Australian Government
Department of Health
Australian Industrial Chemicals Introduction Scheme

Straight run gas oils

Evaluation statement

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Table of contents

Contents

AICIS evaluation statement 4

Subject of the evaluation 4

Chemicals in this evaluation 4

Reason for the evaluation 4

Parameters of evaluation 4

Summary of evaluation 4

Summary of introduction, use and end use 4

Human health 5

Proposed means for managing risk 6

Workers 6

Conclusions 8

Supporting information 9

Grouping rationale 9

Chemical identity 9

Relevant physical and chemical properties 11

Introduction and use 11

Australia 11

International 12

Existing Australian regulatory controls 13

AICIS 13

Public 13

Workers 13

International regulatory status 13

Exposure standards 13

Health hazard information 14
Toxicokinetics 14
Acute toxicity 14
Corrosion/Irritation 15
Sensitisation 16
Repeat dose toxicity 17
Genotoxicity 18
Carcinogenicity 19
Reproductive and development toxicity 20
Other 21
References 22

AICIS evaluation statement

Subject of the evaluation

Straight run gas oils

Chemicals in this evaluation

Name	CAS registry number
Distillates (petroleum), straight-run middle	64741-44-2
Gas oils (petroleum), straight-run	64741-43-1
Distillates (petroleum) heavy straight run	68915-96-8
Distillates (petroleum), full-range straight-run middle	68814-87-9

Reason for the evaluation

An evaluation is required to provide information on the risks to human health.

Parameters of evaluation

These chemicals are a group of straight run gas oils that are listed on the Australian Inventory of Industrial Chemicals (the Inventory). This evaluation is a human health risk assessment for all identified industrial uses of these chemicals in this group. These chemicals have been evaluated as a group as they are expected to have similar toxicological properties and uses.

Summary of evaluation

Summary of introduction, use and end use

The chemical identified by CAS No. 64741-44-2 has reported use in Australia in the printing industry and in fuel and oil products with an introduction volume between 100,000 and 999,999 tonnes. Information from Australian datasheets indicates use of the chemical in heating oils, fuel, defoaming, high flash kerosene, fuel injector cleaner, and wood treatment and preservative products.

Internationally, a range of commercial and site limited uses have been identified including in plastic and rubber products, paints and coatings, lubricants and greases, and fuels. Some domestic uses in paints and coatings and auto products have been identified for CAS No 64741-44-2. This chemical has also been identified as having potential to migrate from food packaging. Although cosmetic use has been flagged in some sources, based on the weight of evidence this use is considered unlikely.

Human health

Summary of health hazards

The critical health effects for risk characterisation will likely depend on the composition of the chemicals, but could include:

- systemic acute effects from inhalation exposure
- local effects including skin irritation
- carcinogenicity.

These chemicals also have the potential to cause chemical pneumonitis if aspirated.

The systemic toxicity of high boiling petroleum substances (HBPS), such as the chemicals in this group, can be correlated with concentrations of PACs (polycyclic aromatic compounds), particularly those composed of 3, 4, 5, 6 and/or 7 fused aromatic rings. However, other compositional characteristics could also influence toxicity. Straight run gas oils are reported to have lower aromatic and olefin contents than gas oils produced through secondary processing. The boiling point specifications for these fuels essentially limit the aromatics to 1, 2 and 3 ring compounds with minimal 4 ring or higher PACs.

Based on the available data, the chemicals in this group are not expected to produce significant systemic adverse effects after repeated dermal exposure but are expected to produce local adverse skin irritation effects. Prolonged exposure to straight run gas oil can result in severe dermal irritation. This repeated dermal damage can result in the development of dermal tumours.

In vitro genotoxicity testing has given some indications of genotoxicity. However, the two available in vivo chromosome aberration assays of limited reliability were reported as negative.

Developmental effects, particularly the increased incidence of foetal death and resorption, are associated with aromatics containing 3 or more rings, while other constituents of these substances (aliphatic constituents and 1 and 2 ring aromatics) do not make any significant contribution to the developmental toxicity of these substances. In general, the chemicals in this group contain low levels of PACs with 3–7 rings. While similar effects were observed in studies with these chemicals, these were only observed in the presence of maternal toxicity. Whilst these chemicals have not been tested for the effects of reproductive toxicity, reproductive effects are considered to be a less sensitive endpoint than developmental toxicity for other HBPS.

Hazard classifications relevant for worker health and safety

These chemicals satisfy the criteria for classification according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) for hazard classes relevant for work health and safety as follows (UNECE 2017). This does not consider classification of physical hazards and environmental hazards.

Health hazards	Hazard category	Hazard statement
Acute toxicity – inhalation	Acute Tox. 4	H332: Harmful if inhaled
Skin Irritation	Skin Irrit. 2	H315: Causes skin irritation
Aspiration	Asp. Tox. 1	H304: May be fatal if swallowed and enters the airways
Carcinogenicity	Carc. Cat. 2	H351: suspected of causing cancer

Summary of health risk

Public

Based on the available use information, the public may be exposed to the chemicals by incidental skin and eye contact with these chemicals during use of domestic products.

