HYDROTREATED LIGHT PETROLEUM DISTILLATE

This dossier on hydrotreated light petroleum distillate presents the most critical studies pertinent to the risk assessment of this substance in its use in drilling muds and hydraulic fracturing fluids. This dossier does not represent an exhaustive or critical review of all available data. The majority of information presented in this dossier was obtained from the ECHA database that provides information on chemicals that have been registered under the EU REACH (ECHA). Where possible, study quality was evaluated using the Klimisch scoring system (Klimisch et al., 1997).

Screening Assessment Conclusion – Hydrotreated light petroleum distillate was not identified in chemical databases used by NICNAS as an indicator that the chemical is of concern and is not a PBT substance. The substance was assessed as a tier 2 chemical for acute and chronic toxicity. Therefore, hydrotreated light petroleum distillate is classified overall as a **tier 2** chemical and requires a hazard assessment and qualitative assessment of risk.

1 BACKGROUND

Hydrotreated light petroleum distillate is a complex combination of hydrocarbons obtained by treating a petroleum fraction with hydrogen in the presence of a catalyst. It consists of hydrocarbons having carbon numbers predominantly in the range of C9 through C16 and boiling in the range of approximately 150°C to 290°C (302°F to 554°F).

Representative substances are expected to be readily biodegradable. They are highly insoluble in water and have high adsorption potential. They have a low potential to bioaccumulate.

The substance has low acute toxicity by the oral and dermal route. It is not irritating to the skin and eyes, but it is a skin sensitiser. Aside from minor changes in body weight, no adverse effects were seen in animals given repeated doses by the oral route. The substance is not genotoxic when tested in both *in vitro* and *in vivo* assays. There is no indication that this substance will cause malformations or have an adverse effect on reproduction and development. The substance is of low acute concern to aquatic organisms.

2 CHEMICAL NAME AND IDENTIFICATION

Chemical Name (IUPAC): 1,4-bis(propan-2-yl)benzene; 7,7-dimethylhexadecane; octadecane
CAS RN: 64742-47-8
Molecular formula: Not available (UVCB substance)
Molecular weight: Not available (UVCB substance)

Synonyms: Distillates, petroleum, hydrotreated light

3 PHYSICO-CHEMICAL PROPERTIES

Hydrotreated light petroleum distillate is a UVCB substance containing aliphatic (linear, branched, and/or cyclic paraffins) molecules of carbon and hydrogen. Physical and chemical properties were not available for the UVCB hydrocarbon. As a result, information was obtained from a read-across substance (hydrodesulfurized kerosine). Key physical and chemical properties for the substance are shown in Table 1.

Table 1 Overview of the Physico-chemical Properties of Hydrodesulfurized Kerosine (CAS No. 64742-81-0)

Property	Value	Klimisch score	Reference
Physical state at 20°C and 101.3 kPa	Liquid	2	ECHA
Melting Point	-49°C (pour point) @ 101.3 kPa.	2	ECHA
Boiling Point[1]	90 to 320°C @ 101.3 kPa	2	ECHA
Density	770 to 850 kg/m^3 @ 15°C	2	ECHA
Vapour Pressure	<1,000 to 37,000 Pa at 37.8°C	2	ECHA
Partition Coefficient (log K_{ow})	1.99 – 18.02 @ 20°C	2	ECHA
Water Solubility	0.000009 – 0.00645 g/L @ 25 °C	-	OECD
Viscosity	1.1 to 2.5 mm^2/s @ 20°C (kinematic)	2	ECHA

4 DOMESTIC AND INTERNATIONAL REGULATORY INFORMATION

A review of international and national environmental regulatory information was undertaken (Table 2). This chemical is listed on the Australian Inventory of Chemical Substances – AICS (Inventory). No conditions for its use were identified. No specific environmental regulatory controls or concerns were identified within Australia and internationally for hydrotreated light petroleum distillates.

Table 2 Existing International Controls

Convention, Protocol or other international control	Listed Yes or No?
Montreal Protocol	No
Synthetic Greenhouse Gases (SGG)	No
Rotterdam Convention	No
Stockholm Convention	No
REACH (Substances of Very High Concern)	No
United States Endocrine Disrupter Screening Program	No
European Commission Endocrine Disruptors Strategy	No

5 ENVIRONMENTAL FATE SUMMARY

A. Summary

Representative substances are expected to be readily biodegradable. They are highly insoluble in water and have high adsorption potential. They have a low potential to bioaccumulate.

While sediment and soil are expected to be the main targets for environmental distribution, biodegradation potential is expected to offset sorption. In fact, fugacity modelling suggest that

[1] CAS numbers in this category indicate a boiling point range of 90-320 deg Celsius.

accumulation in sediment is expected to be several orders of magnitude less than 1%, relative to soil, water and air compartments.

B. Partitioning

Based on Henry's Law Constant values > 4.76 x 10^4 Pa-m^3/mol @25 °C, members of this group have the potential to volatilise from water or moist soil surfaces. These chemicals are unlikely to degrade by hydrolysis as they lack a functional group that is hydrolytically reactive. However, in the air, category members have the potential to rapidly degrade through indirect photolytic processes (OECD, 2012).

C. Biodegradation

Kerosines are readily to inherently biodegradable. In the supporting OECD 301 study, naphtha solvents were readily biodegraded in 28 days but not within the 10-day window. The mean of three samples was 61% theoretical biological oxygen demand on Day 28. In a valid OECD 301F supporting study Kerosine Mid-Blend was not considered readily biodegradable in 28 days, with less than 60% degradation on day 28 (58.6%). However, according to USEPA guidance for biodegradability, it is considered inherently biodegradable because significant degradation occurred). On the basis of this and the known properties of hydrocarbons in the range C9 to C16, kerosines are often considered not readily biodegradable; but as they can be degraded by microorganisms, they are regarded as being inherently biodegradable.

If a chemical is found to be inherently or readily biodegradable, it is categorised as Not Persistent since its half-life is substantially less than 60 days (DoEE, 2017).

