# Screening Assessment
# Petroleum Sector Stream Approach

## Low Boiling Point Naphthas
[Site-restricted]

**Chemical Abstracts Service Registry Numbers**

*64741-54-4*
*64741-55-5*
*64741-64-6*
*64741-74-8*
*64742-22-9*
*64742-23-0*
*64742-73-0*
*68410-05-9*
*68410-71-9*
*68410-96-8*
*68476-46-0*
*68477-89-4*
*68478-12-6*
*68513-02-0*
*68514-79-4*
*68606-11-1*
*68783-12-0*
*68919-37-9*
*68955-35-1*
*101795-01-1*

**Environment Canada**
**Health Canada**

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## Synopsis

Pursuant to section 74 of the *Canadian Environmental Protection Act, 1999* (CEPA 1999), the Ministers of the Environment and of Health have conducted a screening assessment of the following site-restricted low boiling point naphthas (LBPNs):

| CAS RN[a] | DSL Name[b] |
|---|---|
| 64741-54-4 | Naphtha (petroleum), heavy catalytic cracked |
| 64741-55-5 | Naphtha (petroleum), light catalytic cracked |
| 64741-64-6 | Naphtha (petroleum), full-range alkylate |
| 64741-74-8 | Naphtha (petroleum), light thermal cracked |
| 64742-22-9 | Naphtha (petroleum), chemically neutralized heavy |
| 64742-23-0 | Naphtha (petroleum), chemically neutralized light |
| 64742-73-0 | Naphtha (petroleum), hydrodesulfurized light |
| 68410-05-9 | Distillates (petroleum), straight-run light |
| 68410-71-9 | Raffinates (petroleum), catalytic reformer ethylene glycol-water countercurrent exts |
| 68410-96-8 | Distillates (petroleum), hydrotreated middle, intermediate boiling |
| 68476-46-0 | Hydrocarbons, C3-11, catalytic cracker distillates |
| 68477-89-4 | Distillates (petroleum), dependanizer overheads |
| 68478-12-6 | Residues (petroleum), butane splitter bottoms |
| 68513-02-0 | Naphtha (petroleum), full-range coker |
| 68514-79-4 | Petroleum products, hydrofiner-powerformer reformates |
| 68606-11-1 | Gasoline, straight-run, topping-plant |
| 68783-12-0 | Naphtha (petroleum), unsweetened |
| 68919-37-9 | Naphtha (petroleum), full-range reformed |
| 68955-35-1 | Naphtha (petroleum), catalytic reformed |
| 101795-01-1 | Naphtha (petroleum), sweetened light |

[a] CAS RN = Chemical Abstracts Service Registry Number. The CAS RN is the property of the American Chemical Society and any use or redistribution, except as required in supporting regulatory requirements and/or for reports to the government when the information and the reports are required by law or administrative policy, is not permitted without the prior, written permission of the American Chemical Society.
[b] DSL = Domestic Substances List.

These substances were identified as high priorities for action during the categorization of the DSL, as they were determined to present the greatest potential or intermediate potential for exposure of individuals in Canada and were considered to present a high hazard to human health. Some of the components of these substances met the ecological categorization criteria for persistence, bioaccumulation potential and inherent toxicity to non-human organisms, but none of them met all of the criteria. These substances were included in the Petroleum Sector Stream Approach (PSSA) because they were related to the petroleum sector and are all complex mixtures.

LBPNs are a group of complex petroleum mixtures that generally serve as blending constituents in gasoline or are intermediate products of distillation or extraction processes, which subsequently undergo further refining. Final fuel products usually consist of a mixture of LBPNs as well as other high-quality hydrocarbons that have been isolated during processing at refinery or upgrader facilities. The compositions of LBPNs vary depending on the source of crude oil or bitumen. As such, LBPNs are considered to be of Unknown or Variable composition, Complex reaction products or Biological materials (UVCBs). In order to predict overall behaviour of these complex substances for purposes of assessing the potential for ecological effects, representative structures have been selected from each chemical class in the mixture.

Based on the available information, all of these LBPNs are likely to have high proportions of $C_4$–$C_6$ hydrocarbons that are considered to be persistent in air, based on criteria defined in the *Persistence and Bioaccumulation Regulations* of CEPA 1999.

None of the LBPNs considered here contain components that are considered to be bioaccumulative based on criteria in the *Persistence and Bioaccumulation Regulations* of CEPA 1999.

Experimental and modelled ecotoxicological data indicate that many of these LBPNs are moderately toxic to aquatic organisms. It is likely that the toxicity observed in experimental studies is due to the presence of mono- and di-aromatic and alkylated aromatic hydrocarbons; however, the lack of data on the proportions of these components makes it impossible to confirm.

Site-restricted LBPNs were identified as a high priority for action because they were considered to present a high hazard to human health. A critical effect for the initial categorization of site-restricted LBPN substances was carcinogenicity, based primarily on classifications by other international agencies. Furthermore, benzene, a genotoxic carcinogen, is known to be a constituent of LBPN substances. Several studies also confirmed skin tumour development in mice following repeated dermal application of LBPN substances. However, LBPNs demonstrated limited evidence of genotoxicity in *in vivo* and *in vitro* assays, as well as limited potential to adversely affect reproduction and development. Information on additional LBPN substances in the PSSA that are similar from a processing and physical-chemical perspective was considered for characterization of human health effects.

The LBPNs considered in this screening assessment have been identified as site-restricted (i.e., they are a subset of LBPNs that are not expected to be transported off refinery or upgrader facility sites). According to information submitted under section 71 of CEPA 1999, and other sources of information, these LBPNs are consumed on-site or are blended into substances leaving the site under different CAS RNs. In addition, a number of regulatory and non-regulatory measures are already in place in Canada, which minimize releases of site-restricted petroleum sector substances, including provincial/territorial operating permit requirements, and best practices and guidelines put

in place by the petroleum industry at refinery and upgrader facilities. Accordingly, environmental and general population exposure to these substances is not expected, and therefore harm to human health or the environment is not expected.

Therefore, it is concluded that these site-restricted LBPNs are not entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity, or that constitute or may constitute a danger to the environment on which life depends, or that constitute or may constitute a danger in Canada to human life or health.

Based on the information available, it is concluded that site-restricted LBPNs listed under CAS RNs 64741-54-4, 64741-55-5, 64741-64-6, 64741-74-8, 64742-22-9, 64742-23-0, 64742-73-0, 68410-05-9, 68410-71-9, 68410-96-8, 68476-46-0, 68477-89-4, 68478-12-6, 68513-02-0, 68514-79-4, 68606-11-1, 68783-12-0, 68919-37-9, 68955-35-1 and 101795-01-1 do not meet any of the criteria set out in section 64 of CEPA 1999.

Because these substances are listed on the DSL, their import and manufacture in Canada are not subject to notification under subsection 81(1) of CEPA 1999. Given the potential hazardous properties of these substances, there is concern that new activities that have not been identified or assessed could lead to these substances meeting the criteria set out in section 64 of the Act. Therefore, application of the Significant New Activity provisions of the Act to these substances if being considered, so that any proposed new manufacture, import or use of these substances outside a petroleum refinery or upgrader facility is subject to further assessment, to determine if the new activity requires further risk management consideration.

# Introduction

The *Canadian Environmental Protection Act, 1999* (CEPA 1999) (Canada 1999) requires the Minister of the Environment and the Minister of Health to conduct screening assessments of substances that have met the categorization criteria set out in the Act to determine whether these substances present or may present a risk to the environment or to human health.

Based on the information obtained through the categorization process, the Ministers identified a number of substances as high priorities for action. These include substances that

- met all of the ecological categorization criteria, including persistence (P), bioaccumulation potential (B) and inherent toxicity to aquatic organisms (iT), and were believed to be in commerce in Canada; and/or
- met the categorization criteria for greatest potential for exposure (GPE) or presented an intermediate potential for exposure (IPE) and had been identified as posing a high hazard to human health based on classifications by other national or international agencies for carcinogenicity, genotoxicity, developmental toxicity or reproductive toxicity.

A key element of the Government of Canada's Chemicals Management Plan (CMP) is the Petroleum Sector Stream Approach (PSSA), which involves the assessment of approximately 160 petroleum substances that are considered high priorities for action. These substances are primarily related to the petroleum sector and are considered to be of Unknown or Variable composition, Complex reaction products or Biological materials (UVCBs).

Screening assessments focus on information critical to determining whether a substance meets the criteria as set out in section 64 of CEPA 1999. Screening assessments examine scientific information and develop conclusions by incorporating a weight of evidence approach and precaution.[1]

## Grouping of Petroleum Substances

The high-priority petroleum substances fall into nine groups of substances based on similarities in production, toxicity and physical-chemical properties (Table A1.1 in

[1] A determination of whether one or more of the criteria of section 64 are met is based upon an assessment of potential risks to the environment and/or to human health associated with exposures in the general environment. For humans, this includes, but is not limited to, exposures from ambient and indoor air, drinking water, foodstuffs, and the use of consumer products. A conclusion under CEPA 1999 on the petroleum substances in the CMP is not relevant to, nor does it preclude, an assessment against the hazard criteria specified in the *Controlled Products Regulations*, which is part of the regulatory framework for the Workplace Hazardous Materials Information System for products intended for workplace use. Similarly, a conclusion based on the criteria contained in section 64 of CEPA 1999 does not preclude actions being taken under other sections of CEPA or other acts.

Appendix 1). In order to conduct screening assessments, each high-priority petroleum substance was placed into one of five categories ("streams") depending on its production and uses in Canada:

0. substances concluded not to be relevant to the petroleum sector and/or not in commerce;
1. site-restricted substances, which are substances that are not expected to be transported off refinery, upgrader or natural gas processing facility sites[2];
2. industry-restricted substances, which are substances that may leave a petroleum-sector facility and may be transported to other industry facilities (for example, for use as a feedstock, fuel or blending component), but that do not reach the public market in the form originally acquired;
3. substances that are primarily used by industries and consumers as fuels;
4. substances that may be present in products available to the consumer.