Gas oils used as ingredients in products available to consumers are refined to contain a low level of PACs. Given that normal precautions to avoid prolonged contact are expected and these chemicals are likely to be present at concentrations <30%, these chemicals are unlikely to pose a risk from these uses. Although one of the chemicals has been identified as being present in food contact materials, exposure from migration from these materials has been estimated to be very low (0.33 ug/kg bw/day) (Government of Canada 2019). Therefore, there are no identified risks to the public that require management.

Workers

During product formulation and packaging, dermal, ocular and inhalation exposure might occur, particularly where manual or open processes are used. These could include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. Worker exposure to these chemicals at lower concentrations could also occur while using formulated products containing these chemicals. The level and route of exposure will vary depending on the method of application and work practices employed. Good hygiene practices to minimise incidental oral exposure are expected to be in place.

Given the critical systemic acute, local health effects and systemic effects following prolonged dermal contact, these chemicals could pose a risk to workers. Control measures to minimise dermal and inhalation exposure are needed to manage the risk to workers (see **Proposed means for managing risks** section).

Proposed means for managing risk

Workers

Recommendation to Safe Work Australia

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

Classification of chemicals in this group as an aspiration hazard should only be applied if the kinematic viscosity criteria for classification are met (Note 9 should apply).

Carcinogenicity classifications need not apply if it can be shown that the substance contains less than 3% DMSO extract as measured by the IP346 assay; the classification should also be subject to Note 10.

The recommended classification and labelling entry should have the following notes appended:

- ‘Note 9 (The aspiration hazard classification should only be applied if the kinematic viscosity criteria for aspiration classification in the GHS is met.)’
- ‘Note 10 (The chemical is a substance of unknown or variable composition, complex reaction product, or biological material (UVCB). The hazards of the chemical may depend on the composition. For more information refer to the assessment report published on the AICIS website.)'

Information relating to safe introduction and use

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

Control measures that could be implemented to manage the risk arising from exposure to these chemicals include, but are not limited to:

- using closed systems or isolating operations
- using local exhaust ventilation to prevent these chemicals from entering the breathing zone of any worker
- minimising manual processes and work tasks through automating processes
- adopting work procedures that minimise splashes and spills
- cleaning equipment and work areas regularly
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with these chemicals.

Measures required to eliminate or manage risk arising from storing, handling and using these hazardous chemicals depend on the physical form and how these chemicals are used.

These control measures may need to be supplemented with:

- conducting health monitoring for any worker who is at significant risk of exposure to these chemicals, if valid techniques are available to monitor the effect on the worker’s health

Personal protective equipment should not solely be relied upon to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk.

Model codes of practice, available from the Safe Work Australia website, provide information on how to manage the risks of hazardous chemicals in the workplace, prepare an SDS and label containers of hazardous chemicals. Your Work Health and Safety regulator should be contacted for information on Work Health and Safety laws and relevant Codes of Practice in your jurisdiction.

Conclusions

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

Considering the proposed means of managing risks, the Executive Director is satisfied that the identified human health risks can be managed within existing risk management frameworks. 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 and the proposed means of managing the risks identified during this evaluation are implemented.

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

Supporting information

Grouping rationale

This group of chemicals includes straight run gas oils, which are UVCBs (unknown variable composition or biological substances) crude oil distillates consisting of a complex combination of various branched and straight chain hydrocarbons of varying chain length distributions, and naphthenic, aromatic, polycyclic aromatic, and paraffinic content. While the varying chain length distributions of the chemicals could be expected to produce differences between the chemicals, the critical health effects of these chemicals are expected to be similar due to their comparable composition consisting of common classes of hydrocarbons.

The systemic toxicity of high boiling petroleum substances (HBPS), such as chemicals in this group, can be correlated with concentrations of polycyclic aromatic compounds (PACs), particularly those composed of 3, 4, 5, 6 and/or 7 fused aromatic rings. However, other compositional characteristics could also influence toxicity (TERA 2008).

Straight run gas oils are reported to have lower aromatic and olefin content than gas oils produced through secondary processing. Due to the boiling point specifications of these fuels, the aromatics are limited to 1, 2 and 3 ring compounds with minimal 4 ring or higher PACs. The PAC content profile of the chemicals in this group are summarised in the table below, which represents the PAC content in dimethylsulfoxide (DMSO) extracts of the straight run gas oils (API 2012b).

CAS registry number	Total PAC Content (% weight)	1 Aromatic Rings Content (% weight)	2 Aromatic Rings Content (% weight)	3–7 Aromatic Rings Content (% weight)
64741-44-2	3.4–9.7	0.1–0.4	1.9–6.3	0.2–4.4
64741-43-1	3.3–8.8	0.0–0.1	0.6–3.6	2.0–6.6
68915-96-8	4.7–7.8	0.0–0.2	0.5–1.6	3.4–7.0
68814-87-9	4.3–14.0	0.1–0.7	2.6–9.8	1.8–4.2

Information on gas oils produced from secondary processing has been included in this evaluation. As these generally have higher levels of PACs, this is expected to represent worst case toxicity for chemicals in this group.

