Gasolines: Human health tier II assessment

13 February 2015

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Gasoline, natural	8006-61-9
Gasoline, natural gas, natural	68425-31-0
Gasoline, vapor recovery	68514-15-8
Gasoline, pyrolysis, debutanizer bottoms	68606-10-0
Gasoline, straight run, topping plant	68606-11-1
Gasoline	86290-81-5

Preface

This assessment was carried out by staff of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) using the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework.

The IMAP framework addresses the human health and environmental impacts of previously unassessed industrial chemicals listed on the Australian Inventory of Chemical Substances (the Inventory).

The framework was developed with significant input from stakeholders and provides a more rapid, flexible and transparent approach for the assessment of chemicals listed on the Inventory.

Stage One of the implementation of this framework, which lasted four years from 1 July 2012, examined 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This included chemicals for which NICNAS already held exposure information, chemicals identified as a concern or for which regulatory action had been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has three tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach using tabulated electronic data. The Tier II assessment is an evaluation of risk on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted and published separately, using information available at the time, and may be undertaken at different tiers.

This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

For more detail on this program please visit:**www.nicnas.gov.au**

Disclaimer

ACRONYMS & ABBREVIATIONS

Grouping Rationale

This chemicals in this group are described as follows.

Gasoline, natural (CAS No. 8006-61-9): also known as unleaded gasoline, is a complex combination of hydrocarbons separated from natural gas by processes such as refrigeration or absorption. It consists mainly of saturated aliphatic hydrocarbons with carbon numbers ranging between C4 and C8, and boiling between approximately -20 °C to 120 °C (US EPA, 2011 a; ChemID Plus).

Gasoline, natural gas, natural (CAS No. 68425-31-0): a complex combination of hydrocarbons separated as a liquid from natural gas liquids and/or natural gas condensates from which ethane, propane, butane and possibly pentane have been extracted. It consists of hydrocarbons with carbon numbers ranging mainly between C5 and C8. It is a liquid at atmospheric temperature and pressure (US EPA, 2011 a; ChemID Plus).

Gasoline, vapor recovery (CAS No. 68514-15-8): a complex combination of hydrocarbons separated from the gases from vapour recovery systems by cooling. It consists of hydrocarbons with carbon numbers ranging mainly between C4 and C11, and boiling approximately from -20 °C to 196 °C (US EPA, 2011 a; ChemID Plus).

Gasoline, pyrolysis, debutanizer bottoms (CAS No. 68606-10-0): a complex combination of hydrocarbons obtained from the fractionation of depropaniser bottoms. It consists of hydrocarbons with carbon numbers predominantly >C5 (US EPA, 2011 a; ChemID Plus).

Gasoline, straight run, topping plant (Cas No. 68606-11-1): a complex combination of hydrocarbons produced from the topping plant by crude oil (a side distillate coming directly from an atmospheric distillation column) and blended into gasoline product. It boils in the range of approximately 36.1 °C to 193.3 °C (Government of Canada, 2011; US EPA, 2011 a; ChemID Plus).

Gasoline (CAS No. 86290-81-5): a complex combination of hydrocarbons consisting primarily of paraffins, cycloparaffins, aromatic and olefinic hydrocarbons with carbon numbers predominantly >C3 and boiling in the range of 30 °C to 260 °C. In Europe, gasoline is sold under this CAS No. (US EPA, 2011 a; ChemID Plus).

The chemicals in this group are substances of unknown or variable composition, complex reaction products or biological materials (UVCBs) within the low boiling point petroleum naphtha (gasoline) category as defined by the CONservation of Clean Air and Water in Europe (CONCAWE). Gasoline, natural gas, natural (CAS No. 68425-31-0) was not listed by CONCAWE, but has been included in this group due to its similar use, carbon number ranges, and boiling point.

Gasoline is a refined product of petroleum consisting of a mixture of hydrocarbons, additives, and blending agents. The composition of gasolines varies and depends on the crude oils used, the refinery processes available, the overall balance of product demand, and the product specifications. Additives and blending agents are added to the hydrocarbon mixture to improve the performance and stability of gasoline. The typical composition of gasoline hydrocarbons (% volume) consists of 4–8 % alkanes; 2–5 % alkenes; 25–40 % isoalkanes; 3–7 % cycloalkanes; I–4 % cycloalkenes; and 20–50 % total aromatics (ATSDR).

It is expected that the following chemical classes, known as PONA chemicals, will be present as constituents in each chemical of the group:

- (P) normal and branched-chain paraffinic hydrocarbons,
- (O) olefinic hydrocarbons,
- (N) naphthenic hydrocarbons (cycloparaffins), and
- (A) aromatic hydrocarbons (mainly alkylbenzenes),

similar to the low boiling point petroleum naphthas (NICNAS).

The chemicals in this group may contain benzene (CAS No. 71-43-2), albeit at low concentrations compared with other low boiling point petroleum naphthas, at 0.5–2.5 % (US EPA, 2011 b; ATSDR). Automotive gasoline has a reported benzene content range: 0–7 %, or typically 2–3 % (IARC, 1989). Benzene has a number of hazardous properties (NICNAS, 2001). However, if data are available to indicate that the benzene content exceeds the relevant concentration cut offs for the hazardous properties of benzene, appropriate classifications will apply (NICNAS 2001; NICNAS).

Import, Manufacture and Use

Australian

Australian information is available for two chemicals in this category. Gasoline, natural (CAS No. 8006-61-9) and gasoline, pyrolysis, debutanizer bottoms (CAS No. 68606-10-0) have reported commercial use as fuels and are listed on the 2006 High Volume Industrial Chemicals List (HVICL) with a total reported volume of >1,000,000 tonnes and 10,000–99999 tonnes, respectively.

International

The following international uses have been identified through:

- the European Union (EU) Registration, Evaluation and Authorisation of Chemicals (REACH) dossiers;
- Galleria Chemica;
- the Substances and Preparations in the Nordic countries (SPIN) database;
- the United States (US) Environmental Protection Agency's Aggregated Computer Toxicology Resource (ACToR);
- the US National Library of Medicine's Hazardous Substances Data Bank (HSDB); and
- various international assessments (Government of Canada, 2011 & 2013; US EPA, 2011 a; ATSDR).