D. Environmental Distribution

Standard adsorption/desorption studies are not applicable to petroleum UVCB substances. Mackay Level III modeling indicates that category member constituents partition mostly to the sediment and soil compartments rather than air compartment when an equal emission rate (1000 kg/hr) to the air, water, and soil compartment is assumed. When release occurs only to either the air, or soil compartment, constituents are indicated in the modeling to partition largely to the compartment to which they are released. When released to the water compartment, constituents are indicated by the model to partition to either water or sediment (HPVIS). However, based on the member category low solubility, partitioning to sediment would be expected.

E. Bioaccumulation

No experimental studies are available on the substance. Using BCFBAF in EPISuite™, the estimated BCF of a representative substance is 0.893 L/kg based on the Arnot-Gobas model that includes biotransformation and upper trophic. Thus, bioaccumulation is not expected (ECHA). [Kl. score = 2]

6 HUMAN HEALTH HAZARD ASSESSMENT

The information presented within this Section was derived in part from read-across substances: hydrodesulfurized kerosine (CAS No. 64742-81-0) and undiluted JP-8 jet fuel (CAS No. 8008-20-6).

A. Summary

The substance has low acute toxicity by the oral and dermal route. It is not irritating to the skin and eyes, but it is a skin sensitiser. Aside from minor changes in body weight, no adverse effects were seen in animals given repeated doses by the oral route. The substance is not genotoxic when tested in both *in vitro* and *in vivo* assays. There is no indication that this substance will cause malformations or have an adverse effect on reproduction and development. This information was derived in part from products of similar structure or composition.

B. Toxicokinetics

The studies of the pharmacokinetics (i.e. absorption, distribution, metabolism and excretion) of kerosine are scarce. There are some *in vitro* and *in vivo* studies available on jet fuels. However, because jet fuel is a complex mixture, these studies use certain constituents of jet fuels as marker compounds to describe the total jet fuel's pharmacokinetics. There are more data available for a number of kerosine constituents, and these can be used as a basis for understanding the pharmacokinetics of kerosine as a whole. There are three ways in which humans are exposed to kerosine: by inhalation; ingestion; and, dermal contact. Due to the relatively low volatility of kerosine and jet fuels, dermal exposure can be a more important route of exposure than exposure via inhalation. During many operations involving aircraft fuel tanks there is a significant potential for dermal exposure. Ingestion occurs primarily as a consequence of incidental ingestion.

Groups of five male C3H mice were dosed with a single dermal application of 15 or 60 µL kerosine (30% straight-run hydrotreated and 70% hydrocracked kerosine) spiked with radiolabeled naphthalene or tetradecane, and sacrificed after 96 h exposure (Mobil, 1994). Another group of five male C3H mice were exposed by air to the same compounds and doses in a metabolism cage to determine passive inhalation. The results of the dermal exposure show that 5% of the labelled tetradecane and 15% of the labelled naphthalene were absorbed over 96 h. The inhalation experiments showed that 2.8% of the labelled naphthalene was bioavailable. Comparison of these data with a similar dataset obtained with a 25% concentration of the test compounds diluted in mineral oil, revealed that dilution did not affect the absorption of the test compound.

Four groups of eight male Sprague-Dawley rats were exposed to 1, 4, 8,or 16 mL kerosine through the abdominal skin for 2 h at a skin area of 4, 8, 16 or 64 cm2, respectively (Tsujino et al., 2003). Before, during and after the experiment, blood samples were taken and analysed for trimethylbenzenes and aliphatic hydrocarbons. Trimethylbenzenes were detectable in blood within 5-20 min and showed a dose dependent absorption. High concentrations of aliphatic hydrocarbons were detected in the exposed skin as compared to the blood concentration. The aliphatic hydrocarbon levels were dependent on the amount of kerosine exposed per unit area.

The systemic distribution of kerosine components in the blood and tissues of rats following *in vitro* dermal exposures was investigated, using trimethylbenzenes and aliphatic hydrocarbons (C9-C16) as biomarkers (Tsujinoet al., 2002). The trimethylbenzenes were absorbed through the skin and detected in blood and tissues to a greater extent as compared to the aliphatics. The data indicate

that kerosine components are absorbed percutaneously and distributed to the various organs via the blood circulation. Distribution of trimethylbenzenes in blood and tissues following dermal exposure is (at decreasing concentrations): kidney > blood > liver > adipose > brain > spleen > lung = muscle. Distribution of aliphatics in blood and tissues following dermal exposure is (at decreasing concentrations): blood > adipose > muscle > lung > liver > kidney > spleen > brain.

The inhalation studies demonstrate that the volatile kerosine constituents are well absorbed (31 – 54%) and are distributed mainly in the fat tissue. Aromatics were metabolised at a higher rate than naphthenes, n-alkanes, isoalkanes and 1-alkenes. Dermal application of kerosine or jet fuel generally shows that the aromatics and aliphatics are well absorbed into the skin. Subsequently, the aromatics penetrate the skin at a higher rate than the alkanes. SKINPERM calculations indicate that although skin permeation rates of alkanes, naphthenes and aromatics are more or less comparable, the latency times of alkanes are longer than the latency times of naphthenes and aromatics. After absorption, the kerosine constituents are distributed via the blood circulation to the fat tissue and various organs. Studies with oral exposure to kerosine indicate that gastrointestinal absorption of kerosine is slow and incomplete, resulting in low bioavailability.

C. Acute Toxicity

Kerosines are of low acute toxicity, with an oral LD50 greater than 5000 mg/kg (rat), a dermal LD50 greater than 2000 mg/kg (rabbit), and an inhalation LC50 greater than 5.28 mg/L (rat). The most important effects in animals following very high oral doses were slight irritation of the stomach and the gastrointestinal tract. The only adverse effects observed in acute inhalation studies were decreased activity and breathing frequency at very high doses. Dermal application of kerosine did not lead to acute toxic systemic effects. Clinical effects observed were related to dermal irritation rather than to systemic toxicity. The acute toxicity of kerosine is not classified by EU CLP Regulation (EC No. 1272/2008).

Oral

In the key acute oral toxicity study (Klimisch score=1; ARCO, 1992a), groups of fasted (5 per sex), young adult, Sprague Dawley rats were given a single oral dose of undiluted thermocracked kerosine at a dose of 5000 mg/kg bw and observed for 14 days. There were no treatment related mortalities. All of the study animals exhibited one or more of the following clinical signs: nasal discharge, ocular discharge, abnormal stools, lethargy, stained coat, and alopecia. All animals gained weight during study period. At necropsy, one of the ten animals exhibited visual lesions, the remaining nine showed signs of alopecia in the inguinal and/or perineal regions. The oral LD50 was determined to be greater than 5000 mg/kg in males and females.

