ca) received topical applications (25 µL/ear) of the analogue chemical to the entire dorsum of each ear lobe at 25%, 50% and 100% (v/v) concentrations in 20% (v/v) olive oil in acetone for 3 consecutive days. On day 6, 250 µL (20 µCi/mouse) of ^{3}HTdR (80 µCi/mL) solution was injected via the tail vein and the animals were euthanised approximately 5 hours afterward for further processing.

No deaths or signs of systemic toxicity were reported in any treatment group. The analogue chemical produced a Stimulation Index (SI) of greater than 3 when tested at concentrations of 50% or 100% (v/v) (3.23 and 5.97, respectively). It is noted that two negative control substances, Kerosene and n-octadecane, gave SI values of around 3 at 100% concentration, while positive control α-Hexylcinnamaldehyde gave an SI value of greater than 3 when tested at 15% (v/v).

It is noted that recent findings have cast doubt on the reliability of the LLNA for testing the skin sensitisation potential of lipophilic substances (log K_{ow} ≥ 3.5) at high concentrations (Natsch et al. 2023). The findings suggest that skin irritation caused by the lipophilic substances could release cytokines triggering a local inflammation of the skin, resulting in non-specific cell proliferation in the lymph nodes and leading to false positive results from the LLNA.

Therefore, it is likely that the positive SI values obtained with the negative reference substances and with the test substance at 50% and 100% concentration are false positive responses. In this context, the result of the GPMT assay may be considered the more reliable result. In addition, the assessed chemical does not contain structural alerts for skin sensitisation. Therefore, based on the available information, the assessed chemical is unlikely to be a skin sensitiser.

Repeat dose toxicity

Oral

The applicant submitted a combined repeated dose oral toxicity study with a reproduction/developmental toxicity screening test of an analogue chemical (OECD TG 408). Details of the reproduction/developmental toxicity screening test are described in the respective section.

In a sub-chronic repeated dose toxicity study (OECD TG 408), the analogue chemical in arachis oil was administered to groups of Wistar rats (n=10 /sex/dose) by oral gavage for up to 18 weeks, at doses of 0 (control), 50, 250 and 1000 mg/kg bw/day. There were no treatment-related deaths and treatment-related clinical signs were limited to increased salivation following treatment, an observation presumed to reflect the unpleasant taste of the test

substance. Observations for functional and behavioural toxicity together with determinations of haematological and clinical chemistry parameters were unremarkable.

Even though males treated with 1000 mg/kg bw/day showed a statistically significant increase (+13%) in relative liver weight only, no such effect was detected for females, or animals of either sex treated with 250 or 50 mg/kg bw/day. Therefore, this finding was not considered to be biologically or toxicologically significant.

The occurrence of generalised hepatocyte enlargement was significantly increased in females treated at 1000 and 250 mg/kg bw/day but not at 50 mg/kg bw/day. As there was no evidence of an effect on hepatocyte size for male rats at any treatment level, nor any evidence of degenerative changes, the hepatocyte enlargement was considered an adaptive response and not of any toxicological significance.

Kidney tissue from high dose males exhibited globular accumulations of eosinophilic material in the tubular epithelium, shown to contain a2-microglobulin with Mallory-Heidenhain stain. Since a2-microglobulin occurs only in the proximal tubular epithelium of adult male rats, this finding was concluded to be of no biological or toxicological significance to humans. The microscopic appearance of a wide range of other tissues was unremarkable.

The no-observable-adverse-effect level (NOAEL) was established at 1000 mg/kg bw/day in this study, based on no adverse effects noted in rats up to the highest tested dose.

Genotoxicity

In vitro genotoxicity

The analogue chemical was found to be non-mutagenic in a bacterial reverse mutation assay using *Salmonella typhimurium* strains TA98, TA100, TA102, TA1535 and TA1537, with or without metabolic activation (OECD TG 471). No significant increases in the frequency of revertant colonies were recorded for any of the bacterial strains at any tested dose (50, 150, 500, 1500, and 5000 µg/ plate).