In general, the low boiling point petroleum naphtha (gasoline) category consists of petroleum refinery streams. Finished motor fuels also include additives that contain anti-oxidants, metal deactivators, lead scavengers, anti-rust agents, anti-icing agents, upper-cylinder lubricants, detergents and dyes. The end of the production process for motor fuel typically contains more than 150 separate compounds, although as many as 1,000 compounds have been identified in some blends (ATSDR; HSDB).

All chemicals in this group have reported commercial use as fuels, e.g. in internal combustion engines, lubricants and additives, and as fuel additives.

Gasoline (CAS No. 86290-81-5); gasoline, natural (CAS No. 8006-61-9); gasoline, natural gas, natural (CAS No. 68425-31-0); and gasoline, straight run, topping plant (CAS No. 68606-11-1) have reported site-limited uses as intermediates in petroleum refineries, as heat transferring agents and in oil and gas extraction.

Restrictions

Australian

The chemicals in the low boiling point petroleum naphtha category are listed in the *Poisons standard—the Standard for the uniform scheduling of medicines and poisons* (SUSMP) in Schedule 5 (SUSMP, 2014).

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 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.' Schedule 5 chemicals are labelled with 'Caution' (SUSMP, 2014).

For some compositions, the schedule entry for benzene may also be relevant. Benzene is listed in the *Poisons standard—the Standard for the uniform scheduling of medicines and poisons* (SUSMP) in Schedule 7 (SUSMP, 2014).

Schedule 7:

'BENZENE (excluding its derivatives) except:

(a) preparations containing 15 mL/L or less of benzene; or

(b) petrol containing 50 mL/L or less of benzene.'

Schedule 7 chemicals are described as 'Substances with a high potential for causing harm at low exposure and which require special precautions during manufacture, handling or use. These poisons should be available only to specialised or authorised users who have the skills necessary to handle them safely. Special regulations restricting their availability, possession, storage or use may apply.' Schedule 7 chemicals are labelled with 'Dangerous Poison' (SUSMP, 2014).

International

All of the chemicals, except for gasoline, natural gas, natural (CAS No. 68425-31-0) are listed on the EU Cosmetics Regulation 1223/2009 Annex II—List of substances prohibited in cosmetic products, if the chemicals contain >0.1 % (w/w) benzene (CosIng).

Existing Worker Health and Safety Controls

Hazard Classification

All of the chemicals in this group, except for gasoline, natural gas, natural (CAS No. 68425-31-0), are classified as hazardous with the following risk phrases for human health in the Hazardous Substances Information System (HSIS) (Safe Work Australia):

- Carc. Cat. 2; R45 (May cause cancer)
- Muta. Cat. 2; R46 (May cause heritable genetic damage)
- Xn; R65 (May cause lung damage if swallowed).

These classifications are subject to notes H and P.

'**Note H:** The classification and label shown for this substance applies to the dangerous property(ies) indicated by the Risk Phrase(s) in combination with the category(ies) of danger shown. The manufacturers, distributors and importers of this substance shall be obliged to carry out an investigation to make themselves aware of the relevant and accessible data which exists for all other properties to classify and label the substance' (Safe Work Australia).

'**Note P:** The classification as a carcinogen or mutagen need not apply if it can be shown that the substance contains less than 0.1% w/w benzene (EINECS no. 200-753-7). When the substance is classified as a carcinogen or mutagen, Note E shall also apply. When the substance is not classified as a carcinogen or mutagen, at least the Safety Phrases (2-)23-24-62 shall apply. This note applies only to certain complex oil-derived substances in Annex I' (Safe Work Australia).

'**Note E:** For substances ascribed Note E, the Risk Phrases R20, R21, R22, R23, R24, R25, R26, R27, R28 R39, R68 (harmful), R48 and R65 and all combinations of these Risk Phrases should be preceded by the word 'also''(Safe Work Australia).

Exposure Standards

Australian

No specific exposure standards are available for all of the chemicals in this group except for gasoline, natural (CAS No. 8006-61-9), which has an exposure standard of 900 mg/m^3 (300 ppm) (Galleria Chemica).

Additionally, benzene (CAS No. 71-43-2) has an exposure standard of 3.2 mg/m^3 (1 ppm) time weighted average (TWA) (Galleria Chemica).

International

No specific exposure standards are available for most of the chemicals in this group except for gasoline, natural (CAS No. 8006-61-9) and gasoline (CAS No. 86290-81-5). Exposure limits (TWA) of 100–900 mg/m^3 in different countries such as Canada, the USA, Latvia, Iceland, Netherlands and Germany were identified for these chemicals (Galleria Chemica).

Additionally, benzene has a number of exposure standards available internationally (Galleria Chemica).

Health Hazard Information

The chemicals in this group include a large number of individual components including linear and branched alkanes, and alkenes; and aromatic compounds. The aromatic compounds, in general, are more toxic than the aliphatic components. Of these, benzene (CAS No. 71-43-2) (NICNAS, 2001) has the highest toxicity (with reported concentrations of up to 7 % in gasoline) and also serves as a marker for the aromatic content of these UVCBs (refer to **Grouping rationale**).

Hazard information that represents all these group members is available for gasoline, natural (CAS No. 8006-61-9), gasoline, straight run, topping plant (CAS No. 68606-11-1), and gasoline (CAS No. 86290-81-5) (Government of Canada, 2011; US EPA, 2011 a; REACH).

Data from relevant unleaded PONA hydrocarbon mixtures (US EPA, 2011 a) and observations of gasoline exposure in humans (IARC, 1989; HSDB), will be used to infer the properties of these chemicals (read-across) where appropriate.

Human data on the toxicological effects through inhalation exposure from gasoline vapour may be limited due to the lack of data to distinguish these from the effects of the combustion products from gasoline (IARC, 1989).

It should also be noted that in the US, gasoline (including unleaded and leaded gasoline) is not sold under a single CAS number due to the fuel product consisting of a physical blend of numerous petroleum naphtha streams, and thus are identified by their PONA composition, e.g. unleaded gasoline (no CAS No.): paraffins (P): 57.8 % (v/v); olefins (O): 9.9 %; naphthas (N): 3.9 % and aromatics (A): 28.1 % (US EPA, 2011a). Historically on the Australian Inventory of Chemicals (AICS), companies considered unleaded gasoline to be under gasoline, natural (CAS No. 8006-61-9) until gasoline (CAS No. 86290-81-5) was included in AICS in August 2008 (NICNAS, 2008). This indicates that the distinction between the different CAS numbers can, in practice, be difficult.