In supporting studies conducted on kerosine substances, rats were administered single oral gavage doses of the test substance. The results supported an oral LD50 of > 5000 mg/kg in males and females.

Inhalation

In the key acute inhalation toxicity study (Klimisch score = 1; API, 1987a), groups of Sprague-Dawley rats, five males and five females, were exposed by inhalation route to straight-run kerosine for 4 hours to their whole body at a single dose of 5.28 mg/L (vapour, analytical). All except one animal had normal growth rates throughout the study. The one exception on day 8 had a body weight less

than its starting body weight but by the end of the study normal growth had resumed. All animals exhibited decreased activity during the exposure. Otherwise there were no treatment-related clinical signs of toxicity. No macroscopic lesions were observed in any animal at post-mortem and no microscopic changes were observed in any lung section examined. The LC50 was greater than 5.28 mg/L.

In supporting studies conducted on kerosine substances, rats were administered single doses of the test substance via inhalation. The LC50s as measured based on mortality and systemic effects do not indicate classification of kerosine as an acute inhalation toxicant. One supporting study on deodorised kerosine showed a lack of systemic effects after repeated exposure to rats (6 hours each day for 4 days) and resulted in an LC50 of > 7.5 mg/L (Carpenter et al., 1976). Another supporting study on deodorised kerosine showed a lack of systemic effects after a single 6-hour exposure to cats, and resulted in an LC50 of > 6.4 mg/L (Carpenter et al., 1976).

Dermal

In the key acute dermal toxicity study (Klimisch score=1; ARCO, 1992g), groups of young adult New Zealand White rabbits, five males and five females, were dermally exposed to undiluted thermocracked kerosine for 24 hours to 10% of their body surface area at a dose of 2000 mg/kg. Animals were then observed for 14 days. There were no mortalities and all animals gained weight during the study. All of the animals exhibited one or more of the following clinical signs during the observation period: dermal irritation (erythema, edema, eschar, fissuring and/or dried skin) and/or abnormal stools. Apart from skin irritation, there were no other abnormalities noted at necropsy. The dermal LD50 was determined to be greater than 2000 mg/kg in both males and females.

In supporting studies conducted on kerosine substances, rabbits were administered single dermal doses of the test substance, and results supported a dermal LD50 of > 2000 mg/kg in males and females..

D. Irritation

Skin

In the key study, young adult rabbits (6 females) were dermally exposed (occlusive coverage) to 0.5 mL of undiluted kerosine/heating oil for 24 hours on both intact and abraded skin sites. Each of the test sites was evaluated for skin responses for 9 days post-exposure and was scored using the Draize scale. The mean erythema score from 24 to 72 hours was 3.46/4 while the mean edema score from 24 to 72 hours was 2.33/4. While this protocol deviates from current guidelines that state exposure should be semi-occlusive over 4 hours, and to intact skin only, this study is included as key to show the irritating nature of kerosine products.

In another guideline study conducted according to GLP and in accordance with current guidelines, young adult New Zealand White rabbits (3 per sex) were dermally exposed (semi-occlusive coverage) to 0.5 mL of undiluted odourless kerosine, for 4 hours. Animals were observed for seven days after exposure. Irritation was scored based on the Draize method (1959). The mean erythema score from 24 to 72 hours was 0.17/4 while the mean edema score from 24 to 72 hours was 0/4.

Additional supporting studies are provided on straight run kerosine, odourless kerosine, hydrocracked kerosine, hydrodesulfurised kerosine, Jet Fuel A, Jet Fuel A1, JP-5, and Cherry Point Jet

Fuel A. Most of the studies are valid in their methodology, but they differ from the current OECD guidelines in that animals were exposed under occluded conditions for 24 hours instead of semi-occluded conditions for 4 hours. Considering the conditions of the test, results must be interpreted carefully for the purposes of classification and labelling. The mean scores for erythema and edema have been assessed against the deviations, and provided the test would be conducted under standard conditions, the overall weight of evidence indicates that kerosines are irritating to skin. Kerosines are classified as irritating to the skin according to criteria in EU CLP Regulation (EC No. 1272/2008).

Effects on skin irritation/corrosion: irritating

Eyes

A number of well-controlled (GLP) animal experiments performed on a variety of kerosines indicate that none of the kerosines and jet fuels tested were more than slightly irritating to the eyes. In addition, a number of short reports on eye irritation studies on JP-5 and JP-8 show no eye irritation whatsoever in rabbits (6 unwashed eyes; 3 washed eyes): all scores 0.0 for up to 7 days (end of the study). None of the hazard assessments of kerosine and jet fuel constituents have resulted in classification for eye irritation.

In the key study selected for primary eye irritation, 0.1mL of undiluted thermocracked kerosine was instilled into the conjunctival sac of the right eye of three female young adult New Zealand White rabbits and observed through 72 hours. Irritation was scored according to the Draize method (1959). There was no evidence of damage to the cornea or iris for all animals over all scoring periods. Mild conjunctivae indicators such as redness, chemosis, and discharge were evident at the one-hour scoring interval, but not at any of the other scoring intervals. Fluorescein staining scores were zero for all study animals over all scoring periods.

The average irritation score was 0.0 for the cornea, iris and conjunctivae.

Based on the evidence, kerosine is not an eye irritant.

E. Sensitisation

In animal assays for skin sensitisation such as the Magnusson-Kligman GPMT and the Buehler assay, kerosines and jet fuels did not trigger a positive response.

In the key dermal sensitisation study (Klimisch score=1; ARCO, 1992q), thermocracked kerosine in mineral oil was tested on male young adult Pig/Hartley guinea pigs using a modified Buehler technique. During the challenge phase, a second exposure of a 1:4 dilution of thermocracked kerosine to induced test animals did not yield higher response grades, severity, or incidence than those associated with the naive challenge control group exposed to thermocracked kerosine. During the challenge phase, exposure of 0.2% DNCB to induction positive control animals elicited significantly higher response grades, severity indices, and incidence over the naive DNCB challenge control group. The vehicle irritation control group was free of dermal irritation during the challenge phase. Therefore, under the conditions of this study, thermocracked kerosine is not considered a delayed contact sensitiser while DNCB induced an appropriate positive response.