Chemical identity

Chemical name	Distillates (petroleum), straight-run middle
CAS number	64741-44-2
Synonyms	distillate, petroleum, hydrotreated middle gas oil straight run gas oil

Structural formula	Unspecified
Molecular formula	Unspecified
Molecular weight (g/mol)	Unspecified
SMILES	Unspecified
Chemical description	UVCB. A complex combination of hydrocarbons produced by the distillation of crude oil. It consists of hydrocarbons having carbon numbers predominantly in the range of C11 through C20 and boiling in the range of 205°C to 345°C (401°F to 653°F).

Chemical name	Gas oils (petroleum), straight-run
CAS number	64741-43-1
Synonyms	straight run gas oil, petroleum
Structural formula	Unspecified
Molecular formula	Unspecified
Molecular weight (g/mol)	Unspecified
SMILES	Unspecified
Chemical description	UVCB. A complex combination of hydrocarbons produced by the distillation of crude oil. It consists of hydrocarbons having carbon numbers predominantly in the range of C11 through C25 and boiling in the range of approximately 205°C to 400°C (401°F to 752°F).

Chemical name	Distillates (petroleum), heavy straight-run
CAS number	68915-96-8
Synonyms	HS Gasoil straight run gas oil
Structural formula	Unspecified
Molecular formula	Unspecified
Molecular weight (g/mol)	Unspecified
SMILES	Unspecified
Chemical description	A complex combination of hydrocarbons produced by the atmospheric distillation of crude oil. It boils in the

	range of approximately 288°C to 471°C (550°F to 880°F).

Chemical name	Distillates (petroleum), full-range straight-run middle
CAS number	68814-87-9
Synonyms	full range straight run, middle distillate, petroleum atmospheric gasoil light gas oil straight run gas oil
Structural formula	Unspecified
Molecular formula	Unspecified
Molecular weight (g/mol)	Unspecified
SMILES	Unspecified
Chemical description	A complex combination of hydrocarbons produced by the distillation of crude oil. It consists of hydrocarbons having carbon numbers predominantly in the range C9 through C25 and boiling in the range of approximately 150°C to 400°C (302°F to 752°F).

Relevant physical and chemical properties

Chemicals in this group are liquid under ambient pressure (101.3 KPa; 1 atm) and temperature (20°C) with boiling points ranging from 150 to 471°C. Straight run gas oils have a 'diesel fuel odour' and relatively low vapour pressures; the chemical with CAS No. 64741-43-1 has a vapour pressure of 0.4 kPa at 40°C. Chemicals in this group are expected to display relatively low water solubility due to their composition from predominantly non-polar hydrocarbons. The chemicals span a range of viscosities with values reported as 2.1–27 mm^2/s at 40°C (CONCAWE 2020).

Introduction and use

Australia

Current use data derived from the Safety Data Sheets of various registered Australian chemical introducers suggest the chemical with CAS No. 64741-44-2 is used in heating oils, fuel, defoaming, high flash kerosene, fuel injector cleaner, and wood treatment and preservative products.

The chemical with CAS No. 64741-44-2 has been identified by the 2006 Australian High Volume Industrial Chemical List as having an introduction volume in the range 100,000–999,999 tonnes per annum, with use as a solvent in the printing industry and in fuel and oil products (NICNAS 2006). The chemical with CAS No. 64741-43-1 has been identified as a component of hydraulic fracturing products in the period 2005–2009 in a draft letter by the NSW Chief Scientist and Engineer on 'The Likelihood of hydraulic fracturing activities in

NSW' (NSW CSE n.d.). Australian use data is not available for the other chemicals in this group.

International

The following international uses for the chemicals have been identified through:

- European Union (EU) Registration, Evaluation and Authorisation of Chemicals (REACH)
- The Substances in Preparations in Nordic countries (SPIN) database
- The US Chemical Data Reporting under the Toxic Substances Control Act (TSCA) 2012 and 2016
- Consumer product databases
- Government of Canada screening assessment (2019).

These chemicals have a number of site limited and commercial applications including:

- Additives in plastic and rubber products
- Lubricants, greases and oils
- Solvents
- Fuels and related products
- Building and/or construction materials not covered elsewhere
- Paints and coatings
- Electrical and electronic products
- Ink, toner, and colourant products.

Reported maximum concentrations were typically <1% in commercial uses, although concentrations up to 30% were indicated (US EPA 2012; US EPA 2016).

Some of these commercial uses may also be used in domestic applications. Consumer use for CAS No. 64741-44-2) was indicated in North America in paints and coatings (concentrations of <1%), auto products (fuel cleaners; concentration up to 25%) and cleaning waxes (concentration up to 5%) (DeLima Associates; US EPA 2012; US EPA 2016). Potential exposure from contact with food packaging has been identified for CAS No. 647441-44-2. Gas oils used as ingredients in products available to consumers are refined to contain a low level of PACs (Government of Canada 2019).