The analogue chemical was tested for its clastogenic and aneugenic potential in an in vitro mammalian micronucleus test using human lymphocytes (OECD TG 487). The test substance demonstrated no evidence of cytotoxicity in any of the exposure groups. An oily precipitate was observed at 1250 µg/mL and above, but this was not cytotoxic. No increase in the frequency of cells with aberrations or the incidence of polyploidy was recorded in the absence or presence of metabolic activation, up to the maximum dose tested (2500 µg/mL). The results indicate that the assessed chemical is unlikely to be clastogenic or aneugenic to human lymphocytes *in vitro.*

The analogue chemical was tested for its potential to induce mutations at the thymidine kinase locus in mouse lymphoma L5178Y cells (OECD TG 490). The concentrations used in the main experiment (40–640 µg/mL, with and without metabolic activation) were based on data from a preliminary toxicity test. No toxicity was seen up to and including a dose of 5000 µg/mL, however, a cloudy precipitate was observed at 78.13 µg/mL and an oily precipitate formed at 625 ug/mL in the preliminary toxicity test. Therefore, the maximum dose level used for the mutation tests was 640 µg/mL. The mutation frequency was not increased at any dose, with or without metabolic activation. The analogue chemical was therefore considered to be non-mutagenic and non-clastogenic under the conditions of the experiment.

In vivo genotoxicity

The analogue chemical was evaluated for its ability to increase the incidence of micronucleated polychromatic erythrocytes (mnPCEs) in bone marrow of male ICR (CD-1) rats (n = 7/dose) (OECD TG 474). The test substance was administered intraperitoneally (one dose only) at 500, 1000, and 2000 mg/kg bw/day, with one high dose group given a second dose and killed after 48 hours. In all high dose group animals, a hunched posture was observed after administration of the test substance. Even though the presence of the chemical was not demonstrated in the bone marrow, these adverse effects were considered to represent evidence of systemic exposure of treated animals to the test substance.

The test substance did not induce any statistically significant increases in the frequency of cells with micronuclei in polychromatic erythrocytes in bone marrow, indicating that the assessed chemical is not likely to be clastogenic or aneugenic.

Reproductive and development toxicity

In a two-generation reproductive toxicity study (OECD TG 416), the analogue chemical was administered to Wistar rats (n = 28/sex/dose) by oral gavage to serve as the F_0 (parental) generation at dose levels of 0, 50, 250 and 1000 mg/kg bw/day. The study was also designed to assess subchronic toxicity effects following exposure to the analogue chemical and rats (n = 10/sex/dose) from the F_0 generation high dose group were selected for this part of the study.

After 11 weeks of treatment, pairing of animals within each group was undertaken on a one male: one female basis to produce F_1 litters. At weaning of the F_1 offspring, groups of 24 male and 24 female offspring from each dose group were selected to form the F_1 generation. The F_1 generation animals were dosed for 11 weeks prior to pairing to produce F_2 litters. All F_0 males were terminated during week 18, any F_1 females that did not produce litters were terminated by day 25 post-coitum, and the surviving F_0 females and unselected F_1 offspring were terminated by day 21 post-coitum.

No treatment-related unscheduled deaths or adverse effects on body weight gain, food consumption, food efficiency or water consumption were noted. Clinical signs were limited to salivation and increased water intake following dosing in the high and intermediate treatment groups. These observations were considered secondary to the unpleasant taste of the test substance formulations.

Adverse effects were not noted on oestrus cycle, mating cycle and pre-coital intervals, or other reproductive parameters in either generation.

Liver and kidney weights were elevated for high and intermediate dose males from both generations, with treatment-related effects observed microscopically. Hepatic findings consisted of generalised hepatocyte enlargement for females treated at 1000 and 250 mg/kg bw/day from the F_0 generation, and for animals of either sex treated at 1000 mg/kg bw/day from the F_1 generation. Hepatocyte enlargement without any degenerative changes in the liver following the administration of xenobiotics is considered to be adaptive in nature and was not of any toxicological significance. Renal changes were characterised as detailed above in the repeat dose toxicity section.

Adverse effects were not noted on reproductive parameters of either generation. The NOAEL in this study was established as 1000 mg/kg bw/day for reproductive toxicity, based on no adverse effects noted in rats up to the highest tested dose of the analogue chemical. As noted above, the same NOAEL (1000 mg/kg bw/day) was also established for systemic toxicity.

In another study, the developmental toxicity of the analogue chemical was tested in New Zealand White rabbits (OECD TG 414). The analogue chemical in arachis oil was administered once daily, 7 days a week via oral gavage, at doses of 0, 100, 300, 1000 mg/kg bw/day from Day 7 to Day 28 post-coitum, inclusive.