An analysis of the available data determined that approximately 70 high-priority petroleum substances are site-restricted under stream 1, as described above. These occur within four of the nine groupings: heavy fuel oils, gas oils, petroleum and refinery gases, and low boiling point naphthas (LBPNs).

These site-restricted substances were identified as GPE or IPE during the categorization exercise, based on their production volumes reported in the Domestic Substances List (DSL). However, according to information submitted under section 71 of CEPA 1999, voluntary industry submissions, an in-depth literature review, and a search of material safety data sheets, these substances are consumed on-site or are blended into substances leaving the site under different Chemical Abstracts Service Registry Numbers (CAS RNs) (which will also be addressed under the CMP).

This screening assessment addresses 20 site-restricted LBPNs captured under CAS RNs 64741-54-4, 64741-55-5, 64741-64-6, 64741-74-8, 64742-22-9, 64742-23-0, 64742-73-0, 68410-05-9, 68410-71-9, 68410-96-8, 68476-46-0, 68477-89-4, 68478-12-6, 68513-02-0, 68514-79-4, 68606-11-1, 68783-12-0, 68919-37-9, 68955-35-1 and 101795-01-1. The remaining high-priority LBPNs (under 25 different CAS RNs) will be assessed separately, as they belong to streams 2, 3 or 4 (as described above). Health effects were assessed using toxicological data pooled across all 45 LBPN CAS RNs.

Included in this screening assessment is the consideration of information on chemical properties, hazards, uses and exposure, including the additional information submitted under section 71 of CEPA 1999. Data relevant to the screening assessment of these substances were identified in original literature, review and assessment documents, stakeholder research reports and from recent literature searches, up to July 2010 for the ecological section of the document and up to November 2009 for the health effects section. Key studies were critically evaluated; modelling results were used to reach conclusions.

[2] For the purposes of the screening assessment of PSSA substances, a site is defined as the boundaries of the property where a facility is located. In these cases, facilities are either petroleum refineries or upgraders.

Characterizing risk to the environment involves the consideration of data relevant to environmental behaviour, persistence, bioaccumulation and toxicity, combined with an estimation of exposure to potentially affected non-human organisms from the major sources of release to the environment. Conclusions regarding risk to the environment are based on an estimation of environmental concentrations resulting from releases and the potential for a negative impact on non-human organisms. As well, other lines of evidence of environmental hazard are taken into account. The ecological portion of the screening assessment summarizes the most pertinent data on environmental behaviour and effects, and does not represent an exhaustive or critical review of all available data. Environmental models and comparisons with similar petroleum mixtures have been used in the assessment.

Evaluation of risk to human health involves consideration of data relevant to estimation of exposure (non-occupational) of the general population, as well as information on health hazards (based principally on the weight of evidence assessments of other agencies that were used for prioritization of the substance). Decisions for human health are based on the nature of the critical effect and/or margins between conservative effect levels and estimates of exposure, taking into account confidence in the completeness of the identified databases on both exposure and effects, within a screening context. The screening assessment does not represent an exhaustive or critical review of all available data. Rather, it presents a summary of the critical information upon which the conclusion is based.

This screening assessment was prepared by staff in the Existing Substances Programs at Health Canada and Environment Canada and incorporates input from other programs within these departments. The human health and ecological portions of this assessment have undergone external written peer review/consultation. Comments on the technical portions relevant to human health were received from scientific experts selected and directed by Toxicology Excellence for Risk Assessment (TERA), including Patricia Nance (TERA), Dr. Bob Benson (U.S. Environmental Protection Agency), Dr. Stephen Embso-Mattingly (NewFields Environmental Forensics Practice, LLC), Dr. Michael Jayjock (The Lifeline Group) and Dr. Donna Vorhees (Science Collaborative).

Additionally, the draft of this screening assessment was subject to a 60-day public comment period. While external comments were taken into consideration, the final content and outcome of the screening assessment remain the responsibility of Health Canada and Environment Canada.

The critical information and considerations upon which the screening assessment is based are summarized below.

## Substance Identity

LBPNs are a group of complex liquid mixtures containing volatile components and are produced by the refining or upgrading of crude oils or bitumen. Their composition varies depending on the sources of crude oil or bitumen and the processing steps involved.

## Physical and Chemical Properties

The physical and chemical properties of LBPNs vary depending on the sources of crude oil or bitumen and the processing steps involved. LBPNs are volatile liquid hydrocarbons with a typical boiling point range from −20°C to 230°C (CONCAWE 2005). A summary of data on the physical and chemical properties of site-restricted LBPNs is presented in Table 1.

**Table 1. General physical and chemical properties of site-restricted LBPNs**

| CAS RN | Carbon range | Ratio of aromatics to aliphatics (including BTEX) | Boiling point (°C) | References |
|---|---|---|---|---|
| 64741-54-4 | 4–12 | - | 48–249 | ECB 2000a |
| 64741-55-5 | 4–10 | 13:87 | 37–168 | API 2003b |
| | 4–9 | 1.2% benzene; 30–46% alkenes | | ECB 2000b |
| 64741-64-6 | 7–12 | 0:100 | 90–220 | ECB 2000c |
| 64741-74-8 | 4–8 | 40:60 | −10 to 130 | CONCAWE 1992; ECB 2000d; API 2001a |
| 64742-22-9 | 6–12 | 30:70 | 65–230 | CONCAWE 1992; API 2001a |
| 64742-23-0 | 4–11 | 20:80 | −20 to 190 | CONCAWE 1992; API 2001a, 2008a |
| 64742-73-0 | 4–11 | 15:85 | −20 to 190 | CONCAWE 1992; ECB 2000e; API 2001a |
| 68410-05-9 | No data | No data | No data | |
| 68410-71-9 | 6–9 | 10:90 | 20–130 | CONCAWE 1992; API 2001a |
| 68410-96-8 | 5–10 | 40:60 | 127–188 | ECB 2000f |
| 68476-46-0 | 3–11 | 14:86 | 27–204 | CONCAWE 1992; ECB 2000g; API 2001a |
| 68477-89-4 | 4–6 | 0:100 | 25–200 | CONCAWE 1992; API 2001a; PetroTox 2009 |
| | | | −18 to 93 | ECB 2000h |

| CAS RN | Carbon range | Ratio of aromatics to aliphatics (including BTEX) | Boiling point (°C) | References |
|---|---|---|---|---|
| 68478-12-6 | 4–6 | 0:100 | 25–200 | ECB 2000i |
| | | | −18 to 93 | PetroTox 2009 |
| 68513-02-0 | 4–15 | 30:70 | −35 to 275 | API 2001a; Syncrude 2006 |
| 68514-79-4 | 5–12 | 65:35 | 27–210 | CONCAWE 1992; ECB 2000j; API 2001a |
| 68606-11-1 | 5–9 | 38:62<br>8:92 | 30–177 | CONCAWE 1992; ECB 2000k |
| 68783-12-0 | 5–12 | 20:80 | 0–230 | CONCAWE 1992; ECB 2000l; API 2001a |
| 68919-37-9 | 5–12 | 65:35 | 35–230 | CONCAWE 1992; ECB 2000m; API 2003a |
| | 4–10 | | | |
| 68955-35-1 | 4–12 | 63:37 | 30–220 | CONCAWE 1992; ECB 2000n; API 2001a, 2003a |
| 101795-01-1 | 5–8 | 20:80 | 20–130 | ECB 2000o; API 2001a |

BTEX: benzene, toluene, ethylbenzene, xylenes

These LBPNs are complex mixtures with components that predominantly fall in the $C_4$–$C_{12}$ carbon range: alkanes, cycloalkanes, aromatics and, if they are subject to a cracking process, alkenes as well (CONCAWE 2005). Some of the LBPNs in this report are heavily aromatic (up to 65%), others contain up to 40% alkenes, while all of the others are heavily aliphatic in composition, up to 100%. Depending on the specific refining and distillation processes involved, the chemical composition of several CAS RNs is quite restricted, comprising almost exclusively (for example) $C_4$–$C_6$ aliphatics or $C_7$–$C_{12}$ isoalkanes. Others have a much broader range of constituent hydrocarbons, some (for example) being composed of a full spectrum of $C_4$–$C_{12}$ aliphatics and aromatics (see Table A3.1 in Appendix 3 for the detailed analysis of CAS RN 68919-37-9).

In order to predict the overall properties and behaviour of a complex petroleum substance, representative structures were chosen from each chemical class within the mixture (see Table A3.2 in Appendix 3). Nineteen structures were chosen from the database in PetroTox (2009) based on boiling point ranges for each LBPN, the amount of data on each structure and the middle of the boiling point range of similar structures. As the composition of most LBPNs is not well defined, representative structures could not be chosen based on their proportion in the mixture. This lack of general compositional data resulted in the selection of representative structures for alkanes, isoalkanes, alkenes, one- and two-ring cycloalkanes, and one- and two-ring aromatics ranging from $C_4$–$C_{12}$.

Physical and chemical data were assembled from scientific literature and from the EPIsuite (2008) group of environmental models.

Water solubilities range from very low for the longest-chain alkanes to high for the simplest mono-aromatic. In general, the aromatic compounds are more soluble than the same-sized alkanes, isoalkanes and cycloalkanes. This indicates that the components likely to remain in water are the one- and two-ring aromatics ($C_6$–$C_{12}$). The $C_9$–$C_{12}$ alkanes, isoalkanes and one- and two-ring cycloalkanes are likely to be attracted to sediments based on their low water solubilities and moderate to high log octanol–water partition coefficient ($K_{ow}$) and log organic carbon–water partition coefficient ($K_{oc}$) values.

Experimental and modelled vapour pressures for representative structures are moderate to very high and decrease with increasing molecular size. This suggests that losses from soil and water will likely be high and that the air will be the ultimate receiving environment for most of the components of LBPNs.