Chemicals in this group have reported cosmetic use according to REACH dossiers and the Government of Canada screening assessment (REACHa; REACHb; REACHc; REACHd; Government of Canada 2019). However, the chemicals are not listed in the International Nomenclature Cosmetic Ingredient (INCI) Dictionary and were not identified as being used in cosmetic products in the United States of America or in the EWG Skin Deep database (EWG, De Lima Associates; Personal Care Products Council). It is likely that chemicals with more specific composition ranges and greater refinement, rather than chemicals in this evaluation, are being used in cosmetics.

Existing Australian regulatory controls

AICIS

No specific controls are currently available for these chemicals.

Public

Chemicals in this group fall under the scope of the entry for 'Hydrocarbons, Liquid' which is included in *Schedule 5 of The Poisons Standard—The Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP)* as described below (TGA 2022).

Schedule 5:

'HYDROCARBONS, LIQUID, including kerosene, diesel (distillate), mineral turpentine, white petroleum spirit, toluene, xylene and light mineral and paraffin oils (but excluding their derivatives), **except**:

a) toluene and xylene when included in Schedule 6;
b) benzene and liquid aromatic hydrocarbons when included in Schedule 7;
c) food grade and pharmaceutical grade white mineral oils;
d) in solid or semi-solid preparations;
e) in preparations containing 25 per cent or less of designated solvents;
f) in preparations packed in pressurised spray packs;
g) in adhesives packed in containers each containing 50 grams or less of adhesive;
h) in writing correction fluids and thinners for writing correction fluids packed in containers having a capacity of 20 mL or less; or
i) in other preparations when packed in containers with a capacity of 2 mL or less.'

Schedule 5 chemicals are labelled with 'Caution' and are described as 'Substances with a low potential for causing harm, the extent of which can be reduced through the use of appropriate packaging with simple warnings and safety directions on the label.'

Workers

These chemicals are currently not listed on the Hazardous Chemical Information System (HCIS) and no specific exposure standards are available in Australia (SWA) for chemicals in this group.

Industry facilities that introduce or process these chemicals could meet the criteria for major hazard facilities (MHF) due to the quantities of chemicals such as methane, natural gas and liquefied petroleum gas stored, handled or processed. Operators of MHF have specific work health and safety (WHS) duties, in addition to the general WHS duties.

International regulatory status

Exposure standards

While no occupational exposure limits were available for the specific chemicals in this evaluation, time weighted average (TWA) occupational exposure limits for mineral oil were

found to range from 1–5 mg/m^3 in several different countries including Sweden, Iceland, Singapore, Japan, Taiwan, Switzerland, and the United States (Galleria Chemica).

Health hazard information

Toxicokinetics

Currently there appears to be no experimental data in animals or humans to evaluate the adsorption, distribution, metabolism and elimination of chemicals in this group.

Since chemicals in this group are stated to predominantly contain hydrocarbons with carbon numbers in the overall range C9–C25, for the group, the oral absorption of chemicals should be favourable as the molecular weights of alkanes with corresponding carbon numbers (112–304 g/mol) are below 500 g/mol. Similarly, dermal absorption should occur relatively easily due to these chemicals being predominantly composed of chemicals with molecular weights below 500 g/mol. Based on the likely molecular weight profile of chemical constituents of this group of UVCB chemicals, they could be expected to distribute throughout the body to a moderate to high extent. The non-polar lipophilic nature of many of the chemical constituents of UVCB chemicals in this group potentially increases their accumulation potential in adipose tissue; this includes PACs (ECHA 2017). The systemic bioavailability is supported by observations of effects following all routes of exposure.

Acute toxicity

Oral

Based on the current data, the chemicals in this group have low acute oral toxicity.

In an acute oral toxicity study conducted with deviations from OECD TG 401, Sprague Dawley (SD) rats (5 animals/sex), were administered one chemical (CAS No. 64741-44-2) by oral gavage at 5000 mg/kg. The median lethal dose (LD50) was determined to be greater than 5000 mg/kg. Clinical signs of toxicity were observed including ataxia, diarrhoea, hair loss on or around the anus, abdomen, and hind legs; hypoactivity, and lacrimation (REACHa).

In an acute oral toxicity study conducted according to OECD TG 401, employing the limit test regime, SD rats (5 animals/sex) were dosed with one chemical (CAS No. 64741-43-1) at 5000 mg/kg by oral gavage. The LD50 was determined to be greater than 5000 mg/kg and no adverse effects were reported (REACHb).

In general, gas oils produced from secondary processing are considered to have low acute toxicity following oral exposure (NICNAS 2019).

Dermal

Based on the current data, chemicals in this group have low acute dermal toxicity.

In an acute dermal toxicity study conducted with deviations from OECD TG 402, New Zealand White rabbits (NZW) (4 animals/sex) were topically administered one chemical (CAS No. 64741-44-2) to abraded skin (deviation from OECD TG 402 requirements) at 2000 mg/kg. An LD50 greater than 2000 mg/kg was established with clinical signs of toxicity

including oedema, erythema, atonia, and desquamation and fissuring of the skin as well as “slight coriaceousness” of the skin (REACHa).