No treatment-related mortality or changes in any of the maternal parameters investigated (clinical appearance, body weight, food consumption and macroscopic examination) were observed throughout the study period. Six females did not survive until the scheduled necropsy (one in the control group, one at 100 mg/kg bw/day, three at 300 mg/kg bw/day, and one at 1000 mg/kg bw/day). As these premature deaths occurred either as a result of the gavage procedure, symptoms occurring prior to start of the treatment, or were considered incidental, they were determined not to be treatment related.

Increased mean litter incidences of retrocaval ureter were observed in the 300 and 1000 mg/kg bw/day dose groups. Retrocaval ureter is a congenital abnormality of the right ureter, which has been shown, in rare cases to cause clinical symptoms, mainly due to the development of ureterohydronephrosis in humans (Hostiuc et al. 2019). Retrocaval ureters were observed in 0.5%, 2.6%, 6.5% and 4.9% per litter in the control, 100, 300 and 1000 mg/kg bw/day groups, respectively. While the values were above the historical control maximum (4.1% per litter) at 300 mg/kg bw/day (6.5% per litter) and 1000 mg/kg bw/day (4.9% per litter) this was not statistically significant and there was no dose-response relationship. As this concerns a variation with no detrimental effects on development, it was not considered as adverse by the study authors.

No treatment-related changes were observed in any of the remaining developmental parameters investigated in this study (litter size, post-implantation loss, sex ratio, foetal body weights, external, visceral, and skeletal malformations and developmental variations). Based on the lack of adverse treatment-related effects, the maternal and developmental NOAEL was determined to be 1000 mg/kg bw/day in this study.

In another developmental study (OECD TG 414), the analogue chemical in arachis oil was administered to female Wistar Han rats once daily, 7 days a week via oral gavage at doses of 0, 100, 300, 1000 mg/kg bw/day from Day 6 to 20 post-coitum, inclusive (n = 22/dose).

No treatment-related mortality or changes in any of the maternal parameters investigated (clinical appearance, body weight, food consumption, thyroid hormone levels (triiodothyronine (T3), thyroxine (T4), thyroid-stimulating hormone (TSH)), organ weights (thyroid gland), uterine contents, histopathologic examination (thyroid gland), corpora lutea, implantation sites and pre- and post-implantation loss) were observed during the study period.

At 1000 mg/kg bw/day, 3 foetuses (out of 103 examined) of 3 litters (out of 20 examined) were noted with a 7^{th} full rib. This finding was observed in the high dose group only and, as the incidence exceeded available historical control data, it was considered treatment related. However, as this variation has no known detrimental effects on development, it was considered non-adverse by the study authors. No other treatment-related changes were observed in any of the developmental parameters investigated in the study (litter size, sex ratio, foetal body weights, anogenital distance, external, visceral and skeletal malformations and developmental variations). Based on the lack of adverse treatment-related effects observed, the maternal and developmental NOAEL was determined to be 1000 mg/kg bw/day in this study as well.

Environmental exposure

The assessed chemical will be imported into Australia as a finished jet fuel product. The fuel will be transported to storage depots at airports around Australia where it will be pumped into aircraft. The assessed chemical will be combusted as a function of its overall use and it is not expected to be released into the environment.

Accidental spills which occur during transfer and filling processes are expected to be captured and collected for appropriate disposal.

Environmental fate

Partitioning

The assessed chemical is predicted to be slightly water soluble (water solubility ≤ 3.59 mg/L), volatile (vapour pressure = 43 Pa at 25°C) and have a high log K_{OC} value (log K_{OC} > 5.62). If the chemical is released to water, a considerable proportion of the chemical is expected to evaporate and partition to air. The remainder of the assessed chemical is expected to stay in water or partition to, and become immobile in, sediments.

Degradation

A supplied ready biodegradation screening test, performed to OECD TG 301F, demonstrated 79% degradation of the assessed chemical, according to theoretical oxygen demand, after 28 days. This result indicates that the major proportion of the assessed chemical is expected to be susceptible to biodegradation. However, this result does not preclude recalcitrant components forming part of this UVCB substance.