Acute Toxicity

Oral

The chemicals have low oral toxicity based on results from animal tests, and moderate oral toxicity based on human observation data (refer to **Acute toxicity: Observation in humans** section). The available data from animal and human observation studies support the overall classification.

The median lethal doses (LD50s) in Sprague Dawley (SD) rats for CAS Nos. 8006-61-9, 68606-11-1, 86290-81-5, and unleaded gasoline [no CAS No.; P: 57.8 % (v/v); O: 9.9 %; N: 3.9 % A: 28.1 %] were reported to be >2000 mg/kg bw (Government of Canada, 2011; US EPA, 2011 a; REACH).

Dermal

The chemicals have low acute dermal toxicity based on results from animal tests with LD50s in New Zealand White rabbits for CAS Nos. 8006-61-9, 68606-11-1, 86290-81-5, and unleaded gasoline [no CAS No.; P: 57.8 % (v/v); O: 9.9 %; N: 3.9 % A: 28.1 %] reported to be >2000 mg/kg bw (Government of Canada, 2011; US EPA, 2011 a; HSDB; REACH).

Inhalation

The chemicals have low inhalation toxicity based on results from animal tests and human observation data (refer to **Acute toxicity: observation in humans** section).

The median lethal concentrations (LC50s) in SD rats for CAS Nos. 8006-61-9, 68606-11-1, and 86290-81-5 were >5610 mg/m^3 (REACH).

Although human data indicate moderate acute toxicity from inhalation exposure to some of the chemicals in this group, a hazard classification is not warranted for the chemicals in this group since data are insufficient to distinguish the effects of the combustion products from the chemicals (IARC, 1989).

Observation in humans

In humans, ingesting 10–15 g of gasoline, natural (CAS No. 8006-61-9) has been reported to be lethal in children. Another case report noted that ingesting 20–50 g of the chemical may produce symptoms of poisoning, including immediate severe burning of the pharynx and gastric region (HSDB).

It has been reported that intentional or accidental gasoline ingestion often results in the chemical being aspirated into the lungs (due to its high volatility and low surface tension). Thus the most common effect associated with acute gasoline ingestion in humans is aspiration pneumonia, which is associated with respiratory distress, pulmonary oedema, emphysema, and focal alveolar haemorrhage. Death is most likely to result from asphyxia when aspiration pneumonia becomes severe (HSDB).

Several human volunteer studies report low acute inhalation toxicity. Male volunteers exposed to vapours of gasoline, natural (CAS No. 8006-61-9) at nominal concentrations of 200, 500, and 1000 ppm (approximately 960, 2400, and 4800 mg/m^3) over a 30 minute period did not experience systemic effects. However, eye irritation was reported, but was not determined to be dose-dependent even at the highest concentration (REACH).

In another study, human subjects were exposed to vapours of gasoline, natural (CAS No. 8006-61-9), as whole commercial gasoline and gasoline distillate in increasing concentrations (672–53725 mg/m^3) and exposure periods (<10 minutes to eight hours) wherein central nervous system (CNS) effects were monitored. It was reported that increased CNS effects were dose dependent as a function of exposure duration. At 12480 mg/m^3 (within an hour of exposure) and at the highest dose of 53725 mg/m^3 (within five minutes of exposure), the acute symptoms reported included slight dizziness, nausea, headache and intoxication (IARC, 1989; HSDB; REACH).

One-hour inhalation acute exposure to the vapour of gasoline, natural (CAS No. 8006-61-9) at 2000 ppm (approximately 7.6 mg/L) caused dizziness, mucous membrane irritation and anaesthesia (refer to **Irritation: Observation in humans**).

However, other human data indicate that inhalation exposure to gasoline vapour at doses of ≥5000 ppm, (20000 ppm for five minutes) can be lethal. The cause of mortality has been reported to be unclear, although the inhalation of high concentrations of the chemical can lead to asphyxia, leading to respiratory failure and fatal arrhythmia (HSDB).

Corrosion / Irritation

Corrosivity

No data are available.

Respiratory Irritation

No data are available for the chemicals. Human observation data indicate the chemicals in this group could be potential respiratory irritants at high concentrations (refer to **Irritation: Observation in humans** section).

Skin Irritation

The chemicals in this group are shown to have low to moderate skin irritation effects in animal studies and from human observation data (refer to **Irritation: Observation in humans** section).

CAS Nos. 8006-61-9, 68606-11-1, 86290-81-5, and unleaded gasoline [no CAS No.; P: 57.8 % (v/v); O: 9.9 %; N: 3.9 % A: 28.1 %] were found to be slightly irritating to the skin of New Zealand White rabbits (Government of Canada, 2011; US EPA, 2011a; REACH).

The component chemical, benzene (CAS No. 71-43-2), is classified as hazardous with the risk phrase 'Irritating to skin' (R38) with a concentration cut-off of ≥5 % (Safe Work Australia). While benzene vapour levels >60 ppm have been associated with skin irritation, including second degree burns, in humans (NICNAS, 2001), the low concentration of benzene in the gasolines category, up to 7 % (IARC, 1989; ATSDR), is expected to generally be below the classification for this endpoint (refer to **Recommendation** section).

Eye Irritation

The chemicals were found to have low eye irritation potential in rabbits. However, moderate to severe eye irritation at high concentrations (dose dependent) based on human observation data was reported (refer to **Irritation: Observation in humans** section).

CAS Nos. 8006-61-9, 68606-11-1, 86290-81-5, and unleaded gasoline [no CAS No.; P: 57.8 % (v/v); O: 9.9 %; N: 3.9 % A: 28.1 %] are not irritating to the eyes of New Zealand White rabbits (Government of Canada, 2011; US EPA, 2011a; HSDB; REACH).