Based on test data, there was no evidence of skin sensitisation; therefore, kerosine is not classified for skin sensitisation according to EU CLP Regulation (EC No. 1272/2008)

F. Repeated Dose Toxicity

Oral

In the key oral subchronic study (Klimisch score=1; Mattie et al., 2000), male rats were treated for 70 to 90 days with 0 (1mL of distilled water), 750, 1500, or 3000 mg/kg/day of undiluted JP-8 jet fuel, then mated to untreated females (one female at a time). Males were gavaged throughout the cohabitation period and were returned to their individual cage after successful mating. In the second part of the study, female rats were administered the test compound at doses of 0 (1mL of distilled water), 375, 750, or 1500 mg/kg/day undiluted JP-8 jet fuel for 90-day prior to mating, through mating, gestation, delivery, and lactation for a total of 21 week. During mating, they were housed with untreated males.

There were no effects on clinical signs or mortality in either sex. Haematology, clinical chemistry, and urinalysis were measured only in females without any effects noted. Body weights in male rats were decreased in a dose-dependent manner and was likely related to nephropathy, which is specific in male rats treated with hydrocarbons, and not relevant for human exposure. In females, body weight was only significantly reduced in the high-dose group. Absolute and relative liver weights were increased in mid- and high-dose females, but were not likely biologically significant due to the lack of changes in clinical chemistry or histopathology in the liver. The test compound caused perianal dermatitis (high-dose only) and stomach hyperplasia (mid- and high-dose) in the female rats. There was a dose-related decrease in pup weight that was significant in the 750 mg/kg/day group on postnatal day 4 only and in the 1500 mg/kg/day group from postnatal day 4 through postnatal day 21 but had recovered by postnatal day 90. There were no treatment-related effects on reproduction or sperm parameters in males. There were no effects on reproduction, gestation, or litter size in females.

The study LOAEL for systemic effects is 1500 mg/kg/day and the NOAEL for systemic effects is 750 mg/kg/day, based on reduced body weight in dams and in pups. The LOAEL for adult males rats exposed to JP-8 orally was 750 mg/kg/day due to changes in clinical pathology, body weight, organ weights and the same irritation seen in female rats. The decrease in male rat bodyweight is very likely due to the male rat-specific nephropathy and is therefore not taken into account for the derivation of the oral NOAEL. The reproduction NOAEL was 3000 and 1500 mg/kg/day in males and females, respectively.

Inhalation

In a key subchronic inhalation toxicity study (Klimisch score=1; Mattie et al., 1991), JP-8 jet fuel was administered to 95 male Fisher 344 rats, 75 female Fischer 344 rats, and 100 male and female C57BL/6 mice by dynamic whole body vapour exposure at concentrations of 0, 500 or 1000 mg/m3(0, 0.5, or 1.0 mg/L) as a vapour for 24 hours per day, 7 days/week for a total of 90 days. The male rats developed hydrocarbon-induced nephropathy at both treatment concentrations. Male rats had decreased body weight and decreased absolute and relative kidney weight at both treatment concentrations. Female rats were unaffected by treatment. In mice, no significant clinical signs of toxicity were noted that differentiated the groups that were treatment-related. The NOAEC for male rats is difficult to establish, since potential adverse effects may be masked by male rat specific

hydrocarbon nephropathy. However, based on the hydrocarbon-induced nephropathy and reduced body weights and increased kidney weights, the LOAEC in male rats is 500 mg/m3. The LOEC for male mice is also 500 mg/m3, but it was not treatment related. The NOAEC for female rats and mice is greater than or equal to 1000 mg/m3. This was the highest dose tested in the study.

In a subacute inhalation toxicity study (Klimisch score = 1; API, 1986), hydrodesulfurised kerosine vapour was administered to 20 Sprague-Dawley rats/sex/concentration by dynamic whole body exposure at a concentration of 24 mg/m3(0.024 mg/L) for 6 hours per day, 5 days/week for 4 weeks. There were no compound related effects in mortality, clinical signs, body weight, haematology, clinical chemistry, organ weights, or gross and histologic pathology. Therefore, the NOAEC is greater than or equal to 24 mg/m3. This was the highest dose tested in the study.

Dermal

In a key sub-chronic dermal study hydrodesulfurized kerosine was applied at concentrations of 20, 40 or 60% (v/v) at a rate of 1 ml/kg/day to the shorn intrascapular region of groups of 12 individually housed male and female, Sprague-Dawley rats (aged 7-9 weeks). This was equivalent to doses of test material of 165, 330 or 495 mg/kg/day. Dosing was continued for five days a week for 13 weeks. In addition a group of 12 male and 12 female rats of similar age were administered mineral oil at a dose rate of 1 ml/kg/day; these animals served as vehicle controls. 12 rats/sex/group each in the vehicle controls and high dose group were maintained for a 4-week recovery period. Ingestion of the test material was prevented by using a collar and removal of any residual test or control material from the skin. Animals were observed for clinical signs prior to dosing and 1, 6 and 24 hours after the first dose. Subsequently, observations were made prior to each dose being applied.

Prior to the administration of each dose, the treated skin site was evaluated for dermal irritation using the Draize scoring method. Body weights were recorded prior to the first dose and weekly thereafter. An ophthalmic examination was conducted on each rat prior to application of the first dose and again prior to sacrifice at the end of the study. During the week prior to the first dose, each rat was subjected to a functional observation battery (FOB). The FOB was conducted again 1, 6 and 24 hours after the first dose and at 7 and 14 days. During the study, the FOB, motor activity and startle response testing was conducted on all rats at weeks 4, 8 and 12. At week 14 blood samples were collected from 12 animals/sex/group. Full necropsies were performed at week 14 on 6 rats/sex/group and at week 18 on the recovery rats (vehicle and high dose groups). Each full necropsy included an examination of the external surface of the body and its contents. The remaining six rats of each group were anesthetized with an intraperitoneal injection of Pentothal and transcardially perfused in-situ using 10% neutral-buffered formalin and given a limited necropsy. For these rats, no organs were weighed and specific tissues were also collected for subsequent microscopic testing.