Biodegradation estimates (US EPA 2012; calculated using HCBioWin v1.01) of representative components of the assessed chemical indicate that several highly branched components may have half-lives in water and/or soil exceeding domestic thresholds. Each of these components are expected to be present in the substance at ≥ 0.1% (w/w) and collectively account for approximately 8% w/w of the overall substance.

The half-lives of the components of the assessed chemical in air were calculated and range from 4.6–40 hours, based on reactions with hydroxyl radicals (US EPA 2012; calculated using AOPWIN v1.92). The majority of the components have a half-life in air below the domestic threshold value of 2 days (24 hours, assuming 12 hours of sunlight per day) and are not expected to persist in the air compartment. However, up to 1.5% (w/w) of the overall substance has a calculated half-life exceeding the domestic threshold value of 2 days.

While these persistent components will be introduced within the assessed chemical, the overall proportion of these components is not considered to be significant for this introduction (OECD 2002). Therefore, the chemical is assessed as not persistent.

Bioaccumulation

Bioconcentration factor (BCF) estimates were supplied for representative components of the assessed chemical (US EPA 2012; calculated using BCFBAF v3.01). The calculated BCF values ranged from 39–19,054 L/kg using the Meylan log K_{OW} regression method and from 2–1,411 L/kg using the Arnot-Gobas estimation method.

While biotransformation processes of highly branched alkanes are uncertain, fish bioaccumulation studies suggest that biotransformation of highly branched alkanes may mitigate bioaccumulation (Le Bon et al. 1988; Tolls and van Dijk 2002). Therefore, the results from the Arnot-Gobas method have been chosen for the assessed chemical.

As the predicted BCF values for the components of assessed chemical are below 2,000 L/kg, the chemical is assessed as not bioaccumulative. This classification may be reviewed if further information about the bioaccumulation of relevant branched alkanes becomes available.

Predicted environmental concentration (PEC)

The predicted environmental concentration (PEC) has not been calculated as release of the assessed chemical to the aquatic environment is expected to be negligible based on its assessed use patterns.

Environmental effects

Effects on aquatic Life

Acute toxicity

The following measured median lethal loading (LL50) and median effective loading (EL50) values for model organisms were supplied for an analogue of the assessed chemical:

Taxon	Endpoint	Method
Fish	96h LL50 > 1000 mg/L WAF[1]	*Oncorhynchus mykiss* (rainbow trout) Mortality OECD TG 203 Semi-static conditions Nominal loading rate
Invertebrate	48h EL50 > 100 mg/L WAF[1]	*Daphnia magna* (water flea) Immobility OECD TG 202 Static conditions Nominal loading rate
Algae	72h ErL50 > 100 mg/L WAF[1]	*Scenedesmus subspicatus* (green algae) Growth rate OECD TG 201 Static conditions Nominal loading rate
Microorganisms	3h EC50 > 1000 mg/L	Activated sludge from STPs Respiration inhibition OECD TG 209 Nominal concentration

[1] WAF: Water accommodated fraction.

Chronic toxicity

The following measured no-observed-effect loading rate (NOELR) values for model organisms were supplied for an analogue of the assessed chemical:

Taxon	Endpoint	Method
Invertebrates	21d NOELR = 1 mg/L WAF[1]	*Daphnia magna* (water flea) Immobility OECD TG 202 Semi-static conditions Nominal loading rate
Algae	72h NOELR > 100 mg/L WAF[1]	*Scenedesmus subspicatus* (green algae) Growth rate OECD TG 201 Static conditions Nominal loading rate

[1] WAF: Water accommodated fraction.

Effects on sediment dwelling life

The following measured median lethal concentration (LC50) and no-observed-effect concentration (NOEC) values for model organisms were supplied for an analogue of the assessed chemical:

Taxon	Endpoint	Method
Amphipod	10d LC50 = 1200 mg/kg sediment dw 10d NOEC* = 373 mg/ kg sediment dw	*Corophium volutator* (estuarine amphipod) Mortality OSPAR Protocols on Methods for the Testing of Chemicals Used in the Offshore Oil Industry, Part A: A sediment Bioassay using an Amphipod Corophium Static conditions Nominal concentration

* NOEC value based on mortality observations

Predicted no-effect concentration (PNEC)

A predicted no-effect concentration (PNEC) of 20 µg/L was calculated for the assessed chemical in the aquatic environment. This value was derived using the chronic endpoint value for aquatic invertebrates (21d NOELR = 1 mg/L). An assessment factor of 50 was applied to this endpoint as acute toxicity data were provided for three trophic levels and chronic toxicity data was provided for two trophic levels (EPHC 2009).