The component chemical, benzene (CAS No. 71-43-2), is classified as hazardous with the risk phrase 'Irritant: Irritating to eyes' (R36) with a concentration cut-off of ≥5 % (Safe Work Australia). While benzene vapours have been reported to cause eye irritation in humans and rats at concentrations of ≥33 and ≥10 ppm, respectively (NICNAS, 2001), the low concentration of benzene in the gasolines category, up to 7 % (IARC, 1989; ATSDR), is expected to generally be below the classification for this endpoint (refer to **Recommendation** section).

Observation in humans

The chemical gasoline, natural (CAS No. 8006-61-9) is reported to be irritating in vapour or liquid form to human skin, the eyes (conjunctiva) and respiratory tract (mucous membranes) following inhalation exposure (HSDB).

Human volunteers exposed to the vapours of gasoline, natural (CAS No. 8006-61-9) reported no ocular irritation at 140 ppm, but irritation of the eyes and throat were reported at the 270 and 900 ppm. Reported signs of eye irritation included conjunctival hyperaemia (ATSDR; HSDB).

In another human exposure study, eye irritation was reported in volunteers exposed for 30 minutes to gasoline vapours at concentrations of approximately 200, 500 and 1000 pm; the highest concentrations caused the most severe effects (IARC, 1989; HSDB).

Gasoline vapours are reported to cause eye and throat irritation after exposure for several hours (at 160–270 ppm); eye, nose and throat irritation, and dizziness after one hour (at 500–900 ppm); and mild CNS effects within 30 minutes of exposure (at 2000 ppm). Higher concentrations are intoxicating within 4–10 minutes. The threshold for immediate mild toxic effect is 900–1000 ppm (refer to **Acute toxicity: Observation in humans**) (HSDB).

Sensitisation

Respiratory Sensitisation

No data are available.

Skin Sensitisation

The chemicals in this group were not found to induce dermal sensitisation when tested in guinea pigs in various skin sensitisation studies. CAS Nos. 8006-61-9, 68606-11-1, 86290-81-5, and unleaded gasoline [No CAS No.; P: 57.8 % (v/v); O: 9.9 %; N: 3.9 % A: 28.1 %] were found to be non-sensitising to guinea pig skin in the reported studies (Government of Canada, 2011; US EPA, 2011 a; REACH).

Repeated Dose Toxicity

Oral

No data are available for the chemicals in this group.

The component chemical benzene (CAS No. 71-43-2), is classified as hazardous with the risk phrase 'Toxic: Danger of serious damage to health by prolonged exposure by inhalation, in contact with skin and if swallowed' (R48/23/24/25) (Safe Work Australia). Reported concentrations of benzene in the gasolines category of up to 7 % (IARC, 1989; ATSDR), may be within the classification range for this endpoint. Therefore, classification for repeated dose toxicity could be warranted under some circumstances for the chemicals in this group (refer to **Recommendation** section).

Dermal

CAS Nos. 8006-61-9 and 86290-81-5 were applied to the clipped skin of the back of male and female C3H/HeJ mice (15/sex) at a dose of 1000 mg/kg bw/day, twice weekly for an exposure period of 12 months. No systemic effects, except for a non-significant increase in skin tumour incidence (in one female), were reported (Government of Canada, 2011).

In a combined repeated dose and carcinogenicity study, it was reported that unleaded gasoline (unspecified) that was dermally applied to the skin of 50 Swiss mice three times a week for two years did not induce chronic dermal toxicity. Reported symptoms of local toxicity include hyperkeratosis, fibrosis of the dermis, skin ulceration in the treatment areas. However, the incidence of skin carcinomas, liver haemangiomas, lung adenomas, and malignant lymphomas was no greater than the control group (REACH).

The component chemical, benzene (CAS No. 71-43-2), is classified as hazardous with the risk phrase 'Toxic: Danger of serious damage to health by prolonged exposure by inhalation, in contact with skin and if swallowed' (R48/23/24/25) (Safe Work Australia). Reported concentrations of benzene in the gasolines category of up to 7 % (IARC, 1989; ATSDR), may be within the classification range for this endpoint. Therefore, classification for repeated dose toxicity could be warranted under some circumstances for the chemicals in this group (refer to **Recommendation** section).

Inhalation

In general, minimal systemic effects have been observed in SD rats following 90-day and 13-week whole body inhalation exposures to gasoline, natural (CAS No. 8006-61-9), unleaded gasoline blend [No CAS No.; P + N: 45 % (units unspecified); O: 12 %; A: 43 %], and unleaded gasoline blend [No CAS No.; P: 77.4 % (v/v); O: 15.2 %; N: 3.3 % A: 4.2 %]. The no observed adverse effect concentrations (NOAECs) reported in these studies were 14.7–20.3 mg/L (Government of Canada, 2011; US EPA, 2011 a; HSDB). Dose-dependent systemic effects included renal effects (renal lesions such as irreversible tubular dilation and hyaline droplet formation in males only) and haematological changes.

The component chemical, benzene (CAS No. 71-43-2), is classified as hazardous with the risk phrase 'Toxic: Danger of serious damage to health by prolonged exposure by inhalation, in contact with skin and if swallowed' (R48/23/24/25) (Safe Work Australia). This classification is based on bone marrow depression observed with repeated occupational exposure to benzene vapours at ≥7.6 ppm (0.024 mg/L) (NICNAS, 2001). Reported concentrations of benzene in the gasolines category of up to 7 % (IARC, 1989; ATSDR), may be within the classification range for this endpoint. Therefore, classification for repeated dose toxicity could be warranted under some circumstances for the chemicals in this group (refer to **Recommendation** section).

Observation in humans

Human data include reported chronic dermal contact that could result in drying of the skin and lesion formation. Chronic inhalation at a dose >500 ppm (approximately 1.8 mg/L/day) caused symptoms that included vomiting, diarrhoea, insomnia, headache, dizziness, anaemia, and muscle and neurological symptoms (HSDB).

Genotoxicity

The majority of the chemicals are classified as hazardous—Category 2 mutagenic substance—with the risk phrase ‘May cause heritable genetic damage’ (T; R46) in the HSIS (Safe Work Australia). This classification need not apply if it can be shown that the chemical contains less than 0.1 % w/w benzene. The available data support the overall classification, including the lack of classification for low benzene formulations.