In an acute dermal toxicity study conducted similar to OECD TG 402 (with deviations), NZW rabbits (5 animals/sex) were dermally administered 2000 mg/kg of one chemical (CAS No. 64741-43-1) under occlusive conditions for 24 hours. An LD50 greater than 2000 mg/kg was determined, and no fatalities were reported during the 14 day observation period. Signs of toxicity and adverse effects included eschar, erythema, oedema, and abnormal stools. Abnormalities of the gastrointestinal tract were reported in one animal while lung abnormalities were reported in another at necropsy (REACHb).

In general, gas oils produced from secondary processing are considered to have low acute toxicity following dermal exposure (NICNAS 2019).

Inhalation

Based on the current data, the chemicals in this group have moderate acute inhalation toxicity, warranting hazard classification.

In an acute inhalation toxicity study conducted according to OECD TG 403, SD rats (5 animals/sex/dose) were administered aerosolised chemical (CAS NO. 64741-44-2) via whole body inhalation exposure for 4 hours at either 5 mg/L or at 0, 3.3, 4.78, 6.55, or 7.58 mg/L. A median lethal concentration (LC50) value of 1.78 mg/L was determined, with clinical signs of toxicity including decreased activity, partially closed eyes, wet and oily coat, and respiratory distress. Dark red lungs were reported in all test animals that died within 1–2 days of exposure and diffuse moderate or marked pulmonary congestion and perivascular oedema and damaged alveolar walls were observed in all test animals that died during the study. Test animals exposed to concentrations greater than 1.5 mg/L “exhibited chronic inflammatory changes in the lungs” (API 2012a).

In an acute inhalation toxicity study conducted according to OECD TG 403 (limit test), SD rats (5 animals/sex) were administered aerosolised chemical (CAS No. 64741-44-2) by nose inhalation for 4 hours at a concentration of 2.53 mg/L. An LC50 greater than 2.53 mg/L was established, and no deaths were reported during the study. Signs of clinical toxicity included laboured breathing during exposure which increased as exposure progressed. Discolouration of the lungs, alopecia and enlarged kidneys in some animals was reported at necropsy (REACHa).

In general, gas oils are considered to have low to moderate acute toxicity following inhalation exposure (NICNAS). Differences in toxicity could occur, depending on variations in aerosol particle size and subsequent deposition in the lungs. LC50 values of <5 mg/L, following exposure for 4 hours, have been reported for gas oils produced by secondary processing (NICNAS 2019).

Corrosion/Irritation

Skin irritation

Based on the current data, chemicals in this group may be irritating to the skin. Given that effects were observed when tested under occlusive patch conditions and for longer periods of time than specified in the OECD TG 404 conditions, irritant responses might be more pronounced than would be expected in a standard study. While the available data are not sufficient for hazard classification, effects reported following repeated dermal exposure (see

Repeat dose toxicity – Dermal section) are considered sufficient to warrant classifying the chemical for local dermal irritation effects.

In an acute dermal irritation test purportedly conducted according to EPA OPPTS 870.2500 and with some deviations from OECD TG 404, male NZW rabbits (n=6) were administered 0.5 mL of the chemical (CAS No. 64741-43-1) under occlusive conditions at 4 shaved sites per animal for 24 hours and they were observed up to 7 days post treatment with the chemical. Mean scores of 2.28 and 1.83 (over observations at 24 and 72 hours) for erythema and oedema, respectively were reported to be irreversible within the 7 day observation period for 5 out of 6 animals. Dry skin was observed in all test animals throughout the observation period (REACHb).

In an acute dermal corrosion study conducted with deviations from OECD TG 404, NZW rabbits (n=6) were administered 0.5 mL of the chemical (CAS No. 64741-44-2) on either abraded or unabraded skin on each rabbit for a duration of 24 hours. Mean scores were 1.8 and 1.58 (over observations at 24 and 72 hours) for erythema and oedema, respectively. Effects were reversible within 14 days (REACHa).

In general, gas oils are considered to be slightly to moderately irritating to the skin (NICNAS 2019).

Eye irritation

Based on the available data the chemicals are considered to be, at most, slightly irritating to eyes.

In a study conducted with deviations from OECD TG 405, NZW rabbits were administered 0.1 mL of the chemical (CAS No. 64741-44-2) in one eye. For 6 animals, eyes remained unflushed after treatment with the chemical, whereas 3 animals had their eyes flushed for one minute, at 20-30 minutes after administration of the chemical. Observations of test animals occurred at 1, 24, 48, 72 hours and 7 days post treatment. While the mean irritation scores over 24, 48 and 72 hours post treatment for corneal opacity, conjunctivae, and iris, were all reported as zero, slight conjunctival irritation was observed at 24 hours. However, this effect was fully reversible within 48 hours (REACHa).

In an eye irritation study conducted with deviations from OECD TG 405, male NZW rabbits (n=3) were dosed with 0.1 mL of the test chemical (CAS No. 64741-43-1) in one eye and observed for signs of irritation at 1, 24, 48, and 72 hours post treatment. Eyes were not washed after treatment. Individual animal scores were not reported; however, mean scores (over 24, 48 and 72 hours) for both corneal opacity and iris was zero. The mean conjunctivae score (not specified) was 0.67 (out of a maximum of 20), with full reversibility of this effect within 48 hours after treatment (REACHb).