Categorisation of environmental hazard

The categorisation of the environmental hazards of the assessed chemical according to domestic environmental hazard thresholds is presented below:

Persistence

Not Persistent (Not P). The assessed chemical passes a ready biodegradation screening test but may contain persistent components. These components are not considered to be a significant proportion of the assessed chemical for the purpose of classification (OECD 2002). Therefore, the assessed chemical is categorised as Not Persistent.

Bioaccumulation

Not Bioaccumulative (Not B). Based on calculated BCF values below domestic thresholds, the constituents of the assessed chemical are not predicted to bioaccumulate. Therefore, the assessed chemical is categorised as Not Bioaccumulative.

Toxicity

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

Environmental risk characterisation

Based on its assessed use, the chemical is not expected to be released to the environment. Therefore, a Risk Quotient (PEC/PNEC) for the aquatic compartment could not be calculated.

While some minor components of the assessed chemical may be persistent, the proportion of these components is not considered significant. The assessed chemical is categorised as not persistent, and it is not expected to bioaccumulate or be toxic to aquatic life.

The hazards of the assessed chemical are not expected to differ significantly from other existing jet fuel substances available for use in Australia, based on physical property considerations (Gary 2007). The maximum introduction of 80,000 tonnes of the assessed chemical is not expected to increase the total volume of this class of substances in Australia but replace approximately 1% of the current introduction of aviation turbine fuels, based on 2018-2019 sales figures for the demand-driven market (Commonwealth of Australia 2020).

Therefore, based on the assessed hazard characteristics (not P, not B, not T) and the assessed use pattern, the environmental risk from the assessed chemical can be managed within existing frameworks.

References

Commonwealth of Australia (2020), *Australian Petroleum Statistics Issue 281, December 2019*, accessed January 2023.

EPHC (2009) Environment Protection and Heritage Council, 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.

Gary J, Handwerk G and Kaiser M (2007). *Petroleum Refining: Technology and Economics* (Fifth ed). CRC Press, Taylor and Francis Group, Florida. ISBN 978-0-203-90792-4.

Hostiuc S, Rusu MC, Negoi I, Grigoriu M and Hostiuc M (2019) 'Retrocaval ureter: a meta-analysis of prevalence', *Surg Radiol Anat*., 41(11):1377-1382, doi: 10.1007/s00276-019-02269-w.

Le Bon AM, Cravedi JP and Tulliez JE (1988) 'Biotransformation of hydrocarbons by fish: Metabolic pathways of pristane in trout', *Chemosphere*, 17(5): 1063-1075, doi: 10.1016/0045-6535(88)90077-X.

Natsch A, Kleinstreuer N and Asturiol D (2023) 'Reduced specificity for the local lymph node assay for lipophilic chemicals: Implications for the validation of new approach methods for skin sensitisation', *Regul Toxicol Pharmacol*., 138:105333. doi: 10.1016/j.yrtph.2023.105333.

Nilsen OG, Haugen OA, Zahlsen K, Halgunset J, Helseth A, Aarset H and Eide I (1998) 'Toxicity of n-C9 to n-C13 alkanes in the rat on short term inhalation', *Pharmacol Toxicol*., 62(5): 259-66, doi: 10.1111/j.1600-07731988.tb01884.x.

OECD (Organisation for Economic Co-operation and Development) (2002) *Harmonised Integrated Classification System for Human Health and Environmental Hazards of Chemical Substances and Mixtures*, OECD, accessed January 2023.

Tolls J and van Dijk J (2002) 'Bioconcentration of n-dodecane and its highly branched isomer 2,2,4,6,6-pentamethylheptane in fathead minnows', *Chemosphere*, 47(10): 1049-1057, doi: 10.1016/S0045-6535(02)00013-9.

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*, UNECE, accessed December 2022.

US EPA (United States Environmental Protection Agency) (2012) *Estimation Programs Interface (EPI) SuiteTM for Microsoft Windows® (version 4.11)*, US EPA, accessed January 2023.