## Sources

Site-restricted LBPNs are produced in Canadian refineries and upgraders. The CAS RN descriptions (NCI 2006), typical process flow diagrams (Figures A2.1-A2.20 in Appendix 2) (Hopkinson 2008), and information collected under section 71 of CEPA 1999 (Environment Canada 2008, 2009) indicate that these 20 LBPNs are intermediate streams within both refineries and upgraders or are blended to make other products under a new CAS RN (Figures A2.5, A2.6 and A2.20 show blending streams). As such, these LBPNs are not expected to be transported off of facility sites. Quantities produced were reported under section 71 of CEPA 1999 (Environment Canada 2008, 2009) by the petroleum refining and upgrading industry but are considered to be confidential. However, these data are not critical to this screening assessment, since release to the environment is not expected.

CAS RN 64741-54-4 and CAS RN 64741-55-5 refer to products of a catalytic cracking process (Figures A2.1 and A2.2 in Appendix 2).

CAS RN 64741-64-6 represents a bottom substance from distillation of alkylation products (Figure A2.3 in Appendix 2).

CAS RN 64741-74-8 often refers to an overhead distillate from a fractionation column in a thermal cracking unit (coking or visbreaking) (Figures A2.4a and A2.4b in Appendix 2).

CAS RN 64742-22-9 and CAS RN 64742-23-0 refer to a heavy naphtha and a light naphtha, respectively. Both are treated by an alkali solvent to remove acid compounds via a neutralization reaction (Figures A2.5 and A2.6 in Appendix 2).

CAS RN 64742-73-0 represents a bottom substance discharged from a distillation column fed with hydrodesulphurized light naphtha (Figures A2.7a and A2.7b in Appendix 2).

CAS RN 68410-05-9 refers to a product of the atmospheric distillation tower (Figure A2.8 in Appendix 2).

CAS RN 68410-71-9 refers to a raffinate from an extraction column where aromatic compounds are removed from the product of a catalytic reforming process (Figure A2.9 in Appendix 2).

CAS RN 68410-96-8 refers to a bottom residue discharged from a stabilization column treated with the product of a hydrotreating process of straight-run heavy naphtha (Figures A2.10a and A2.10b in Appendix 2).

CAS 68476-46-0 represents a distillate derived from the main distillation column (Figure A2.11 in Appendix 2).

CAS RN 68477-89-4 refers to an overhead product ($C_5$ and less) from a distillation column treated with the product of a catalytic cracking process (Figure A2.12 in Appendix 2).

CAS RN 68478-12-6 refers to a bottom product from a distillation column where isobutane is separated from *n*-butane and heavier compounds (Figures A2.13a and A2.13b in Appendix 2).

CAS RN 68513-02-0 represents an overhead distillate from a fractionation column in a coking unit (Figure A2.14a and A2.14b in Appendix 2).

CAS RN 68514-79-4 refers to a bottom substance discharged from a distillation column fed with hydrotreated heavy naphtha from a hydrofiner-powerformer process (Figure A2.15 in Appendix 2).

CAS RN 68606-11-1 refers to a side distillate coming directly from an atmospheric distillation column; it is normally blended into gasoline products (Figure A2.16 in Appendix 2).

CAS RN 68783-12-0 is a generic description of naphthas produced from various distillation processes in a refinery, including straight-run naphthas from an atmospheric distillation column, naphtha distillates from cracking units (catalytic cracking, thermal cracking, hydrocracking) and naphtha upgrading units (isomerization, alkylation, polymerization, reformer) (Figures A2.17a and A2.17b in Appendix 2).

CAS RN 68919-37-9 and CAS RN 68955-35-1 represent a bottom substance of a distillation column fed with effluent from a catalytic reforming process (Figures A2.18 and A2.19 in Appendix 2).

CAS RN 101795-01-1 refers to a product after mercaptans and other acid compounds are removed by a sweetening process (Figure A2.20 in Appendix 2).

## Uses

According to the information collected through the *Notice with respect to certain high priority petroleum substances* (Environment Canada 2008) and the *Notice with respect to potentially industry-limited high priority petroleum substances* (Environment Canada 2009), published under section 71 of CEPA 1999, the LBPN substances listed in this screening assessment were identified as either being consumed at the facility or blended into substances leaving the site under different CAS RNs. Although these substances were identified by multiple use-codes established during the development of the DSL, it has been determined from information submitted under section 71 of CEPA 1999 (Environment Canada 2008, 2009), voluntary submissions from industry, an in-depth literature review and a search of material safety data sheets that these site-restricted LBPNs are not expected to be transported off refinery or upgrader facility sites.

## Releases to the Environment

Potential releases of LBPN substances from refineries and upgraders can be characterized as either controlled or unintentional releases. Controlled releases are planned releases from pressure relief valves, venting valves and drain systems that occur for safety purposes or maintenance, are considered part of routine operations and occur under controlled conditions. Unintentional releases are typically characterized as unplanned releases due to spills or leaks from various equipment, valves, piping, flanges, etc. resulting from equipment failure, poor maintenance, lack of proper operating practices, adverse weather conditions or other unforeseen factors. Refinery and upgrader operations are highly regulated and regulatory requirements established under various jurisdictions, as well as voluntary non-regulatory measures implemented by the petroleum industry, are in place to manage these releases (SENES 2009).

### Controlled Releases

The site-restricted LBPN CAS RNs in this screening assessment originate from distillation or extraction columns in refineries or upgraders, as either a distillate or a residue (bottom product). Thus, the potential locations for the controlled release of LBPNs are relief valves, venting valves or drain valves on the piping (e.g., columns and vessels) in the vicinity of the equipment.

Under typical operating conditions, controlled releases of site-restricted LBPNs would be captured in a closed system,[3] according to defined procedures, and then returned to the

[3] For the purposes of the screening assessment of PSSA substances, a closed system is defined as a system within a facility that does not have any releases to the environment, and where losses are collected and either recirculated or destroyed.

processing facility. In cases where the amount of the substance is small or its concentration is dilute, the site-restricted LBPN is sent to the facility wastewater treatment plant. In both cases, exposure of the general population or the environment is not expected from the site-restricted LBPN substances under the CAS RNs listed in this screening assessment, as they are not expected to be transported off refinery or upgrader facility sites.

**Unintentional Releases**

Unintentional releases (including fugitive releases) occur from equipment (e.g., pumps, storage tanks), seals, valves, piping, flanges, etc., during processing and handling of petroleum substances, and can be greater in situations of poor maintenance or operating practice. Regulatory and non-regulatory measures are in place to reduce these events (SENES 2009). Rather than being specific to one substance, these measures are developed in a more generic way in order to reduce unintentional releases of all substances in the petroleum sector.

For the Canadian petroleum industry, requirements at the provincial/territorial level typically prevent or manage the unintentional releases of petroleum substances and streams within a facility (through the use of operating permits) (SENES 2009).

At the federal level, unintentional releases of some petroleum substances are addressed under the *Fisheries Act*; the *Petroleum Refinery Liquid Effluent Regulations and Guidelines* set the discharge limits of oil and grease, phenol, sulphides, ammonia nitrogen and total suspended matter, as well as testing requirements for acute toxicity in the final petroleum effluents entering Canadian waters.

Additionally, existing occupational health and safety legislation specifies measures to reduce occupational exposures of employees, and some of these measures also serve to reduce unintentional releases (CanLII 2001).

Non-regulatory measures (e.g., guidelines, best practices) are also in place at petroleum sector facilities to reduce unintentional releases. Such control measures include appropriate material selection during the design and setup processes; regular inspection and maintenance of storage tanks, pipelines and other process equipment; the implementation of leak detection and repair or other equivalent programs; the use of floating roofs in above-ground storage tanks to reduce the internal gaseous zone; and the minimal use of underground tanks, which can lead to undetected leaks (SENES 2009).

## Environmental Fate

Given that these are site-restricted LBPNs which are not expected to be transported off refinery or upgrader facility sites, only general data on the environmental behaviour of these CAS RNs are presented in the screening assessment.

# Persistence and Bioaccumulation Potential

## Environmental Persistence

No empirical data are available on the degradation of LBPNs as complex mixtures. However, estimates can be derived from analyzing the biodegradation of the components of LBPNs. Aerobic biodegradation data for individual isoalkanes ($C_9$–$C_{12}$) from an Organisation for Economic Co-operation and Development (OECD) 301F ready biodegradation test indicate that they will be 22% degraded (ultimate biodegradation) over a period of 28 days (ECB 2000e). This equates to a degradation half-life of approximately 78 days in water, assuming that degradation follows first-order kinetics. Numerous researchers have found that the degree of branching in an isoalkane increases its resistance to biodegradation (Atlas 1981). However, Prince et al. (2007a, 2007b) reported that $C_6$–$C_{10}$ components (alkanes, isoalkanes, alkenes, cycloalkanes, one-ring aromatics and two-ring aromatics) in a formulated gasoline had relatively short median half-lives (primary biodegradation)—ranging from 3 to 17 days—in freshwater, salt water and sewage effluent (see Table A3.3 in Appendix 3). They hypothesized that primary biodegradation half-lives were shorter for hydrocarbons in a gasoline mix than for individual components, because indigenous micro-organisms degrade hydrocarbons most effectively when they are presented as a mixed suite of hydrocarbon substrates that allows microbes to use intermediates from different pathways to balance their overall metabolism.

A quantitative structure–activity relationship (QSAR)–based weight of evidence approach (Environment Canada 2007) was also applied using primary biodegradation model BIOHCWIN (2008), the ultimate biodegradation model BIOWIN (2009) and the atmospheric degradation model AOPWIN (2008). BIOWIN (2009) is a general biodegradation estimation model for organic compounds that estimates a variety of biodegradation rates, such as primary and ultimate biodegradation. Primary biodegradation is the transformation of a parent compound to an initial metabolite. Ultimate biodegradation is the transformation of a parent compound to carbon dioxide and water, mineral oxides of any other elements present in the test compound, and new cell material (EPIsuite 2008). The key persistence metric is ultimate biodegradation.

Using an extrapolation ratio of 1:1:4 for water:soil:sediment biodegradation half-lives (Boethling et al. 1995), the half-lives in soil and sediment can be extrapolated from the half-life estimations in water.