Slight reversible eye irritation effects have been reported for gas oils produced by secondary processing (NICNAS 2019).

Sensitisation

Skin sensitisation

Based on the available data, the chemicals in this group are not expected to exhibit skin sensitising potential.

In a skin sensitisation study conducted with multiple deviations from OECD TG 406, male Hartley guinea pigs (n=10) were administered 0.4 mL of the chemical (CAS No. 64741-44-2) under occlusion 3 times for durations of 6 hours once a week for 3 weeks during the induction phase. Subsequently, the test animals were challenged once with the chemical at a concentration of 1% in paraffin oil under occlusion. One animal displayed a reaction to the challenge. All animals from the positive control group (n=20) administered 2,4-dinitrochlorobenzene displayed reactions (REACHa).

Gas oils produced by secondary processing were not skin sensitisers in the guinea pig Buehler test (NICNAS 2019).

Repeat dose toxicity

Oral

No data are available.

Dermal

Based on the available data chemicals in this group are not expected to produce significant systemic adverse effects after repeated dermal exposure but are expected to produce local adverse skin irritation effects after repeated dermal exposure.

The systemic toxicity of high boiling petroleum substances (HBPS), such as chemicals in this group, can be correlated with concentrations of PACs, particularly those composed of 3, 4, 5, 6 and/or 7 fused aromatic rings. However, other compositional characteristics could also influence toxicity (TERA 2008).

In a repeat dose dermal toxicity study conducted with deviations from OECD TG 410, SD rats (n=10/sex/dose) were dermally administered one chemical (CAS No. 64741-43-1) under occlusive conditions at 0, 0.01, 0.10 or 0.50 mL/kg bw/day, 5 days a week for 4 weeks (equivalent to 0, 9.2, 92 and 460 mg/kg bw/day, respectively). The only adverse treatment related effect reported was very slight to slight dermal irritation characterised by dry skin, erythema and/or eschar in 5 treated test animals; these effects were only noted in higher dose animals (≥0.1 mL/kg bw/day). A NOAEL for local skin irritation effects of 0.01 mL/kg bw/day was established, whereas a NOAEL for systemic adverse effects of 0.5 mL/kg bw/day (equivalent to 460 mg/kg bw/day) was established (API 2012b; REACHb)

Effects including increased liver and spleen weights, altered bone marrow function, and liver histopathology have been reported following dermal exposure to CAS No. 64741-44-2. Irritation at the application site in addition to systemic effects was observed in rats at 125 mg/kg bw/day. No further study details are available (CONCAWE 2020).

In general, gas oils produced from secondary processing (which contain higher levels of PAC) are not expected to cause damage to health from repeated dermal exposure. A number of 4 week studies showed slight to moderate skin irritation, but minimal systemic toxicity. Similar to other HBPS, treatment related effects including increased liver weights, reduced thymus weights, and changes in serum chemistry and haematological parameters were observed in 13 week studies (NICNAS 2019).

Inhalation

No data are available for the chemicals in this group and limited data are available for other gas oils.

Whilst microscopic changes in nasal tissue and subacute inflammation of the respiratory mucosa were observed in a 4 week study with a gas oil produced by secondary processing, no histopathological changes or effects on pulmonary function were noted in rats exposed up to 1500 mg/m^3 in a 13 week study with a diesel fuel (which is blended from various gas oils) (NICNAS 2019).

Genotoxicity

While the chemical with CAS No. 64741-44-2 predominantly yielded positive test results in vitro, especially with metabolic activation, the same chemical does not exhibit mutagenicity, specifically clastinogenicity, in vivo. For the remainder of the chemicals in this group, no in vivo studies were identified, and in vitro studies yielded negative results.

In vitro

These chemicals have been tested using the optimised Ames test (modified bacterial reverse mutation assay for complex aromatic hydrocarbon mixtures). Positive results were reported for the chemical with CAS No. 64741-44-2 in *Salmonella typhimurium* strain TA980 with metabolic activation only, at concentrations of 5–60 µL/plate. Negative results were reported for the remainder of the chemicals in the group. The following mutagenicity indices (MI) – defined as the slope of the curve of revertants per µL DMSO extract – were also reported:

- CAS No. 64741-44-2: 1.3
- CAS No. 64741-43-1: 0.15
- CAS No. 68915-96-8: 0.57
- CAS No. 68814-87-9: 0.04 and 0.8.

Petroleum substances containing >3% w/w DMSO extractables (as measured by the IP346 assay) are generally mutagenic in the optimised Ames test (API 2012b). Gas oils produced by secondary processing that contain higher levels of aromatics with ≥3 rings, induced higher mutagenicity indices in modified Ames tests (NICNAS 2019).