There was a generally dose-related increase in the incidence and severity of various skin conditions at the treated site. Males seemed to be more sensitive than females as they were affected at all doses, however, the effects indicated very little irritation. Recovery group animals revealed complete recovery in the females and minimal hyperkeratosis in the high dose group males. At necropsy no substance-related observations were made for males in any group. In the females there was a suggestion of a possible treatment-related effect which occurred in 7 rats across all groups and consisted of skin crusts or ulceration at the site of application of test material. Haematological and serum clinical parameters were unaffected by treatment.

All animals survived until scheduled termination. There were no test substance-related effects on survival, clinical observations (apart from skin irritation), neurobehavioral signs or ophthalmological findings. The NOEL for systemic toxicity was >495 mg/kg/day. The LOEL for slight dermal irritation was 165 mg/kg/day, equivalent to ~ 1mg/cm2.

G. Genotoxicity

In vitro gene mutation in mammalian cells

Key in vitro gene mutation studies in mammalian cells were identified. In a study by the American Petroleum Institute (API, 1984b), cultures of mouse lymphoma cells were exposed to hydrodesulfurised kerosine with or without metabolic activation by Aroclor 1254-induced rat liver S9 fraction. Under non-activation conditions the test material induced a good range of toxicities for evaluation (relative growths ranged from 2.8% to 65.3%). None of the assays induced a mutant frequency that exceeded the minimum criterion (40.8 x 10-6). The test material was not mutagenic under non-activation conditions. In the presence of metabolic activation a wide range of toxicities was induced (6.1 to 107.9% relative growths). The minimum criterion mutant frequency of 69.0 x 10-6 was not exceeded. The test material was therefore considered non mutagenic under activation conditions. In a study by API (1977) (Klimisch score = 1), mouse lymphoma L5178Y cells were exposed to straight-run kerosine in acetone vehicle at concentrations ranging from 0.04 to 0.065 µL/mL (with metabolic activation) or 0.006 to 0.13 µL/mL (without activation). There was no evidence that straight-run kerosine induced mutant colonies over background levels.

In vitro cytogenicity in mammalian cells

Hydrodesulfurised kerosine was tested in the sister chromatid exchange assay using Chinese hamster ovary cells (API, 1988a). The assay was conducted with Aroclor-induced rat liver S-9 activation system. A small but statistically significant increase in the frequency of sister chromatid exchanges was observed at the high and low concentrations with metabolic activation. These increases appeared to be random and of no biological significance. There were no significant increases observed at any concentration in the absence of metabolic activation. Under the conditions of the study, hydrodesulfurised kerosine is considered to be negative in the sister chromatid exchange assay with Chinese hamster ovary cells.

In vivo cytogenicity

Based on weight of evidence kerosine substances were found to be non-mutagenic through cytogenic investigations.

In six in vivo bone marrow cytogenetic studies in the rat, there were no indications of chromosomal aberrations. Although an in vivo Sister Chromatid Exchange study in the mouse gave positive findings in the male group (but not in the females) the positive findings in the males were associated with signs of toxicity (lethargy and weight loss) at the very high top dose used in the study (4000mg/kg), both on the day of the administration of the kerosine and the day after (when they were sacrificed).

In a rat bone marrow micronucleus assay (API, 1985c, Klimisch score = 1), straight run kerosine (CAS# 800-20-6) was administered to Sprague Dawley rats. Straight run kerosine was not considered to induce chromosomal aberrations in bone marrow cells of rats. In another bone marrow

micronucleus assay (API, 1984b, Klimisch score = 1), hydrodesulfurised kerosine (CAS# 64742-81-0) was administered to rats. No clinical signs of toxicity were exhibited by the rats, and there was no significant increase in frequency of micronucleated polychromatic erythrocytes in bone marrow as compared to control. In a study by API (1977) (Klimisch score = 1), straight-run kerosine (CAS# 8008-20-6) was administered to 45 male rats. No significant increase in the frequency of micronucleated polychromatic erythrocytes was observed.

In vivo gene mutation

Key in vivo gene mutation studies were identified. In a sperm cell dominant lethal mutation assay (API, 1980b, Klimisch score = 1), Jet Fuel A was administered via inhalation route to male mice at concentrations of 100 or 400 ppm for a 6-hour exposure period, 5 days per week for 8 weeks. Males were mated with females, and the uteri of pregnant females were examined for living and dead implants. Jet Fuel A did not increase the incidence of post-implantation deaths. In another study by API (1973) (Klimisch score = 1), deodorised kerosine was administered subcutaneously to 10 male Swiss-Webster mice in corn oil vehicle or intraperitoneally to 10 Long-Evans rats undiluted at a dose of 1.0 mL/kg. Males were mated with females, and no pattern of decreased pregnancy rate or increased embryo loss was observed in the females.

H. Carcinogenicity

Kerosine is not carcinogenic when animals are exposed via the oral or inhalation route (ECHA).

Male mice were administered dermally 37.5µL of jet fuel A to the shaved backs of 50 mice per dose, twice a week for 2 years or intermittently so that application of the jet fuel was suspended when dermal irritation was noted in 20% of the group and was resumed when irritation resolved in all but 20% of the affected animals. There was a significant increase in tumours at the application site with continuous treatment compared to the control (0% versus 44%), but not with intermittent treatment (0% versus 2%). With continuous treatment, there was a treatment-related increase in dermal tumour incidence compared to controls. However, stopping treatment during dermal irritation nearly eliminated the carcinogenic effect (ECHA) [Kl. Score = 1].

Male and female mice were administered dermally 25 mg of petroleum-derived jet fuel A to the shaved backs of 25 mice, three times a week for 105 weeks. Due to high mortality, jet fuel A application was discontinued during week 62, but surviving animals were observed until study termination. There was a significant increase in tumours at the application site (0%, 26%, and 26% in the controls, JP-4, and jet A groups). The majority of the tumours were squamous cell carcinomas or fibrosarcomas. At the doses tested, there was a treatment-related increase in dermal tumour incidence when compared to controls. The results of the study indicate that there was a treatment-related increase in dermal tumour incidence when compared to controls, therefore it can be concluded that Jet fuel A has a carcinogenic effect on mice at 25 mg dosage (ECHA) [Kl. Score = 1].