The results of the BIOHCWIN (2008) model indicate that the components of LBPNs have primary degradation half-lives in water ranging from 3.1 to 55.9 days (see Table A3.4 in Appendix 3). Outputs from BIOWIN (2009) indicate that most components of LBPNs undergo ultimate degradation in a period of "weeks" or less, although a time frame of "weeks to months" is indicated for a few of the heavier components ("weeks to months" is equated to a half-life of 37.5 days by Aronson et al. 2006). Using an extrapolation ratio of 1:1:4 for water:soil:sediment biodegradation half-lives

(Boethling et al. 1995), the ultimate degradation half-life in soil for the heavy components is also < 182 days, and the half-life in sediments is < 365 days.

In air, empirical data (Atkinson 1990) show that butane, isobutane, pentane and isopentane are persistent (see Table A3.5a in Appendix 3), with half-lives ranging from 2 to 3.4 days. Predicted atmospheric oxidation half-lives (AOPWIN 2008) for representative structures confirm these data; as well, AOPWIN (2008) predicted that benzene and hexane have half-lives of equal to or greater than 2 days (5.5 days and 2 days, respectively) (see Table A3.5b in Appendix 3). The atmosphere would be an important environmental compartment for these LBPNs due to the high volatility of most of the components.

For all of the LBPNs considered in this report, the $C_4$-$C_6$ components that are highly persistent based on criteria in the *Persistence and Bioaccumulation Regulations* of CEPA 1999 (Canada 2000) likely make up a large proportion of the mixture (see Tables A3.6a, b and c in Appendix 3). For CAS RNs 64742-22-9 and 68410-71-9, it is assumed that they also contain significant proportions of these persistent components, although there are no data to enable an estimate of their compositions. There is nothing to suggest that they would not contain persistent components.

**Potential for Bioaccumulation**

Because no experimental bioaccumulation or bioconcentration data for these LBPNs as mixtures were available, empirical data for the representative structures found in LBPNs and a predictive approach were applied using a bioconcentration factor (BCF) model (BCFBAF 2008). The BCFBAF program incorporates the generic QSAR model of Arnot and Gobas (2003). As well, experimental data for similar substances were considered.

Both experimentally derived and modelled log $K_{ow}$ values for representative structures of the LBPNs (Table A3.2, Appendix 3) suggest that these components have a moderate to high potential to bioaccumulate in biota.

Correa and Venables (1985) exposed a tropical fish (*Mugil curema*) to naphthalene (a $C_{10}$ di-aromatic) in water for 96 hours and found rapid uptake with slower depuration. BCFs in muscle were 81 to 567. A whole fish BCF of 145 was calculated for this species.

The Arnot-Gobas kinetic model (BCFBAF 2008) estimates bioaccumulation factor (BAF) values for the nineteen representative structures ranging from 10–9605 (Table A3.7, Appendix 3). Four of the nineteen components have predicted BAF values in excess of 5000. These representative structures include $C_{12}$ alkanes, $C_{12}$ isoalkanes, $C_{12}$ alkenes and $C_{12}$ 1-ring cycloalkanes. However, experimental data do not indicate significant bioaccumulation by mono-aromatics and di-aromatics (Table 3.8, Appendix 3), with the highest measured BAF being 230 litres per kilogram (L/kg).

The results of the BCF model calculations (see also Table A3.7 in Appendix 3) indicate a generally low bioconcentration potential of these representative structures, with values from 10–2180.

Studies on the bioconcentration potential of many of the representative structures in LBPNs have been conducted in Japan (Table A3.9, Appendix 3) (JNITE 2010). None of the substances considered had a BCF ≥ 5000.

Tolls and van Dijk (2002) measured the BCF value for a $C_{12}$ isoalkane at between 880 and 3500 L/kg, which is consistent with the modelled BCF value for 2,3-dimethyl decane (1910 L/kg), but not the BAF (8232 L/kg). There is some supporting evidence of low BAF values, in that some *n*-alkanes of around $C_{12}$ and some $C_{10}$–$C_{12}$ aromatics and alkylated aromatics are bioaccumulative at low to moderate levels in mussels (Boehm and Quinn 1977) and fish (Colombo et al. 2007) via diet. However, the research data on the accumulation of *n*-alkanes and polycyclic aromatic hydrocarbons (PAHs) in this size range are contrary to the high BAFs predicted by the BAF model (Correa and Venables 1985; Niimi and Dookhran 1989; Wan et al. 2007; Takeuchi et al. 2009). This is likely due to the slower estimated metabolism rate of these compounds or faster estimated uptake rates used in the kinetic mass-balance model compared with the field data.

In this assessment, laboratory, field and modelled data are available for the $C_{12}$ linear and cyclic fractions. In the case of the BCF, both empirical and modelled data agree and suggest a low potential for bioconcentration from water. In the case of accumulation from all exposures including the diet (BAF), greater weight has been placed on the field data because the field data inherently account for factors that are sources of uncertainty in model estimates. The field BAF data indicate that none of the components of these LBPNs would be bioaccumulative based on criteria in the *Persistence and Bioaccumulation Regulations* of CEPA 1999.

## Potential to Cause Ecological Harm

### Ecological Effects Assessment

### A - In the Aquatic Compartment

Experimental aquatic toxicity data were obtained for some of the LBPN CAS RNs considered here (see Table A3.10 in Appendix 3), whereas others were extrapolated from results for similar types of LBPNs. Moderate toxicity (median lethal loading [$LL_{50}$] values of 4.5–32 milligrams [mg]/L) was seen with the water-accommodated fractions in shrimp, *Daphnia magna*, Rainbow Trout and Fathead Minnows (Adema and van den Bos Bakker 1986; PPSC 1995a; CONCAWE 1996; ECB 2000g, 2000h, 2000k). It is likely that the mono-aromatic and di-aromatic hydrocarbons and alkylated aromatics are largely responsible for the toxicity seen in the tests, as $C_9$–$C_{12}$ alkanes and isoalkanes are known not to be especially toxic to aquatic organisms (ECB 2000e). Algae appear to be some of the most sensitive organisms to whole products in water; one algal no-observed-adverse-

effect level (NOAEL) was below 1 mg/L, although the median effective concentration ($EC_{50}$) for growth was 880 mg/L (ECB 2000i). Empirical tests with water-accommodated fractions of LBPNs did not indicate that the substances tested were highly hazardous to aquatic organisms.

CONCAWE developed an aquatic toxicity model specific to petroleum hydrocarbon mixtures, called PetroTox (2009). PetroTox assumes toxicological action via narcosis and therefore accounts for additive effects according to the toxic unit approach (PetroTox 2009). It models the toxicity of petroleum hydrocarbons dissolved in the water fraction for $C_5$–$C_{41}$ compounds; compounds smaller than $C_5$ are considered by the model to be too volatile to remain in water long enough to impart any significant aquatic toxicity, and compounds greater than $C_{41}$ are assumed to be too hydrophobic and immobile to impart any toxicity. PetroTox generates estimates of toxicity as an $LL_{50}$ rather than a median lethal concentration ($LC_{50}$), due to the insolubility of petroleum substances in water. The $LL_{50}$ is the amount of petroleum substance needed to generate a water-accomodated fraction (WAF) that is toxic to 50% of the test organisms. It is not a measure of the concentration of the petroleum components in the WAF.

A range of moderate aquatic toxicity predictions was obtained from the PetroTox (2009) model. The $LL_{50}$ predictions were in the same range as observed in the empirical tests, from 0.5–154 mg/L (see Tables A3.11a and b in Appendix 3). Some of the CAS RNs were predicted to have relatively high toxicity to some aquatic organisms: 64741-64-6, 64742-22-9, 68513-02-0 and 68783-12-0. The most sensitive organism from the PetroTox (2009) tests was *Rhepoxynius abronius*, a marine amphipod known to be sensitive to sediment pollutants. However, PetroTox (2009) predicts toxicity only from water-soluble components, not those that would likely be attracted to sediments.

**B - In Other Environmental Compartments**

Selected endpoints (mortality and reproduction) from studies on small mammals used to evaluate human health effects were also used to bound terrestrial toxicity. Analysis was limited to site-restricted LBPN CAS RNs, obtained from the summary of studies used to evaluate human health effects (see Appendix 4).

Rats exhibited an $LD_{50}$ of 3500 milligrams per kilogram of body weight (mg/kg-bw) when orally dosed with CAS RN 68955-35-1 (API 2008a). CAS RN 64741-55-5 delivered via inhalation at 9041 mg per cubic metre ($mg/m^3$) was considered to be a no-observed-adverse-effect-concentration (NOAEC) for systemic toxicity in rats using a reproductive/developmental toxicity testing protocol (Shreiner et al. 1999; API 2008a). An oral NOAEL of 2000 mg/kg-bw/day was determined for CAS RN 64741-55-5 for reproductive and developmental toxicity in rats (Stonybrook Laboratories, Inc. 1995), and an oral NOAEL of 50 mg/kg-bw/day was determined for CAS RN 68513-74-8 for reproductive and developmental toxicity in rabbits (this was the highest dose tested) (Miller and Schardein 1981). These values do not indicate that these CAS RNs are highly hazardous to terrestrial mammals for these particular endpoints and exposure routes.

**Ecological Exposure Assessment**

Because the LBPNs in this report have been identified as site-restricted, indicating that they are not expected to be transported off refinery or upgrader facility sites, the potential for release to the ecosystem is negligible, and exposure is not expected.

**Characterization of Ecological Risk**

Most of the LBPNs in this report are only moderately toxic to aquatic organisms through their water-soluble components, although the PetroTox model suggests that LBPNs 64741-64-6, 64742-22-9, 68513-02-0 and 68783-12-0 have higher toxicity to some aquatic organisms.

All of these LBPNs contain large proportions of components that are considered to be persistent in the atmosphere based on criteria in the *Persistence and Bioaccumulation Regulations*.

Based on the available field BAF data none of the components of these LBPNs would be bioaccumulative based on criteria in the *Persistence and Bioaccumulation Regulations* of CEPA 1999.