In a mammalian cell gene mutation assay (purportedly conducted according to OECD TG 476) in mouse lymphoma L5178Y cells, one chemical (CAS No. 64741-44-2) was tested at concentrations of 100−1000 nL/mL without metabolic activation, and 3.13−800 nL/mL with metabolic activation. The chemical was reported to be positive and induce mutations with metabolic activation and to be negative in the absence of metabolic activation (REACHa).

Positive results were reported in a mammalian cell gene mutation assay (purportedly conducted according to OECD TG 476) in mouse lymphoma L5178Y cells using one chemical (CAS NO. 64741-44-2) at concentrations of 0.042-0.56 µL/mL without metabolic activation and 0.012-0.16 µL/mL with metabolic activation. The chemical was reported to be positive and induce mutations with and without metabolic activation (REACHa).

In vivo

In a mammalian bone marrow chromosomal aberration study conducted with deviations from OECD TG 475, SD rats (5 animals/sex/dose/time point) were administered one chemical

(CASRN 64741-44-2) at 300, 1000 or 3000 mg/kg in a corn oil vehicle by intraperitoneal injection once. Bone marrow cells were harvested 6, 24 and 48 hours after administration of the chemical. The chemical was reports to be negative for clastogenicity under the conditions of the study as no statistically significant increase in the incidence of chromosome aberrations were reported in the treatment groups compared to the negative control group. No clinical signs of toxicity were reported during the study (REACHa).

In a mammalian bone marrow chromosomal aberration study conducted with deviations from OECD TG 475, SD rats (5/sex/dose/time point) were administered the same chemical (CAS No. 64741-44-2) at 500, 1700, 5000 mg/kg by intraperitoneal injection once. Bone marrow cells were harvested 6, 24 and 48 hours after administration of the chemical. The chemical was determined to be negative for clastogenicity under the conditions of the study as no statistically significant increase in the incidence of chromosome aberrations were reported in the treatment groups compared to the negative control group. No clinical signs of toxicity were reported during the study, except for distress in one male immediately after administration of the chemical at 1700 mg/kg but was reported to have recovered for the remainder of the study (REACHa).

Carcinogenicity

Prolonged exposure to straight run gas oil can result in the development of dermal tumours. Weak tumourigenic activity of straight run middle distillates (with low levels of PACs) is considered a likely consequence of a non-genotoxic process associated with frequent cell damage and repair; no significant increases in tumour incidences were reported under conditions that did not result in skin irritation effects (Nessel 1999). Petroleum substances containing <3% w/w DMSO extractable PACs (as measured by the IP346 assay) are also not considered to be carcinogenic to skin (IPIECA 2010).

While the level of PACs are expected to be relatively low for this group of chemicals, the available analytical data indicate that the reported aromatic content range (specifically for 3-7 aromatic rings) exceeds 3% for each of these chemicals (see **Grouping Rationale** section). Based on the available information, hazard classification is warranted. However, this classification need not apply if it can be shown that the substance contains less than 3% DMSO extract as measured by the IP346 assay.

In a carcinogenicity study not conducted according to OECD TGs, male C3H/HeJ mice (n=50) were dermally administered 50 μL of the chemical (CAS No. 64741-44-2) twice a week for 24 months. A negative solvent (toluene; methylbenzene) control group was used, and a positive control group was administered the chemical benzo-alpha-pyrene. The number of surviving animals (who were administered the chemical) at 18 months was significantly less than the solvent control and untreated groups. While reported observations included dehydration, tilting of the head, traumatic injury (not specified), and distention of the abdomen, these were not consistently observed and not considered to be specifically treatment related. More severe dermal lesions and skin irritation was noted in animals treated with the chemical compared to the solvent control group. Increased incidences of preputial gland swelling and penile prolapse were also reported in almost all male animals exposed to the chemical that were 2 years old or older. Non-neoplastic lesions were reported, including acanthosis, epidermal crusting and cysts, dermal vascularisation and fibrosis, hyperkeratosis, dermal or subcutaneous inflammation, dermal pigmentation and ulceration and abscess. Neoplastic lesions included benign fibromas, papillomas and haemangiomas, with malignant squamous cell carcinomas and fibrosarcomas also reported. The study determined the chemical to be a weak dermal carcinogen (REACHa).

In a carcinogenicity study not conducted according to OECD TGs, 50 male C3H/HeJ mice were dermally administered 25 μL of one chemical (CAS No. 64741-44-2) 3 times a week for the lifetime of the animal starting from 6−10 weeks of age. A negative control group was used and a positive control group (administered the chemical "catalytically cracked clarified oil") was also employed in the study. A statistically significant increase in skin tumour yield was reported; however, the study authors noted that 'non-neoplastic dermal changes including hyperplasia may have contributed to the tumourigenic response'. Signs of skin irritation and injury were also observed including hyperkeratosis, dermatitis and epidermal degeneration and necrosis (REACHa).

It is noted that the only studies available are for the chemical with CAS No. 64741-44-2, demonstrating potential carcinogenicity; this same chemical was reported to be genotoxic according to a modified Ames test, with an MI value of >1. A correlation between the mutagenicity index (MI) for petroleum fractions and dermal carcinogenic potential has been suggested (Roy et al., 1988): oils with MI values <1 are unlikely to be dermally carcinogenic; oils with MI values between 1 and 2 are considered indeterminate; and oils with MI values >2 are considered likely produce skin tumours if tested in mice (API 2012b).