Straight-run kerosine (CAS # 8008-20-6) and hydrodesulfurised kerosine (CAS # 64742-81-0) were tested in standard 2-year bioassays in mice. The animals, 50 per group, were treated twice weekly with 50 µl straight-run kerosine or with hydrodesulfurised kerosine. It was concluded that both straight-run and hydrodesulfurised kerosine were moderate skin carcinogens (ECHA) [Kl. Score = 2].

In the key carcinogenicity study from NTP, JP-5 navy fuel in acetone was administered to 50 mice dermally at dose levels of 0 (vehicle control), 250, or 500 mg/kg bw/day for up to 103 weeks. There

was a significant decrease in survival in females at both treatment doses. Remaining high-dose females were sacrificed at week 90. There was no treatment-related effect on survival in male mice. The LOAEL is 250 mg/kg/day, based on dermatitis and decreased survival in females. No NOAEL can be determined. At the doses tested, there was not a treatment-related increase in tumour incidence when compared to controls (ECHA) [Kl. Score = 1].

The potential influence of skin irritation on tumour development in long-term mouse skin painting studies was investigated as part of the CONCAWE middle distillates programme. The study included straight run hydrotreated kerosine (MD3). The test material was applied to the shorn skin of three groups of 50 male mice for 104 weeks. For the straight run hydrotreated kerosine, skin tumours only developed in the group of animals in which substantial skin irritation occurred during the study. Since no polycyclic aromatic compounds were detected in the straight run kerosine it is concluded that the occurrence of tumours is likely to have been caused by a non-genotoxic mechanism. This conclusion is consistent with reports by others that lighter middle distillates are tumour promotors but not initiators and furthermore that skin irritation plays an important role in skin tumour development. These tumours are probably the consequence of a continuous cycle of cell damage and repair caused by chronic skin irritation. The conclusions gained from this study can be applied to other carcinogenicity studies on kerosines, and they show that tumours are noted in the presence of repeated dermal irritation, and that kerosines lack a genotoxic mechanism of carcinogenicity (ECHA) [Kl. Score = 1].

I. Reproductive Toxicity

There are no specific reproductive toxicity data for the substance but there are data available with ECHA as migrated information which is read-across based on grouping of substances (category approach).

An OECD Guideline 415 One-Generation Reproduction Toxicity study was conducted. This was a reproductive study performed in two parts. In the first part, males were treated for 70 to 90 days with 0 (1mL of distilled water), 750, 1500, or 3000 mg/kg/day of undiluted JP-8 jet fuel, then mated to untreated females (one female at a time). In the second part of the study, female rats were administered the test compound at doses of 0 (1mL of distilled water), 375, 750, or 1500 mg/kg/day undiluted JP-8 jet fuel for 90 -day prior to mating, through mating, gestation, delivery, and lactation for a total of 21 weeks.

There were no changes in clinical signs or mortality in parental animals. Body weights in male rats were decreased in a dose-dependent manner. Terminal body weights were approximately 545 grams, 520 grams, 475 grams, and 315 grams in the control, 750, 1500, and 3000 mg/kg/day, respectively. In females, body weight was only significantly reduced in the high-dose group, but the differences were not significant at terminal sacrifice. The body weight in females at 20 weeks (1 week before sacrifice) was approximately 400 grams, 385 grams, 382 grams, and 335 grams in the control, 375, 750, and 1500 mg/kg/day, respectively. Hematology was not measured in the males and no effects were noted in the females. Clinical chemistry was not measured in the males and no effects were noted in the females. Urinalysis was not measured in the males and no effects were noted in the females. Absolute and relative liver weights were increased in mid- and high-dose females, but were not accompanied by any histological findings. The test compound caused perianal dermatitis (high-dose only) and stomach hyperplasia (mid- and high-dose) in the female rats.

There were no treatment-related effects on reproduction or sperm parameters in males. There were no effects on reproduction, gestation, or litter size in females. The lowest NOAEL based on parental body weight was determined to be 750 mg/kg/day.

The F1 generation was not examined for clinical signs though no mention would suggest no significant signs were noted. No mortality was observed. There were no effects on offspring viability. However, there was a dose-related decrease in pup weight that was significant in the 750 mg/kg/day group on postnatal day 4 only and in the 1500 mg/kg/day group from postnatal day 4 through postnatal day 21. The 1500 mg/kg/day group recovered by postnatal day 90. The NOAEL based on offspring body weight was determined to be 750 mg/kg/day.

J. Reproductive Toxicity/Developmental Toxicity

In a developmental toxicity study, undiluted JP-8 jet fuel was administered to 30 Sprague-Dawley (Crl:CD) rats/dose by gavage at various volumes to achieve dose levels of 0 (sterile water), 500, 1000, 1500, or 2000 mg/kg bw/day from days 6 through 15 of gestation.

There was a significant decrease in maternal weight gain with doses of 1000 mg/kg/day or greater. Maternal necropsy weight was significantly different than the control in the 1500 and 2000 mg/kg/day groups. There were no apparent clinical signs of toxicity. Reproductive endpoints were not assessed in this study because females were pregnant prior to treatment and did not deliver, so only developmental endpoints can be assessed. Thirteen females (one 1000 mg/kg/day; three 1500 mg/kg/day, and nine 2000 mg/kg/day) were found dead. Although there appears to be a dose-dependent increase in the mortality, necropsy found the cause of death to be related to the presence of the test compound in the lungs indicating dosing into the lungs instead of the gastrointestinal tract. The maternal LOAEL is 1000 mg/kg/day, based on reduced body weight gain. The maternal NOAEL is 500 mg/kg/day.

There was a significant decrease in fetal weight in both male and female fetuses dosed with 1500 and 2000 mg/kg/day. The test compound did not significantly increase the incidence of malformations or variations compared to the control nor was the sex ratio altered. The developmental LOAEL is 1500 mg/kg/day, based on reduced fetal weight. The developmental NOAEL is 1000 mg/kg/day. It can be concluded that the test substance is not toxic to development.

This study received a Klimisch score of 1 and is classified as reliable without restrictions because it was carried out in a method equivalent/similar to OECD TG 414.

K. Derivation of Toxicological Reference and Drinking Water Guidance Values

The toxicological reference values developed for the substance follow the methodology discussed in enHealth (2012). The approach used to develop drinking water guidance values is described in the Australian Drinking Water Guidelines (ADWG, 2011).