Based on information obtained from a variety of sources (voluntary industry submissions, an in-depth literature review, and a search of material safety data sheets), the LBPNs considered in this screening assessment have been identified as site-restricted - i.e., they are not expected to be transported off refinery or upgrader facility sites. These LBPNs are consumed on-site or are blended into other substances leaving the site under different CAS RNs. Measures (including provincial/territorial operating permit requirements, and best practices and guidelines put in place by the petroleum industry) are in place to minimize releases from refineries and upgrader facilities. As a result of these factors, the likelihood of exposure, and potential for risk, of organisms in the environment to LBPNs under these CAS RNs is considered to be low.

**Uncertainties in Evaluation of Ecological Risk**

As the site-restricted LBPNs are UVCBs, their specific chemical compositions are not well defined. LBPN streams under the same CAS RN can vary significantly in the number, identity and proportion of constituent compounds, depending on operating conditions, feedstocks and processing units.

Modelling of the physical and chemical properties of LBPNs, as well as their persistence, bioaccumulation and toxicity, is based on representative structures. The physical and chemical properties of 19 representative structures were used to estimate the overall behaviour of the LBPNs. Given that a variety of representative structures may be derived for the same LBPN, it is recognized that structure-related uncertainties exist for these substances. However, the limited number of hydrocarbons theoretically present in LBPNs (based on boiling point ranges and carbon ranges) reduces this uncertainty. The lack of

specific proportions of representative structures in CAS RNs also creates uncertainty in estimating certain properties, such as toxicity.

As these substances are classified as site-restricted, environmental releases and exposures are expected to be negligible. However, CAS RN specific monitoring data were not identified to verify this assumption.

The lack of data on the composition of two of the CAS RNs (68410-05-9 and 68410-96-8) resulted in uncertainty regarding their behaviour in the environment, including persistence.

## Potential to Cause Harm to Human Health

### Health Effects Assessment

Given the limited number of studies available that evaluated the health effects of site-restricted LBPNs, an adequately representative toxicological data set specifically for the site-restricted LBPNs could not be obtained. Therefore, to characterize the toxicity of these site-restricted substances, additional LBPNs in the PSSA that are similar from both a process perspective as well as a physical and chemical perspective were also evaluated for their toxicological effects. As both the site-restricted and the additional LBPN substances have similar physical and chemical as well as toxicological properties, the toxicological data across CAS RNs were used to construct a toxicological profile to represent all LBPNs. Accordingly, the toxicity of LBPNs is represented as a group, not by individual CAS RNs.

Appendix 4 contains a summary of available health effects information on LBPNs in experimental animals. A summary of key studies selected to represent the toxicity of site-restricted LBPNs follows.

LBPNs have low acute toxicity by the oral (median lethal dose [$LD_{50}$] in rats > 2000 mg/kg-bw), inhalation ($LD_{50}$ in rats > 5000 mg/m$^3$) and dermal ($LD_{50}$ in rabbits > 2000 mg/kg-bw) routes of exposure (CONCAWE 1992; Rodriguez and Dalbey 1994a, 1994b, 1994c, 1994d; API 2008a). This oral $LD_{50}$ value is lower than the 5000 mg/kg-bw value identified in CONCAWE (1992) and API (2008a). Most LBPNs are mild to moderate eye and skin irritants in rabbits, with the exception of heavy catalytic cracked and heavy catalytic reformed naphthas, which have higher primary skin irritation indices (API 1980a, 1985a, 1985b, 1985c, 1986a, 1986b, 1986c, 1986d, 2008a; CONCAWE 1992; Rodriguez and Dalbey 1994e, 1994f, 1994g, 1994h, 1994i). LBPNs do not appear to be skin sensitizers, but a poor response in the positive control was also noted in these studies (API 1980a, 1985b, 1986a, 1986b, 1986c, 1986d, 1986e, 1986f).

The lowest-observed-adverse-effect concentration (LOAEC) and lowest-observed-adverse-effect level (LOAEL) values identified following short-term (2–89 days) and

subchronic (greater than 90 days) exposure to the LBPN substances are listed in Table 2. These values were determined for a variety of endpoints after considering the toxicity data for all LBPNs in the PSSA. Most of the studies were carried out by the inhalation route of exposure. Renal effects, including increased kidney weight, renal lesions (renal tubule dilation, necrosis) and hyaline droplet formation, observed in male rats exposed orally or by inhalation to most LBPNs, were considered species- and sex-specific (Carpenter et al. 1975; Halder et al. 1984, 1985; Phillips and Egan 1984; Research and Environmental Division 1984; Gerin et al. 1988; Schreiner et al. 1998, 1999, 2000a; McKee et al. 2000; API 2005, 2008b, 2008c). These effects were determined to be due to a mechanism of action not relevant to humans—specifically, the interaction between hydrocarbon metabolites and alpha-2-microglobulin, an enzyme not produced in substantial amounts in female rats, mice and other species, including humans. The resulting nephrotoxicity and subsequent carcinogenesis in male rats were therefore not considered in deriving LOAEC/LOAEL values.

**Table 2. LOAECs/LOAELs identified for a variety of endpoints in experimental animals following short-term or subchronic exposure to LBPNs**

| Route of exposure | Effects observed[1] | Lowest LOAEC/LOAEL | CAS RN | Reference |
|---|---|---|---|---|
| Inhalation | Decreased growth rate | 1327 mg/m$^3$ | 64742-95-6 | McKee et al. 1990 |
| | Brain enzyme changes | 1327 mg/m$^3$ | 8006-61-9 | Chu et al. 2005 |
| | Oxidative stress in the liver | 4679 mg/m$^3$ | 64742-48-9 | Lam et al. 1994 |
| | Decreased survival | 363 mg/m$^3$ | 8052-41-3 | Rector et al. 1966 |
| | Biochemical | 575 mg/m$^3$ | 64742-48-9 | Savolainen and Pfaffli 1982 |
| | Inflammatory response of the respiratory tract | 214 mg/m$^3$ | 8052-41-3 | Riley et al. 1984 |
| | Hematological | 1800 mg/m$^3$ | 64742-95-6 | Shell Research Ltd. 1980 |
| Oral | Decreased growth rate; biochemical | 500 mg/kg per day | 64742-95-6 | Bio/Dynamics Inc. 1991a |
| | Hematological | 500 mg/kg per day | 64742-95-6 | Bio/Dynamics Inc. 1991b |
| Dermal | Skin irritation | 30 mg/kg-bw per day | 64741-55-5 | Mobil 1988a |
| | Biochemical | 1500 mg/kg-bw per day | 64742-48-9 | Zellers 1985 |
| | Hematological | 500 mg/kg-bw per day | 64742-48-9 | Zellers 1985 |
| | Decreased growth rate | 200 mg/kg-bw per day | 64741-54-4 | API 1986g |
| | Decreased survival | 1000 mg/kg-bw per day | 68955-35-1 | API 1986h |

[1] See Appendix 4 for additional details.

Only a limited number of studies of short-term and subchronic duration were identified for site-restricted LBPNs. The lowest LOAEC identified in these studies, via the inhalation route, is 5475 mg/m$^3$, based on a concentration-related increase in liver weight in both male and female rats following a 13-week exposure to light catalytic cracked naphtha (API 1987a). Shorter exposures of rats to this test substance resulted in nasal irritation at 9041 mg/m$^3$ (Schreiner et al. 1999; API 2008a). No systemic toxicity was reported following dermal exposure to light catalytic cracked naphtha, but skin irritation and accompanying histopathological changes were increased, in a dose-dependent manner, at doses as low as 30 mg/kg-bw per day when applied 5 days per week for 90 days in rats (Mobil 1988a).

No non-cancer chronic toxicity studies (≥ 1 year) were identified for site-restricted LBPNs and very few non-cancer chronic toxicity studies were identified for other LBPNs. An LOAEC of 200 mg/m$^3$ was noted in a chronic inhalation study that exposed mice and rats to unleaded gasoline (containing 2% benzene). This inhalation LOAEC was based on ocular discharge and ocular irritation in rats. At the higher concentration of 6170 mg/m$^3$, increased kidney weight was observed in male and female rats (increased kidney weight was also observed in males only at 870 mg/m$^3$). Furthermore, decreased body weight in male and female mice was also observed at 6170 mg/m$^3$ (MacFarland et al. 1984). A LOAEL of 714 mg/kg-bw was identified for dermal exposure based on local skin effects (inflammatory and degenerative skin changes) in mice following application of naphtha for 105 weeks. No systemic toxicity was reported (Clark et al. 1988).

Although few genotoxicity studies were identified for the site-restricted LBPNs, the genotoxicity of several other LBPN substances has been evaluated using a variety of *in vivo* and *in vitro* assays. While *in vivo* genotoxicity assays were negative overall, the *in vitro* tests exhibited mixed results as described below.

For *in vivo* genotoxicity tests, LBPNs exhibited negative results for chromosomal aberrations and micronuclei induction (API 1985d, 1985e, 1985f, 1985g, 1985h, 1985i, 1986i; Gochet et al. 1984; Khan 1984; Khan and Goode 1984), but exhibited positive results in one sister chromatid exchange assay (API 1988a), although this result was not considered definitive for clastogenic activity as no genetic material was unbalanced or lost (API 2008a). Mixtures that were tested, which included a number of light naphthas, displayed mixed results (i.e., both positive and negative for the same assay) for chromosomal aberrations and negative results for the dominant lethal mutation assay (API 1977a). Unleaded gasoline (containing 2% benzene) was tested for its ability to induce unscheduled deoxyribonucleic acid (DNA) synthesis (UDS) and replicative DNA synthesis (RDS) in rodent hepatocytes and kidney cells. UDS and RDS were induced in mouse hepatocytes via oral exposure and RDS was induced in rat kidney cells via oral and inhalation exposure (Loury et al. 1986, 1987). Unleaded gasoline (benzene content not stated) exhibited negative results for chromosomal aberrations and the dominant lethal mutation assay (API 1977b, 1977c, 1980b; Dooley et al. 1988; Conaway et al. 1984) and mixed results for atypical cell foci in rodent renal and hepatic cells (Short et al. 1989; Standeven et al. 1994, 1995; Standeven and Goldsworthy 1993).