Reproductive and development toxicity

Developmental effects, particularly the increased incidence of foetal fatality and resorption, are associated with aromatics containing 3 or more rings; other constituents of these substances (aliphatic constituents and 1- and 2 ring aromatics) do not make any significant contribution to the developmental toxicity of these substances (McKee et al., 2014). In general, the chemicals in this group contain low levels of PACs with 3–7 rings. Available analytical data indicate that the aromatic content can vary. However, given that effects are observed in the presence of maternal toxicity, the data do not meet the criteria for hazard classification. Whilst the chemicals have not been tested for reproductive toxicity, available data for other HBPS do not indicate that reproductive effects would be a more sensitive endpoint than developmental toxicity.

Certain petroleum stream chemicals have been shown to be developmentally toxic via dermal exposure. Effects include increased incidence of early and total resorptions and decreased foetal body weight (IPIECA 2010; Murray et al. 2013). Similar embryotoxic effects have been described in laboratory animals exposed to PACs such as benz[alpha]anthracene, benzo[alpha]pyrene, and naphthalene (IPCS 1998). Some effects have been observed in developmental toxicity studies with CAS No. 64741-43-1.

In a non-guideline reproductive toxicity study, female SD rats (15 animals/dose) were dermally administered one chemical (CAS No. 64741-43-1) at 1, 259, or 1036 mg/kg bw/day from 7 days prior to mating through to gestational day (GD) 20; a negative control group (n=20) was also included in the study. Reduced body weight, body weight gain, and food consumption as well as dermal irritation were observed in dams in the 259 and 1036 mg/kg bw/day groups. Females in the 1036 mg/kg bw/day group failed to deliver any live pups, while statistically significant decreases in the mean weight of pups at birth and lactation day 4 compared to controls were reported at doses of 259 mg/kg bw/day. No adverse effects were seen on mating capability, gestation length, delivery or number of implantation sites. A LOAEL of 259 mg/kg bw/day was determined for maternal toxicity on the basis of body weight, body weight gain, food consumption, vaginal discharge and dermal irritation. A LOAEL of 259 mg/kg bw/day was determined for developmental toxicity based on statistically significant decreases in mean pup weight at birth and lactation day 4 (API 2012b; REACHb).

In a developmental toxicity study purportedly conducted according to OECD TG 414, pregnant female Crl:CD BR VAF/plus rats (dams) (25 animals/dose) were administered the same chemical (CAS No. 64741-43-1) via dermal application in an acetone vehicle at 0, 50, 250, or 500 mg/kg bw/day from GD 0-19. The test material was reported to contain 8.7% 3-7 ring PAC. Skin irritation effects were reported in all treatment groups including effects such as erythema, oedema, atonia and desquamation. The acetone vehicle may confound some of the observed skin irritation effects due to its capacity to cause skin dryness and cracking following repeated exposure (NICNAS 2013). A maternal toxicity LOAEL of 50 mg/kg bw/day was established on the basis of skin irritation effects. Statistically significant reductions in body weight and food consumption were observed at 250 and 500 mg/kg bw/day, potentially indicating signs of systemic rather than local maternal toxicity at these doses. Adverse developmental effects in pups included statistically significant decreases in body weight and statistically significant increases in teratogenic effects such as eye malformations, non-dose related cleft palate and increased incidence of hydronephrosis in pups of dams at 250 and 500 mg/kg bw/day. Furthermore, statistically significant reductions in the number of live foetuses, average litter size, and statistically significant increases in the number of resorptions compared to controls were reported at doses of 250 and 500 mg/kg bw/day. The LOAEL for developmental toxicity is 250 mg/kg bw/day (API 2012b; REACHb).

In developmental toxicity study conducted similarly to OECD TG 414, pregnant SD rats (12–15 animals/dose) were dermally dosed with the same chemical (CAS No. 64741-43-1) at 0, 50, 150 or 500 mg/kg bw/day from GD 0–20. Indications of maternal toxicity included significant reductions in body weight and body weight gain at 500 mg/kg/day. A maternal toxicity LOAEL of 50 mg/kg bw/day was determined based on dermal irritation. Developmental toxicity in pups was reported in the 150 and 500 mg/kg bw/day groups, manifesting as significantly reduced pup body weight from lactation days 0 to 4 in both groups, and reduced pup survival on lactation day 4 at 500 mg/kg bw/day. A developmental toxicity LOAEL of 150 mg/kg bw/day was determined based on reduced pup weight (REACHb).

Other

The chemicals could have the potential to cause chemical pneumonitis if aspirated (Mckee et al., 2014). The viscosity depends on the carbon number range (API HPV Testing Group, 2012). The chemicals in this group could meet the criteria for classification for aspiration toxicity. The threshold kinematic viscosity value for classification as an aspiration hazard is 20.5 mm^2/s at 40°C (UNECE 2017).

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