Several in vitro assays for some of the chemicals gave negative results (Government of Canada, 2011 & 2013; US EPA, 2011 a; HSDB; REACH) from the following:

- bacterial mutation assays (various *Salmonella typhimurium* strains) in the absence and presence of metabolic activation for CAS Nos. 8006-61-9 and unleaded gasoline (No CAS No.; PONA composition unspecified); and
- chromosomal aberrations in mouse lymphoma assays with and without metabolic activation [doses up to 1.04 µg/mL for unleaded gasoline (No CAS No.; PONA composition unspecified)].

The chemicals gave largely negative results in several in vivo genotoxicity assays which included the following:

- positive results for induction of sister chromatid exchange in SD, Crl:CD, IGS and BR rats [inhalation exposure to unleaded gasoline (no CAS No.; PONA composition unspecified)];
- positive results for induction of sister chromatid exchange in SD rats [inhalation exposure to unleaded gasoline (no CAS No.; P: 48.7 % (v/v); O: 9.0 %; N: 6.3 % A: 36.0 %)];
- negative results for the induction of bone marrow chromosomal aberrations in SD rats [intraperitoneal (i.p.) injection of unleaded gasoline (no CAS No.; P: 57.8 % (v/v); O: 9.9 %; N: 3.9 % A: 28.1 %)];
- negative results for the induction of bone marrow chromosomal aberrations in CD-1 mice [inhalation exposure of unleaded gasoline (no CAS No.; P: 57.8% (v/v); O: 9.9 %; N: 3.9 % A: 28.1 %)]; and
- negative results for micronuclei induction in SD, Crl:CD, IGS and BR rats [inhalation exposure to unleaded gasoline (no CAS No.; P: 48.7 % (v/v); O: 9.0 %; N: 6.3 % A: 36.0 %)].

The component chemical, benzene, is classified as hazardous—Category 2 mutagenic substance—with the risk phrase ‘May cause heritable genetic damage’ (T; R46) in the HSIS (Safe Work Australia). Reported concentrations of benzene in the gasolines category of up to 7 % (IARC, 1989; ATSDR), may be within the classification range for this endpoint. Therefore, classification for repeated dose toxicity could be warranted under some circumstances for the chemicals in this group (refer to **Recommendation** section).

Carcinogenicity

The majority of the chemicals are classified as hazardous—Category 2 carcinogenic substance—with the risk phrase ‘May cause cancer’ (T; R45) in the HSIS (Safe Work Australia). This classification need not apply if it can be shown that the chemical contains less than 0.1 % w/w benzene. The available data from animal and human observation studies support the overall classification.

Several inhalation studies reported the carcinogenic potential of unleaded gasoline with a 2 % benzene content in animals (Government of Canada, 2011). The chemicals gasoline, natural (CAS No. 8006-61-9) and gasoline [no CAS No.; P: 57.8 % (v/v); O: 9.9 %; N: 3.9 % A: 28.1 %], were carcinogenic in Fischer 344 rats and B6C3F1 mice on inhaling vapour at concentrations of 50, 275 or 1500 ppm (approximately 0, 0.2, 1.1 or 5.9 mg/L). The two studies reported an increased incidence of renal and hepatocellular carcinomas, sarcomas and adenomas (Government of Canada, 2011; US EPA, 2011 a; HSDB).

Studies in C3H/HeJ and Swiss-Webster mice exposed dermally to 0.05 mL of gasoline [no CAS No.; P: 57.8 % (v/v); O: 9.9 %; N: 3.9 % A: 28.1 %], twice a week for 131 weeks, or 0.05 mL of gasoline (CAS No. 86290-81-5), twice a week for two years, reported no treatment-related effects in the incidence of systemic or dermal tumours (Government of Canada, 2011; US EPA, 2011 a; REACH).

The component chemical, benzene, is classified as hazardous—Category 1 carcinogenic substance—with the risk phrase ‘May cause cancer’ (T; R45) in the HSIS (Safe Work Australia). Reported concentrations of benzene in the gasolines category of up to 7 % (IARC, 1989; ATSDR), may be within the classification range for this endpoint. Therefore, classification for repeated dose toxicity could be warranted under some circumstances for the chemicals in this group (refer to **Recommendation** section).

Observation in humans

Occupational exposure to gasoline, natural (CAS No. 8006-61-9) has been reported in occupations such as service station attendants and motor vehicle mechanics. However, detailed data are not available to distinguish the effects of the combustion products from gasoline, thus there is limited evidence of carcinogenicity in humans (IARC, 1989).

A cohort study reported the mortality rates of cancer associated with occupational gasoline exposure to oil distribution workers were below national rates, but there were slightly elevated number of deaths from neoplasms of the lymphatic and haematopoietic tissues. Another cohort study reported a moderately increased incidence of pancreatic cancer among service station workers (IARC, 1989).

US and Swedish mortality studies reported dose-dependent elevated risks for some types of lymphopoietic and testicular cancers in motor vehicle mechanics; and leukaemia, aleukaemia (acute leukaemia), liver tumours (hepatocellular carcinoma), stomach and kidney cancer in service station workers or garage workers (IARC, 1989).

In several US and Danish case studies on cancer in the lower urinary tract, it was reported that there were possibly increased risks of bladder cancer from occupational exposure associated with the oil and gasoline industries (IARC, 1989).

In one case-control study, an increase in the risk for leukaemia in the offspring of pregnant women exposed to hydrocarbons (not specifically of gasoline) during pregnancy was reported. However paternal exposure was not well characterised as there was no consistent link between paternal occupation and risk for childhood cancer (IARC, 1989).

The International Agency for Research on Cancer (IARC) has classified gasoline (CAS No. 8006-61-9) as 'Possibly carcinogenic to humans (Group 2B)' based on inadequate evidence in humans and limited evidence in animals (IARC, 1989).

Reproductive and Developmental Toxicity

The chemicals in this group are not expected to be reproductive or developmental toxins.

In two-generation reproductive studies, SD rats exposed by inhalation to gasoline, natural (CAS No. 8006-61-9), unleaded gasoline [no CAS No.; P: 48.7 % (v/v); O: 9.0 %; N: 6.3 % A: 36.0 %], and CAS Nos. 68606-11-1 and 86290-81-5, showed no treatment-related adverse effects on reproductive parameters at doses up to 20 mg/L (US EPA, 2011 a; REACH).