For *in vitro* genotoxicity studies, LBPNs were negative for six out of seven Ames tests, and were also negative for UDS and for forward mutations (Riccio and Stewart 1991; Blackburn 1981; Blackburn et al. 1986, 1988; Gochet et al. 1984; Brecher 1984a; Brecher and Goode 1984a; Papciak and Goode 1984). LBPNs exhibited mixed or equivocal results for the mouse lymphoma and sister chromatid exchange assays, as well as for cell transformation (API 1985d, 1985j, 1985k, 1985l, 1985m, 1985n, 1985o, 1985p, 1986j, 1986k, 1986l, 1987b, 1988b; Kirby et al. 1979; Gochet et al. 1984; Brecher 1984b; Brecher and Goode 1984b; Tu and Sivak 1981; Jensen and Thilager 1978; Roy 1981) and positive results for one bacterial DNA repair assay (Haworth 1978). Mixtures that were tested, which included a number of light naphthas, displayed negative results for the Ames and mouse lymphoma assays (API 1977a). Gasoline exhibited negative results for the Ames test battery, the sister chromatid exchange assay and for one mutagenicity assay (API 1977b; Farrow et al. 1983; Dooley et al. 1988; Conaway et al. 1984; Richardson et al. 1986). Mixed results were observed for UDS and the mouse lymphoma assay (API 1977b, 1988c; Farrow et al. 1983; Conaway et al. 1984; Dooley et al. 1988; Loury et al. 1986, 1987).

While the majority of *in vivo* genotoxicity results for LBPN substances are negative, the potential for genotoxicity of LBPNs as a group cannot be discounted based on the mixed *in vitro* genotoxicity results.

No inhalation studies assessing the carcinogenicity of the site-restricted LBPNs were identified. Only unleaded gasoline has been examined for its carcinogenic potential, in several inhalation studies (MacFarland et al. 1984; Short et al. 1989; Standeven and Goldsworthy 1993; Standeven et al. 1994, 1995). In one study, rats and mice were exposed to 0, 200, 870 or 6170 mg/m$^3$ of a 2% benzene formulation of the test substance, via inhalation, for approximately 2 years. A statistically significant increase in hepatocellular adenomas and carcinomas, as well as a non-statistical increase in renal tumours, were observed at the highest dose in female mice. A dose-dependent increase in the incidence of primary renal neoplasms was also detected in male rats, but this was not considered to be relevant to humans, as discussed previously (MacFarland et al. 1984). In other studies, no renal cell tumours were observed after 1 year in male and female rats exposed to lower concentrations (0, 27, 183 or 791 mg/m$^3$) for 24 or 65–67 weeks (Short et al. 1989). Carcinogenicity was also assessed for unleaded gasoline, via inhalation, as part of initiation/promotion studies. In these studies, unleaded gasoline did not appear to initiate tumour formation, but did show renal cell and hepatic tumour promotion ability, when rats and mice were exposed, via inhalation, for durations ranging from 13 weeks to approximately 1 year using an initiation/promotion protocol (Short et al. 1989; Standeven and Goldsworthy 1993; Standeven et al. 1994, 1995). However, further examination of data relevant to the composition of unleaded gasoline demonstrated that this is a highly-regulated substance; it is expected to contain a lower percentage of benzene and has a discrete component profile when compared to other substances in the LBPN group.

Both the European Commission and the International Agency for Research on Cancer (IARC) have classified LBPN substances as carcinogenic. All of these substances were

classified by the European Commission (2008) as Category 2 (R45: *may cause cancer*) (benzene content ≥ 0.1% by weight). IARC has classified gasoline, an LBPN, as a Group 2B carcinogen (*possibly carcinogenic to humans*) and "occupational exposures in petroleum refining" as Group 2A carcinogens (*probably carcinogenic to humans*). In both IARC classifications, several LBPN substances, including some that are site-restricted, were included: CAS RNs 64741-46-4, 64741-54-4, 64741-55-5, 64741-64-6, 64741-74-8 and 68919-37-9 were identified by IARC as major components of gasoline, while CAS RNs 64741-41-9, 64741-46-4, 64741-54-4, 64741-55-5, 64741-63-5, 64741-64-6, 64741-68-0, 64741-69-1, 64741-74-8, 64742-82-1, 68410-05-9 and 68919-37-9 were listed in "occupational exposures in petroleum refining" (IARC 1989a, b).

LBPNs potentially contain the volatile component benzene. The most likely average benzene concentration in naphthas is approximately 1%, and measured benzene concentrations ranged from non-detected in isomerized naphthas to 20% in reformates (UN 2009). Benzene was assessed by the Government of Canada under CEPA, 1988 (Canada 1993) and was determined to be harmful to human health based on carcinogenicity. This substance was subsequently added to the List of Toxic Substances - Schedule 1 of CEPA 1999. Other organizations have drawn similar conclusions. IARC classified benzene as a Group 1 carcinogen (*carcinogenic to humans*) (IARC 1987, 2004, 2007) and the European Commission has recommended that all LBPNs containing ≥ 0.1% benzene by weight be classified as Category 2 carcinogens, even in the absence of stream-specific experimental animal data (ECB 2007; CONCAWE 2005; UN 2009). This is consistent with the approach used to categorize petroleum streams during the categorization exercise conducted for substances on the DSL under CEPA 1999 (Health Canada 2008).

Several studies were conducted on experimental animals to investigate the dermal carcinogenicity of LBPNs. The majority of these studies were conducted through exposure of mice to doses ranging from 694–1351 mg/kg-bw, for durations ranging from 1 year to the animals' lifetime or until a tumour persisted for 2 weeks. Given the route of exposure, the studies specifically examined the formation of skin tumours. Results for carcinogenicity via dermal exposure are mixed. Both malignant and benign skin tumours were induced with heavy catalytic cracked naphtha, light catalytic cracked naphtha, light straight-run naphtha and naphtha (API 1986m, 1986n; Blackburn et al. 1986, 1988; Witschi et al. 1987; Clark et al. 1988; Broddle et al. 1996). Significant increases in squamous cell carcinomas were also observed when mice were dermally treated with Stoddard solvent (US EPA 1984), but the latter was administered as a mixture (90% test substance), and the details of the study were not available. In contrast, insignificant increases in tumour formation or no tumours were observed when light alkylate naphtha, heavy catalytic reformed naphtha, sweetened naphtha, light catalytically cracked naphtha or unleaded gasoline was dermally applied to mice (API 1986m, 1986n, 1986o, 1988d; Skisak et al. 1994; Broddle et al. 1996). Negative results for skin tumours were also observed in male mice dermally exposed to sweetened naphtha using an initiation/promotion protocol (Skisak et al. 1994).

Therefore, after consideration of the carcinogenicity data set, there is evidence for carcinogenicity for some LBPN substances in experimental animals following dermal exposure. There also appears to be evidence of tumour formation in rodents following inhalation exposure to gasoline. However, no inhalation studies examining site-restricted, or other, LBPN substances were identified.

No reproductive or developmental toxicity was observed for the majority of LBPN substances evaluated. Most of these studies were carried out by inhalation exposure in rodents.

NOAEC values for reproductive toxicity following inhalation exposure ranged from 1701 mg/m$^3$ (CAS RN 8052-41-3) to 27 687 mg/m$^3$ (CAS RN 64741-63-5) for the LBPNs group evaluated, and from 7690 mg/m$^3$ to 27 059 mg/m$^3$ for the site-restricted light catalytic cracked and full-range catalytic reformed naphthas (API 1978, 2008a, 2008b, 2008c, 2008d; Phillips and Egan 1981; Schreiner 1984; McKee et al. 1990; Dalbey et al. 1996; Bui et al. 1998; Schreiner et al. 1999, 2000b; Roberts et al. 2001). However, a decreased number of pups per litter and higher frequency of post-implantation loss were observed following inhalation exposure of female rats to hydrotreated heavy naphtha (CAS RN 64742-48-9) at a concentration of 4679 mg/m$^3$, 6 hours per day, from gestational days 7–20 (Hass et al. 2001). For dermal exposures, NOAEL values of 714 mg/kg-bw (CAS RN 8030-30-6) and 1000 mg/kg-bw per day (CAS RN 68513-02-0) were noted (Clark et al. 1988; ARCO 1994). For oral exposures, no adverse effects on reproductive parameters were reported when rats were given site-restricted light catalytic cracked naphtha at 2000 mg/kg on gestational day 13 (Stonybrook Laboratories, Inc. 1995).

For most LBPNs, no treatment-related developmental effects were observed by the different routes of exposure (API 1977d, 1978, 2008b, 2008c, 2008d; Litton Bionetics 1978; Miller and Schardein 1981; Phillips and Egan 1981; Schreiner 1984; Clark et al. 1988; Mobil 1988b; ARCO 1994; Stonybrook Laboratories 1995; Dalbey et al. 1996; Bui et al. 1998; Schreiner et al. 1999, 2000b; Roberts et al. 2001). However, developmental toxicity was observed for a few naphthas. Decreased fetal body weight and an increased incidence of ossification variations were observed when rat dams were exposed to light aromatized solvent naphtha, by gavage, at 1250 mg/kg-bw per day (Bio/Dynamics, Inc. 1991c). In addition, pregnant rats exposed by inhalation to hydrotreated heavy naphtha at 4679 mg/m$^3$ delivered pups with higher birth weights. Cognitive and memory impairments were also observed in the offspring (Hass et al. 2001).

Although a number of epidemiological studies have reported increases in the incidence of a variety of cancers, the majority of these studies are considered to contain incomplete or inadequate information. Limited data, however, are available for skin cancer and leukemia incidence, as well as mortality among petroleum refinery workers (Hendricks et al. 1959; Lione and Denholm 1959; McCraw et al. 1985; Divine and Barron 1986; Nelson et al. 1987; Wong and Raabe 1989). IARC (1989b) therefore concluded that there is limited evidence supporting the view that working in petroleum refineries entails a carcinogenic risk (Group 2A carcinogen). IARC (1989a) also classified gasoline as a

Group 2B carcinogen; it considered the evidence for carcinogenicity in humans from gasoline to be inadequate and noted that published epidemiological studies had several limitations, including a lack of exposure data and the fact that it was not possible to separate the effects of combustion products from those of gasoline itself. Similar conclusions were drawn from other reviews of epidemiological studies for gasoline (US EPA 1987a, 1987b). Thus, the evidence gathered from these epidemiological studies is considered to be inadequate to conclude on the effects of human exposure to LBPN substances.