<u>Non-Cancer</u>

The NOAEL for reduced maternal body weight is 500 mg/kg/day, based on reduced body weight in dams and in pups treated under a repeat dose regimen. The NOAEL from this study will be used for determining the oral Reference dose (RfD) and the drinking water guidance value.

Oral Reference Dose (oral RfD)

Oral RfD = NOAEL / (UF_A x UF_H x UF_L x UF_{Sub} x UF_D)

Where:
UF_A (interspecies variability) = 10
UF_H (intraspecies variability) = 10
UF_L (LOAEL to NOAEL) = 1
UF_{Sub} (subchronic to chronic) = 10
UF_D (database uncertainty) = 1

Oral RfD = 500 /(10 x 10 x 1 x 10 x 1) = 500/1,000 = 0.5 mg/kg-day

Drinking water guidance value

Drinking water guidance value = (animal dose) x (human weight) x (proportion of intake from water) / (volume of water consumed) x (safety factor)

Using the oral RfD,

Drinking water guidance value = (oral RfD) x (human weight) x (proportion of water consumed) / (volume of water consumed)

where:
Human weight = 70 kg (ADWG, 2011)
Proportion of water consumed = 10% (ADWG, 2011)
Volume of water consumed = 2L (ADWG, 2011)

Drinking water guidance value = (0.500 x 70 x 0.1)/2 = 1.8 mg/L

Cancer

There are no carcinogenicity studies on the substance or related hydrocarbons. Thus, a cancer reference value was not derived.

L. HUMAN HEALTH HAZARD ASSESSMENT OF PHYSICO-CHEMICAL PROPERTIES

The substance does not exhibit the following physico-chemical properties:

- Explosivity
- Oxidizing potential

The substance is classified as a “Flammable Liquid Category 3”

7 ENVIRONMENTAL EFFECTS SUMMARY

A. Summary

The substance is of low acute concern to aquatic organisms.

B. Aquatic Toxicity

Acute Studies

Table 3 lists the results of acute aquatic toxicity studies on hydrotreated light petroleum distillate surrogates.

Table 3 Acute Aquatic Toxicity Studies on Hydrotreated Light Petroleum Distillate Surrogate[2]

Test Species	Endpoint	Results (mg/L)	Klimisch score	Reference
Oncorhynchus mykiss	96-hour LL_{50}	2-5	1	ECHA
Daphnia magna	48-hour EL_{50}	1.4	1	ECHA
Raphidocelis subcapitata	72-hour EC_{50}	<1-3 (average of 2)	1	ECHA
Selenastrum capricornutum	72-hour EC_{50}	3.7	2	ECHA

Chronic Studies

There are no long-term toxicity studies on fish. A single long term study on invertebrates is discussed below.

In a 21-day semi-static chronic reproductive toxicity test (OECD 211; KS = 1) on *Daphnia magna*, hydrodesulfurised kerosine was evaluated using water accommodated fraction methodology. The actual loading rates were 0 (control), 0.08, 0.19, 0.48, 1.2 and 3.0 mg/L. Under the conditions of this test, the 21-day chronic reproductive NOEL for kerosine is 0.48 mg/L. The LOEL is 1.2 mg/L. The EL_{50} based on reproduction is 0.89 mg/L (ECHA).

C. Terrestrial Toxicity

There are no terrestrial toxicity studies for this substance.

[2] Hydrodesulfurized Kerosine (CAS No. 64742-81-0)

D. Calculation of PNEC

The PNEC calculations for hydrotreated light petroleum distillate follow the methodology discussed in DEWHA (2009).

PNEC water

Experimental results are available from acute tests on three trophic levels. There is one long term study on a single trophic level organism, *D. magna*.

On the basis that the data consists of short-term studies from three trophic levels and a long-term study from one trophic level, an assessment factor of 100 is applied to the 21-day chronic reproductive NOEL for kerosine of 0.48 mg/L. The $PNEC_{aquatic}$ is 0.005 mg/L.

PNEC sediment

There are no toxicity data for sediment-dwelling organisms. Therefore, the $PNEC_{sed}$ was calculated using the equilibrium partitioning method. The $PNEC_{sed}$ is 0.36 mg/kg sediment wet weight.

The calculations are as follows:

$PNEC_{sed} = (K_{sed\text{-}water}/BD_{sed}) \times 1000 \times PNEC_{water}$
$= (93.4/1280) \times 1000 \times 0.005$
$= 0.36$ mg/kg

Where:
$K_{sed\text{-}water}$ = suspended matter-water partition coefficient (m^3/m^3) [calculated]
BD_{sed} = bulk density of sediment (kg/m^3) = 1,280 [default]

$K_{sed\text{-}water} = 0.8 + [0.2 \times Kp_{sed}/1000 \times BD_{solid}]$
$= 0.8 + [0.2 \times 193/1000 \times 2400]$
$= 93.4\ m^3/m^3$

And:
Kp_{sed} = solid-water partition coefficient (L/kg).[calculated]
BD_{solid} = bulk density of the solid phase (kg/m^3) = 2,400 [default]

$Kp_{sed} = K_{oc} \times f_{oc}$
$= 4818 \times 0.04$
$= 193$ L/kg

Where:
K_{oc} = organic carbon normalized distribution coefficient (L/kg). The K_{oc} for hydrodesulfurized kerosine calculated from EPISUITE™ using the MCI is 4818 L/kg.
F_{oc} = fraction of organic carbon in sediment = 0.04 [default].

PNEC soil

There are no experimental toxicity testing results available for the substance or its noted surrogates. Therefore, the $PNEC_{soil}$ was calculated using the equilibrium partitioning method. The $PNEC_{soil}$ is 0.32 mg/kg soil dry weight.

The calculations are as follows:

$PNEC_{soil} = (Kp_{soil}/BD_{soil}) \times 1000 \times PNEC_{water}$
$= (96.4/1500) \times 1000 \times 0.005$
$= 0.32$ mg/kg

Where:
Kp_{soil} = soil-water partition coefficient (m3/m3)
BD_{soil} = bulk density of soil (kg/m3) = 1,500 [default]

$Kp_{soil} = K_{oc} \times f_{oc}$
$= 4818 \times 0.02$
$= 96.4\ m^3/m^3$

And:
K_{oc} = organic carbon normalised distribution coefficient (L/kg). The K_{oc} for hydrodesulfurized kerosine calculated from EPISUITE™ using the MCI is 4818 L/kg.
F_{oc} = fraction of organic carbon in soil = 0.02 [default].