Several developmental studies on SD rats that were exposed by inhalation to gasoline, natural (CAS No. 8006-61-9), unleaded gasoline [no CAS No.; P: 48.7 % (v/v); O: 9.0 %; N: 6.3 % A: 36.0 %], and CAS Nos. 68606-11-1 and 86290-81-5, showed no treatment-related adverse effects on developmental parameters at doses up to 20 mg/L (US EPA, 2011 a; REACH).

Other Health Effects

Neurotoxicity

Several neurotoxicity studies reported that SD rats exposed to vapours of the chemical identified as unleaded gasoline [no CAS No.; P: 77.4 % (v/v); O: 15.2 %; N: 3.3 % A: 4.2 %] through inhalation did not show treatment-related adverse effects. However human data from several case studies indicate that unleaded gasoline causes transient CNS effects (US EPA, 2011 a; REACH).

Risk Characterisation

Critical Health Effects

The critical health effects of the chemicals are dependent on the composition of benzene. Effects include systemic long-term effects (carcinogenicity and mutagenicity) and systemic acute effects (potential acute toxicity from inhalation exposure, skin and eye irritation) and potential respiratory irritation. The chemicals could also cause harmful effects following repeated oral, dermal and inhalation exposure. Components other than benzene are associated with a range of hazardous properties. However, exposure to chemicals is expected to be very limited, and so only the most severe effect will contribute to the likely risk.

Public Risk Characterisation

Apart from the hazards that are due to individual constituents, the chemicals in this group are all aspiration hazards and CNS depressants, so the public will be exposed to small amounts of vapour while refuelling cars. The risks from exposure to the chemical is dependent on benzene content, which is low in these chemicals. The *Poison standard* includes hydrocarbon solvents containing benzene at 15 mL/L or greater in Schedule 7; these should not be available to the public (refer to **Restrictions: Australian** section). Therefore, the public risk from these chemicals are not considered to be unreasonable.

There is limited general population exposure to unintentional releases of the gasoline blending constituents in the vicinity of petroleum refineries. These releases are likely to contribute to ambient background levels of hazardous components such as benzene. However, industrial emissions of benzene are not considered a significant source of public exposure (NICNAS, 2001).

Companies introducing and processing the chemicals are likely to implement control measures to reduce fugitive emissions on site as a consequence of occupational and environmental legislative requirements, such as licence conditions and occupational exposure standards. Based on data reported to the National Pollutant Inventory (NPI) for Australian refineries, fugitive emissions of volatile organic compounds have generally reduced over recent years (NPI).

Occupational Risk Characterisation

The chemicals in this group have widespread use, and occupational exposure, particularly to vapours, will be of concern. Exposed workers will mostly be those involved in gasoline distribution and sale.

Given the critical systemic acute and chronic health effects, the chemicals could pose an unreasonable risk to workers unless adequate control measures to minimise oral, dermal, ocular and inhalation exposure are implemented. The chemicals should be appropriately classified and labelled to ensure that a person conducting a business or undertaking (PCBU) at a workplace (such as an employer) has adequate information to determine the appropriate controls.

Air monitoring should include benzene.

The data available support an amendment to the hazard classification in the HSIS (refer to **Recommendation** section).

NICNAS Recommendation

Assessment of these chemicals is considered to be sufficient, provided that the recommended amendments to the classification are adopted, and labelling and all other requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory.

introducing or processing the chemicals should continually seek to reduce fugitive emissions as far as reasonably practicable.

Regulatory Control

Work Health and Safety

Although the chemicals are classified as UVCBs, the producers of these chemicals may have constituent profiles and compositions for each chemical in the group. If this is the case, then the hazards of the UVCBs and the relevant classification(s) should be determined based on the application of mixture rules.

The chemicals are recommended for classification and labelling under the current Approved Criteria and adopted GHS as below. This assessment does not consider classification of physical and environmental hazards.

For skin and eye irritation, and chronic health effects, the classification will be dependent on the concentration of benzene as follows.

Irritation/Corrosivity

In the absence of specific test data for chemicals in this group with high benzene content, the classification should be determined based on the levels of benzene.

Repeated dose toxicity

In the absence of specific test data, the classification should be determined based on the levels of benzene.

Genotoxicity

In the absence of specific test data, the classification should be determined based on the levels of benzene.

Carcinogenicity

In the absence of specific test data, the classification should be determined based on the levels of benzene.

The classification criteria for mixtures (GHS, 2009; Safe Work Australia, 2004 should be applied to benzene, based on its concentration in these UVCB substances. The classifications depend on benzene content, except for the aspiration hazard (R65) and CNS depression (R67). The classifications below represent the highest possible classifications for each endpoint under these rules. Should empirical data become available for any member of the group indication that a lower (or higher) classification is appropriate for the specific chemical, this may be used to amend the default classification for that chemical.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Harmful: may cause lung damage if swallowed (Xn; R65)*	May be fatal if swallowed and enters airways - Aspi. Cat. 1 (H304)
Irritation / Corrosivity	Irritating to eyes (Xi; R36) Irritating to skin (Xi; R38)	Causes serious eye irritation - Cat. 2A (H319) Causes skin irritation - Cat. 2 (H315)
Repeat Dose Toxicity	Toxic: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed (T; R48/23/24/25)	Causes damage to organs through prolonged or repeated exposure - Cat. 1 (H372)
Genotoxicity	Muta. Cat 2 - May cause heritable genetic damage (T; R46)*	May cause genetic defects - Cat. 1B (H340)
Carcinogenicity	Carc. Cat 2 - May cause cancer (T; R45)*	May cause cancer - Cat. 1B (H350)
Other Health Effects	Vapours may cause drowsiness and dizziness (R67)	May cause drowsiness or dizziness - Specific target organ tox, single exp Cat. 3 (H336)

[a] Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2004)].

[b] Globally Harmonized System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third Edition.