**Characterization of Risk to Human Health**

Site-restricted LBPNs were identified as a high priority for action because they were considered to present a high hazard to human health. A critical effect for the initial categorization of site-restricted LBPN substances was carcinogenicity, based primarily on classifications by other international agencies. These substances are classified by the European Commission (2008) as Category 2 (benzene content ≥0.1% by weight), and by IARC as Group 2A and 2B (IARC 1989a, b). However, the LBPNs considered in this report have been identified as site-restricted (i.e., indicating that they are not expected to be transported off refinery or upgrader facility sites), and therefore general population exposure is not expected. Accordingly, the likelihood of exposure to Canadians is considered to be low; hence, the risk to human health is likewise considered to be low.

**Uncertainties in Evaluation of Risk to Human Health**

As the site-restricted LBPNs are considered to be UVCBs, their specific compositions are not well defined. LBPN streams under the same CAS RN can vary significantly in the number, identity and proportion of constituent compounds, depending on operating conditions, feedstocks and processing units. Consequently, it is difficult to obtain a truly representative toxicological dataset for individual CAS RNs. For this reason, all available toxicological data on LBPN substances with similar processing as well as physical and chemical properties were pooled across CAS RNs to develop a comprehensive toxicity profile. Specific physical and chemical properties of some LBPN substances were not available; therefore, properties of representative LBPNs were used as needed.

The scope of this screening assessment does not involve full investigation of the mode of induction of effects.

The PSSA screening assessments evaluate substances that are complex mixtures (UVCBs) composed of a number of components in various proportions due to the source of the crude oil or bitumen and its subsequent processing. Monitoring information or provincial release limits from petroleum facilities target broad releases (such as oils and greases) to water or air. These widely encompassing release categories do not allow for detection of individual complex mixtures or production streams. As such, the monitoring of broad releases cannot provide sufficient data to associate a detected release with a specific substance identified by a CAS RN, and the proportion of releases attributed to individual CAS RNs cannot be defined.

## Conclusion

Based on the available information, all of the LBPNs in this report are likely to have high proportions of $C_4$–$C_6$ hydrocarbons that are considered to be persistent in air, based on criteria in the *Persistence and Bioaccumulation Regulations* of CEPA 1999.

Based on the available information, none of the LBPNs considered here contain components that are considered to be bioaccumulative based on criteria in the *Persistence and Bioaccumulation Regulations* of CEPA 1999.

Based on the information presented in this screening assessment, the basis for initial categorization for human health hazard was carcinogenicity. Genotoxicity assays *in vivo* were essentially negative. Mixed results, however, were obtained *in vitro*, suggesting that some LBPNs have the potential to be mutagenic. LBPNs also appear to have limited potential to adversely affect reproduction and development.

The LBPNs listed in this screening assessment (64741-54-4, 64741-55-5, 64741-64-6, 64741-74-8, 64742-22-9, 64742-23-0, 64742-73-0, 68410-05-9, 68410-71-9, 68410-96-8, 68476-46-0, 68477-89-4, 68478-12-6, 68513-02-0, 68514-79-4, 68606-11-1, 68783-12-0, 68919-37-9, 68955-35-1 and 101795-01-1) are restricted to refinery and/or upgrader facilities; therefore, exposure of the general population and the environment is not expected. It is concluded that these site-restricted LBPNs are not entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity; that constitute or may constitute a danger to the environment on which life depends; or that constitute or may constitute a danger in Canada to human life or health.

It is therefore concluded that these site-restricted LBPNs do not meet the criteria set out in section 64 of CEPA 1999.

Because these substances are listed on the DSL, their import and manufacture in Canada are not subject to notification under subsection 81(1) of CEPA 1999. Given the potential hazardous properties of these substances, there is concern that new activities that have not been identified or assessed could lead to these substances meeting the criteria set out in section 64 of the Act. Therefore, application of the Significant New Activity provisions of the Act to these substances if being considered, so that any proposed new manufacture, import or use of these substances outside a petroleum refinery or upgrader facility is subject to further assessment, to determine if the new activity requires further risk management consideration.

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# Appendix 1: Description of the Nine Groups of Petroleum Substances

**Table A1.1. Description of the nine groups of petroleum substances**

| Group[1] | Description | Example |
|---|---|---|
| Crude oil | Mixture of aliphatic and aromatic hydrocarbons and small amounts of inorganic compounds, naturally occurring under the Earth's surface or under the sea floor | Crude oil |
| Petroleum and refinery gases | Mixture of light hydrocarbons primarily from $C_1$ to $C_5$ | Propane |
| Low boiling point naphthas | Mixture of hydrocarbons primarily from $C_4$ to $C_{12}$ | Gasoline |
| Gas oils | Mixture of hydrocarbons primarily from $C_9$ to $C_{25}$ | Diesel |
| Heavy fuel oils | Mixture of heavy hydrocarbons primarily from $C_{20}$ to $C_{50}$ | Fuel Oil No. 6 |
| Base oils | Mixture of hydrocarbons primarily from $C_{15}$ to $C_{50}$ | Lubricating oils |
| Aromatic extracts | Mixture of primarily aromatic hydrocarbons from $C_{15}$ to $C_{50}$ | Feedstock for benzene production |
| Waxes, slack waxes and petrolatum | Mixture of primarily aliphatic hydrocarbons from $C_{12}$ to $C_{85}$ | Petrolatum |
| Bitumen or vacuum residues | Mixture of heavy hydrocarbons having carbon numbers greater than $C_{25}$ | Asphalt |

[1] Groupings were based on classifications developed by CONservation of Clean Air and Water in Europe (CONCAWE) and a contractor's report commissioned by the Canadian Petroleum Products Institute (CPPI) (Simpson 2005).

# Appendix 2: Process Flow Diagrams for Low Boiling Point Naphthas

Red dotted line indicates the process relevant to the particular CAS RN.
FCCU: fluid catalytic cracking unit; LPG: liquified petroleum gas

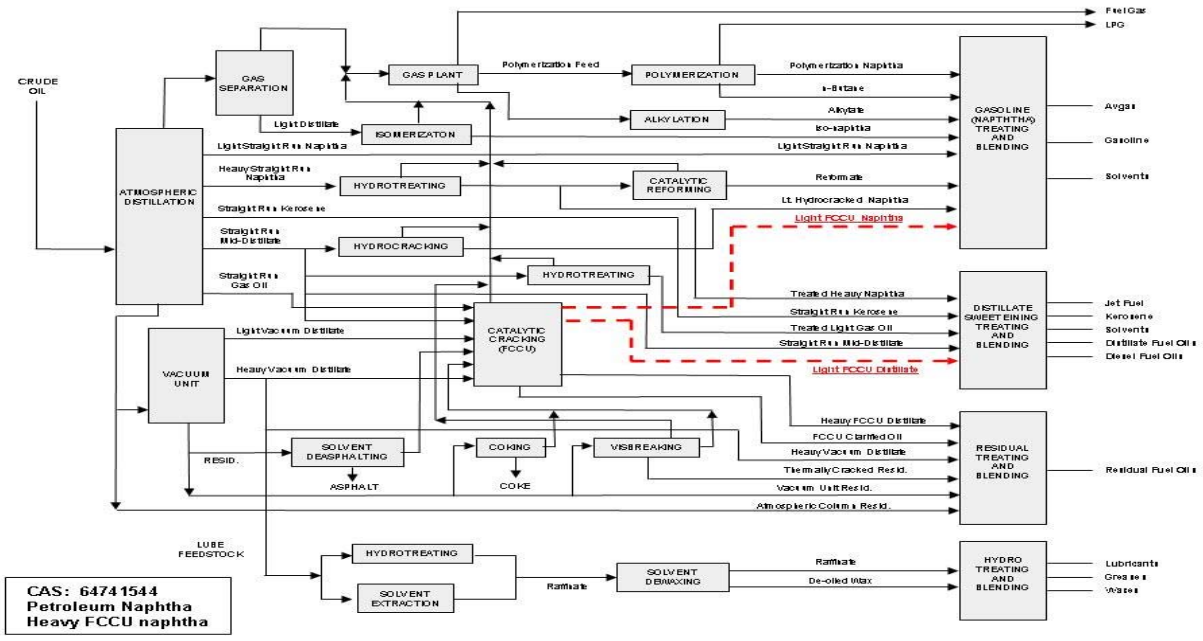


**Figure A2.1. Process flow diagram for CAS RN 64741-54-4 (Hopkinson 2008)**
CAS RN 64741-54-4 is shown to be a processing intermediate formed after processing in the FCCU (fluid catalytic cracking unit) in a refinery.