8 CATEGORISATION AND OTHER CHARACTERISTICS OF CONCERN

A. PBT Categorisation

The methodology for the Persistent, Bioaccumulative and Toxic (PBT) substances assessment is based on the Australian and EU REACH Criteria methodology (DEWHA, 2009; ECHA, 2008).

The substance or similar compounds are readily biodegradable; thus they do not meet the screening criteria for persistence.

Based on the estimated BCF values, derived from EPISuite estimates (BCF = 3.162 L/kg wet-weight) the substance does not meet the screening criteria for bioaccumulation.

The NOEC values from acute and chronic aquatic toxicity studies on the substance indicate it does not meet the screening criteria for toxicity.

Therefore, hydrotreated light petroleum distillates are not PBT substances.

B. Other Characteristics of Concern

No other characteristics of concern were identified for hydrotreated light petroleum distillates.

9 SCREENING ASSESSMENT

Chemical Name	CAS No.	Overall PBT Assessment [1]	Chemical Databases of Concern Assessment Step		Persistence Assessment Step		Bioaccumulative Assessment Step	Toxicity Assessment Step			Risk Assessment Actions Required[3]
			Listed as a COC on relevant databases?	Identified as Polymer of Low Concern	P criteria fulfilled?	Other P Concerns	B criteria fulfilled?	T criteria fulfilled?	Acute Toxicity [2]	Chronic Toxicity[2]	
Hydrotreated Light Petroleum Distillates	64742-47-8	Not a PBT	No	No	No	No	No	No	2	2	2

Footnotes:

1 - PBT Assessment based on PBT Framework.

2 - Acute and chronic aquatic toxicity evaluated consistent with assessment criteria (see Framework).

3 – Tier 1 – Hazard Assessment only.

Notes:

NA = not applicable

PBT = Persistent, Bioaccumulative and Toxic

B = bioaccumulative

P = persistent

T = toxic

10 REFERENCES, ABBREVIATIONS AND ACRONYMS

A. References

ADWG (2011). National Water Quality Management Strategy. Australian Drinking Water Guidelines, Section 6, Australian Government, National Health and Medical Research Council, Natural Resource Management Ministerial Council.

AUS (2018). Australian Code for the Transport of Dangerous Goods by Road & Rail Edition 7.6, 2018. Commonwealth of Australia National Transport Commission, Level 3, 600 Bourke Street MELBOURNE, VIC, 3000.

BASF (2012). GPS Safety Summary: Fatty acids, C8-C16, 2-ethylhexyl ester. Available at: http://www.safety-summaries.basf.com/group/corporate/safety-summaries/en/literature-document:/GPS+Safety+Summaries--Fatty+acids+C8+16+2+ethylhexyl+ester-English.pdf.

Bookstaff, R.C., Stuard, S.B., Ward, S.R., Pesik, P.K., and Henwood, S.M. (2004). The safety of ethyl oleate is supported by a 91-day feeding study in rats. Regul. Toxicol. Pharmacol. 39: 202-213.

Department of the Environment, Water, Heritage and the Arts [DEWHA] (2009). Environmental risk assessment guidance manual for industrial chemicals, Department of the Environment, Water, Heritage and the Arts, Commonwealth of Australia.

Department of the Environment and Energy [DoEE]. (2017). Chemical Risk Assessment Guidance Manual: for chemicals associated with coal seam gas extraction, Guidance manual prepared by Hydrobiology and ToxConsult Pty Ltd for the Department of the Environment and Energy, Commonwealth of Australia, Canberra.

ECHA. ECHA REACH database: http://echa.europa.eu/information-on-chemicals/registered-substances

enHealth Human Risk Assessment [HHRA] (2012). Environmental Health Risk Assessment, Guidelines for Assessing Human Health Risks from Environmental Hazards. Office of Health Protection of the Australian Government Department of Health.

European Chemicals Agency [ECHA] (2008). Guidance on Information Requirements and Chemical Safety Assessment, Chapter R11: PBT Assessment, European Chemicals Agency, Helsinki, Finland.

Klimisch, H.J., Andreae, M., and Tillmann, U. (1997). A systematic approach for evaluating the quality of experimental and toxicological and ecotoxicological data. Regul. Toxicol. Pharmacol. 25:1-5.

OECD (2012). SIDS INITIAL ASSESSMENT PROFILE. C9-C14 Aliphatic [≤2% aromatic] Hydrocarbon Solvents Category. CoCAM 3, 16-18 October 2012.

U.S. Environmental Protection Agency [EPA] (2017). EPISuite™ v. 4.11, United States Environmental Protection Agency, Office of Pollution Prevention and Toxics and Syracuse Research Corporation. Available at: https://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface.

B. Abbreviations and Acronyms

°C	degrees Celsius
°F	degrees Fahrenheit
AICS	Australian Inventory of Chemical Substances
BCF	bioconcentration factor
BCFBAF	bioconcentration factor/bioaccumulation factor
COC	constituent of concern
DEWHA	Department of the Environment, Water, Heritage and the Arts
EC	effective concentration
ECHA	European Chemicals Agency
EL	effect level
EU	European Union
IUPAC	International Union of Pure and Applied Chemistry
kg/m^3	kilogram per cubic metre
KI	Klimisch scoring system
KOCWIN™	USEPA organic carbon partition coefficient estimation model
KOWWIN	USEPA modelling program to estimate the organic carbon-normalised sorption coefficient for soil and sediment
kPa	kilopascal
L/kg	litres per kilogram
LL	Lethal loading
MCI	molecular connectivity index
mg/L	milligrams per litre
NOEC	no observed effective concentration
OECD	Organisation for Economic Co-operation and Development
Pa	Pascal

Pa.s64742	pascal second
PBT	Persistent, Bioaccumulative and Toxic
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
SGG	Synthetic Greenhouse Gases
USEPA	United States Environmental Protection Agency
UVCB	Unknown or Variable Composition, Complex Reaction Products and Biological Materials