[*] Existing Hazard Classification. No change recommended to this classification

Advice for industry

Control measures

Control measures to minimise the risk from oral, dermal, ocular and inhalation exposure to the chemicals should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate, or minimise risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemicals are used. Examples of control measures which could minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- using local exhaust ventilation to prevent the chemicals from entering the breathing zone of any worker;
- health monitoring for any worker who is at risk of exposure to the chemicals, if valid techniques are available to monitor the effect on the worker's health;
- air monitoring to ensure control measures in place are working effectively and continue to do so;
- minimising manual processes and work tasks through automating processes;
- work procedures that minimise splashes and spills;
- regularly cleaning equipment and work areas; and
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemicals.

Guidance on managing risks from hazardous chemicals are provided in the *Managing risks of hazardous chemicals in the workplace—Code of practice* available on the Safe Work Australia website.

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. Guidance in selecting personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

Obligations under workplace health and safety legislation

Information in this report should be taken into account to help meet obligations under workplace health and safety legislation as adopted by the relevant state or territory. This includes, but is not limited to:

- ensuring that hazardous chemicals are correctly classified and labelled;
- ensuring that (material) safety data sheets ((M)SDS) containing accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of the chemicals are prepared; and
- managing risks arising from storing, handling and using a hazardous chemical.

Your work health and safety regulator should be contacted for information on the work health and safety laws in your jurisdiction.

Information on how to prepare an (M)SDS and how to label containers of hazardous chemicals are provided in relevant codes of practice such as the *Preparation of safety data sheets for hazardous chemicals—Code of practice* and *Labelling of workplace hazardous chemicals—Code of practice*, respectively. These codes of practice are available from the Safe Work Australia website.

A review of the physical hazards of these chemicals has not been undertaken as part of this assessment.

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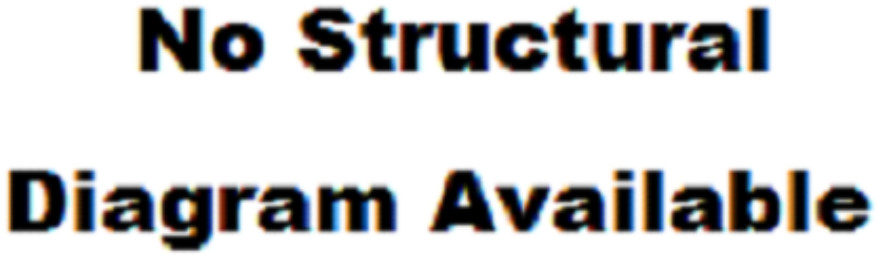
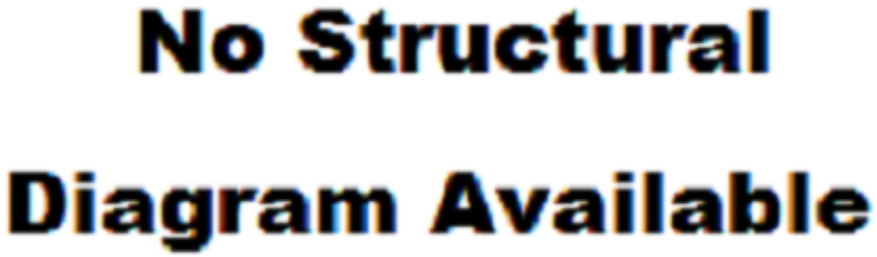
Last Update 13 February 2015

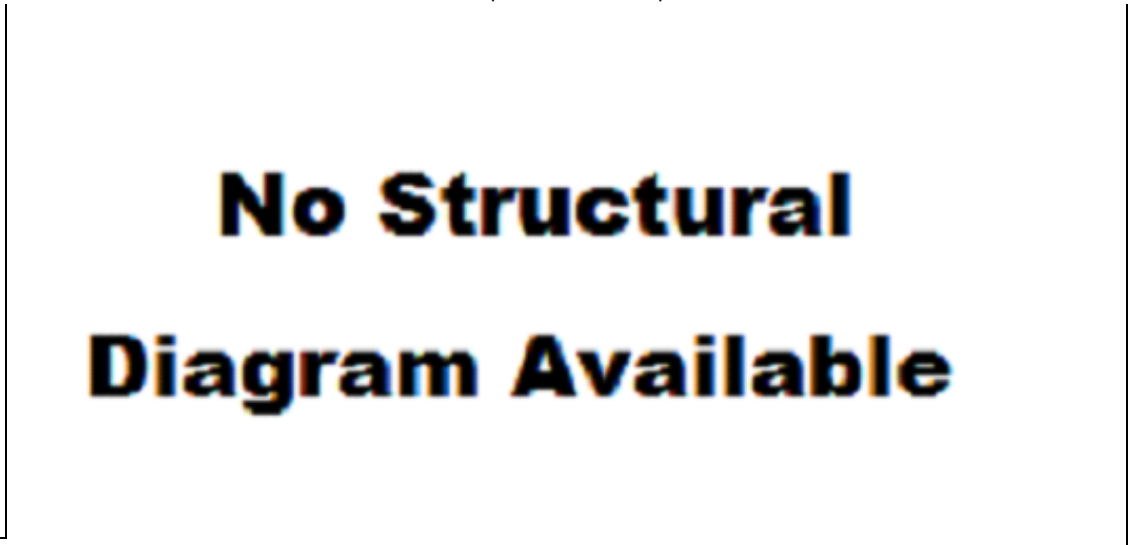
Chemical Identities

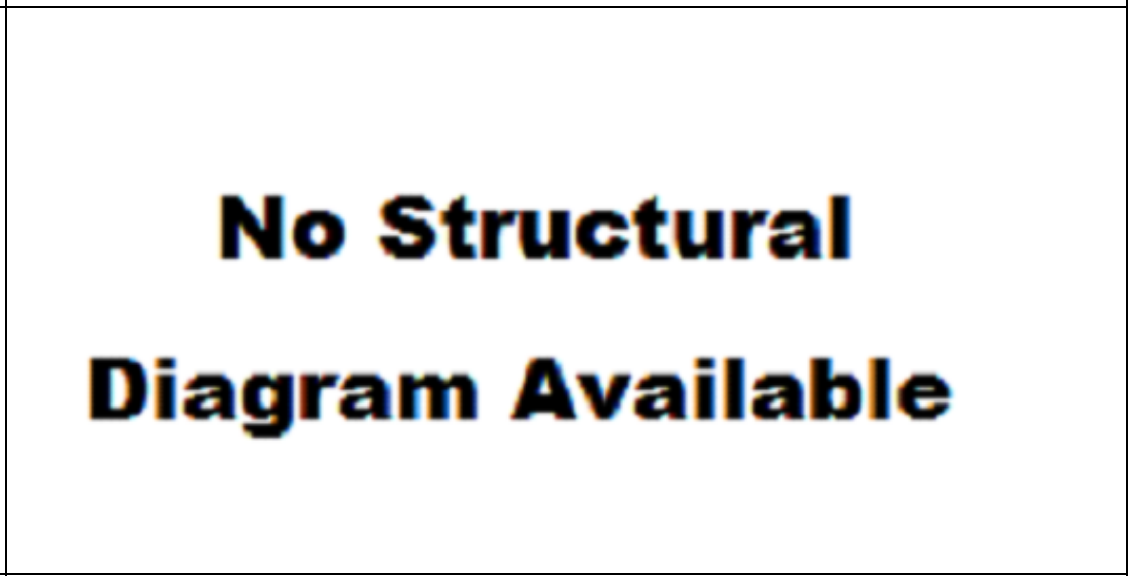
Chemical Name in the Inventory and Synonyms	**Gasoline, natural** light gasoline cracked gasoline white gasoline polymer gasoline automobile regular unleaded gasoline
CAS Number	8006-61-9

Structural Formula	
Molecular Formula	Unspecified
Molecular Weight	N/A

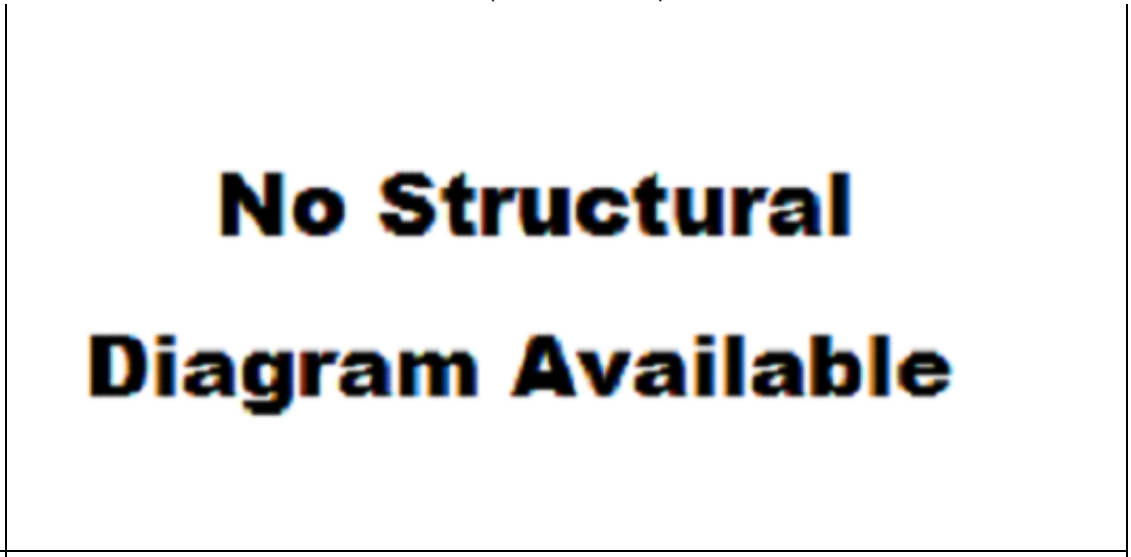
Chemical Name in the Inventory and Synonyms	**Gasoline, natural gas, natural** natural gasoline, natural gas ethyl silicate, partially hydrolyzed
CAS Number	68425-31-0
Structural Formula	
Molecular Formula	Unspecified
Molecular Weight	N/A

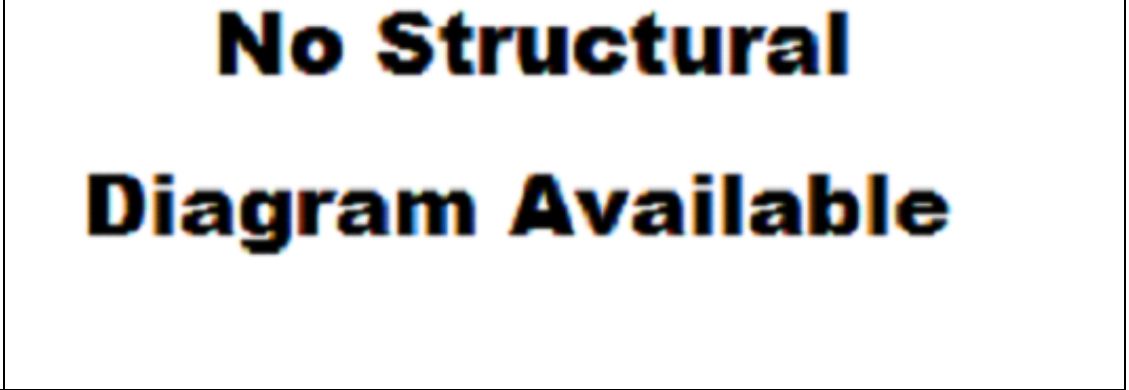
Chemical Name in the Inventory and Synonyms	**Gasoline, vapor recovery** recovered gasoline vapor recovery gasoline
CAS Number	68514-15-8
Structural Formula	

	
Molecular Formula	Unspecified
Molecular Weight	N/A

Chemical Name in the Inventory and Synonyms	**Gasoline, pyrolysis, debutanizer bottoms** pyrolysis gasoline pentane aromatics debutanizer bottoms pyrolysis gasoline
CAS Number	68606-10-0
Structural Formula	
Molecular Formula	Unspecified
Molecular Weight	N/A

Chemical Name in the Inventory and Synonyms	**Gasoline, straight run, topping plant** raw, straight run gasoline topping plant straight run gasoline
CAS Number	68606-11-1
Structural Formula	

	
Molecular Formula	Unspecified
Molecular Weight	N/A

Chemical Name in the Inventory and Synonyms	**Gasoline** motor fuel petrol motor spirits natural gasoline automotive gasoline
CAS Number	86290-81-5
Structural Formula	
Molecular Formula	Unspecified
Molecular Weight	N/A

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