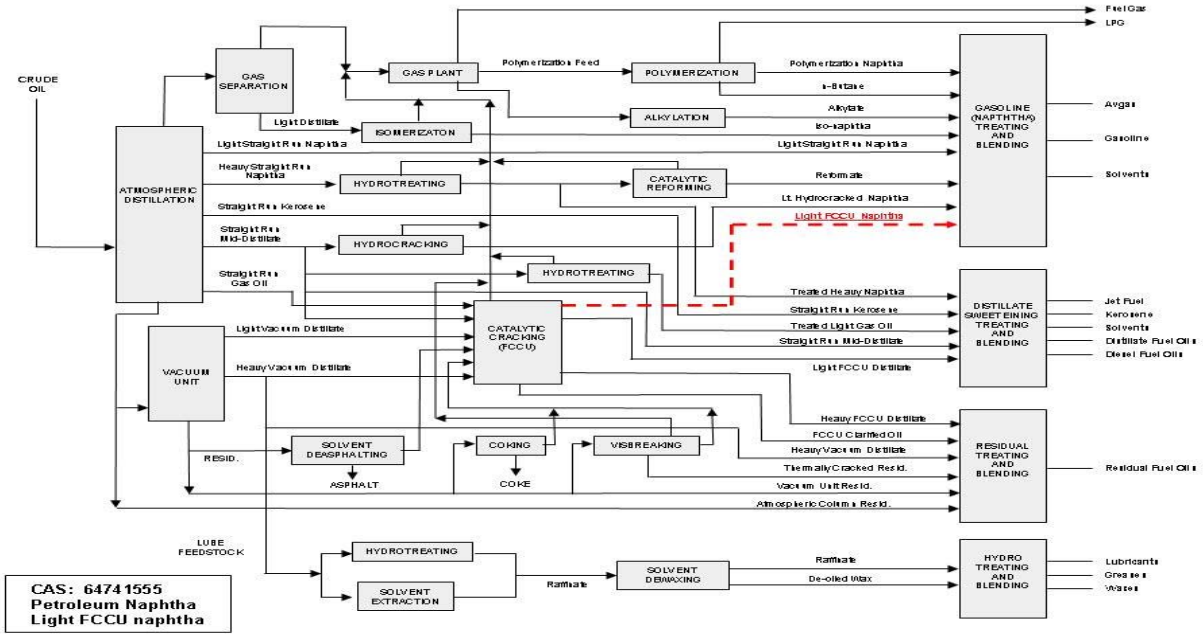


**Figure A2.2. Process flow diagram for CAS RN 64741-55-5 (Hopkinson 2008)**
CAS RN 64741-55-5 is shown to be a processing intermediate formed after processing in the FCCU in a refinery.

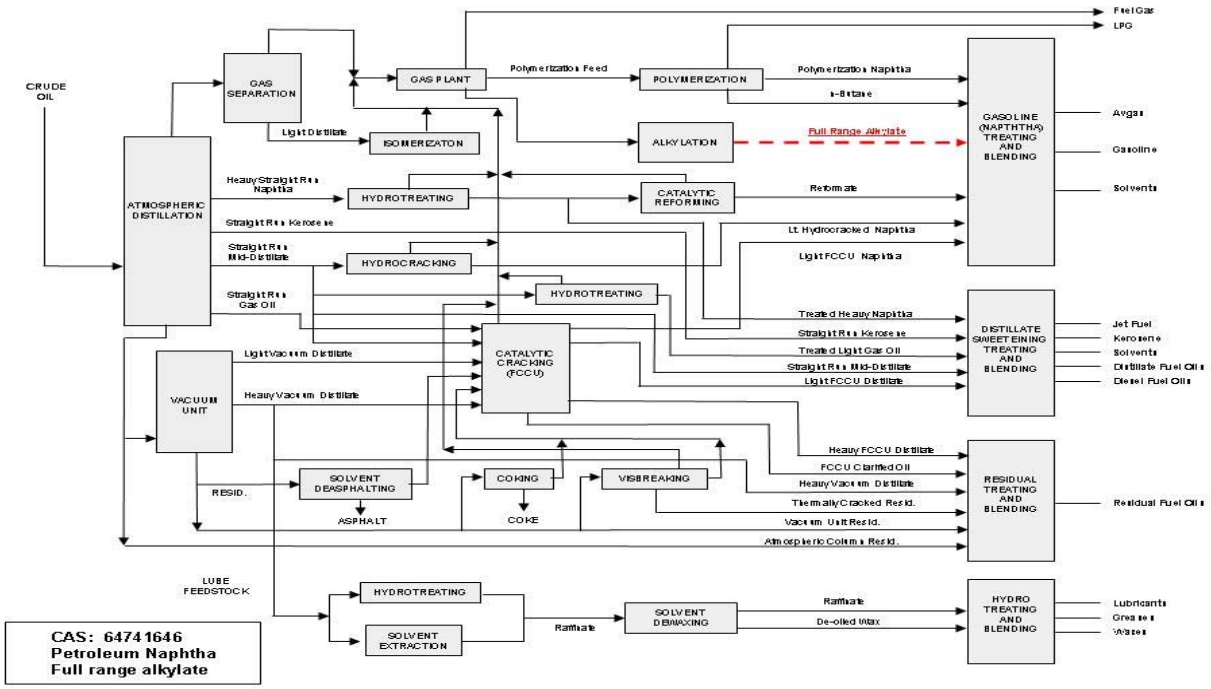


**Figure A2.3. Process flow diagram for CAS RN 64741-64-6 (Hopkinson 2008)**
CAS RN 64741-64-4 is shown to be a processing intermediate formed in an alkylation unit in a refinery.

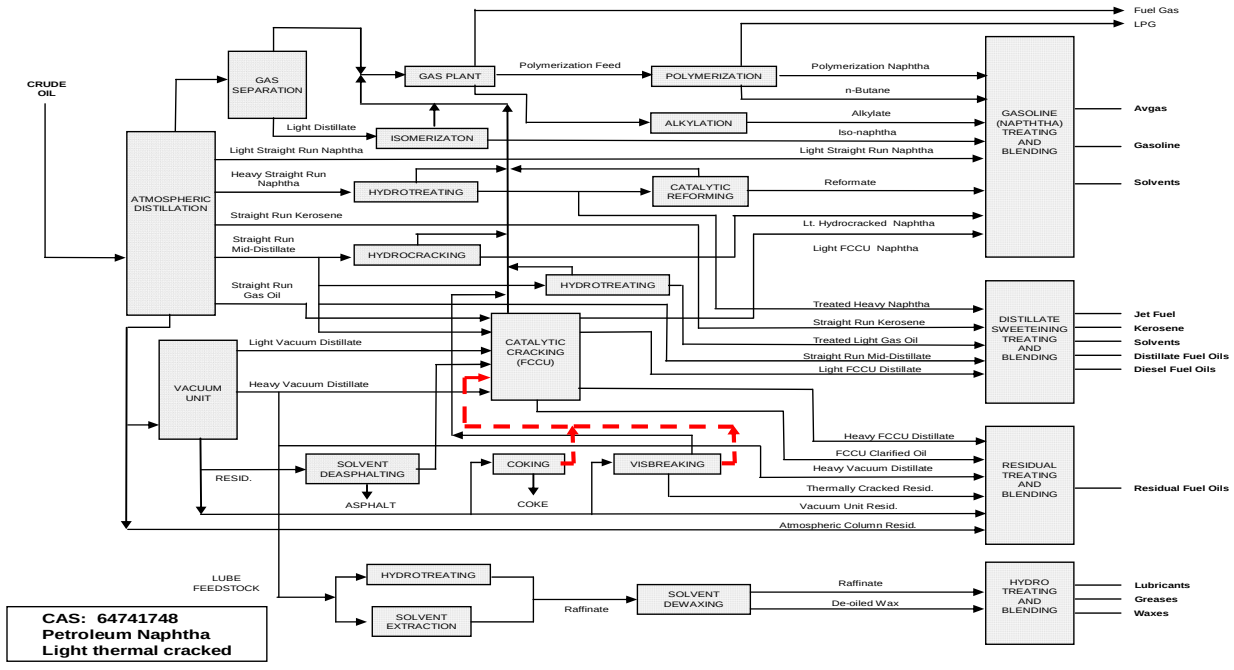


**Figure A2.4a. Process flow diagram for CAS RN 64741-74-8, refinery (Hopkinson 2008)**
CAS RN 64741-74-8 is shown to be a processing intermediate (distillate) formed after fractionation in a thermal cracking unit (coking or visbreaking) in a refinery.

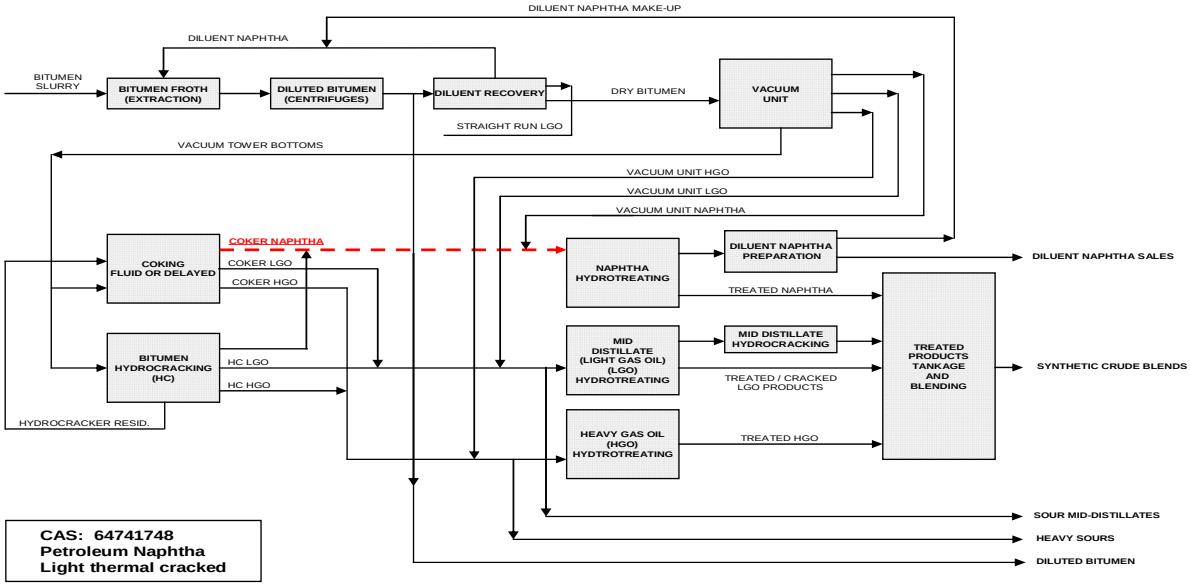


**Figure A2.4b. Process flow diagram for CAS RN 64741-74-8, upgrader (Hopkinson 2008)**
CAS RN 64741-74-8 is shown to be a processing intermediate (distillate) formed after fractionation in a thermal cracker (coker) in an upgrader.

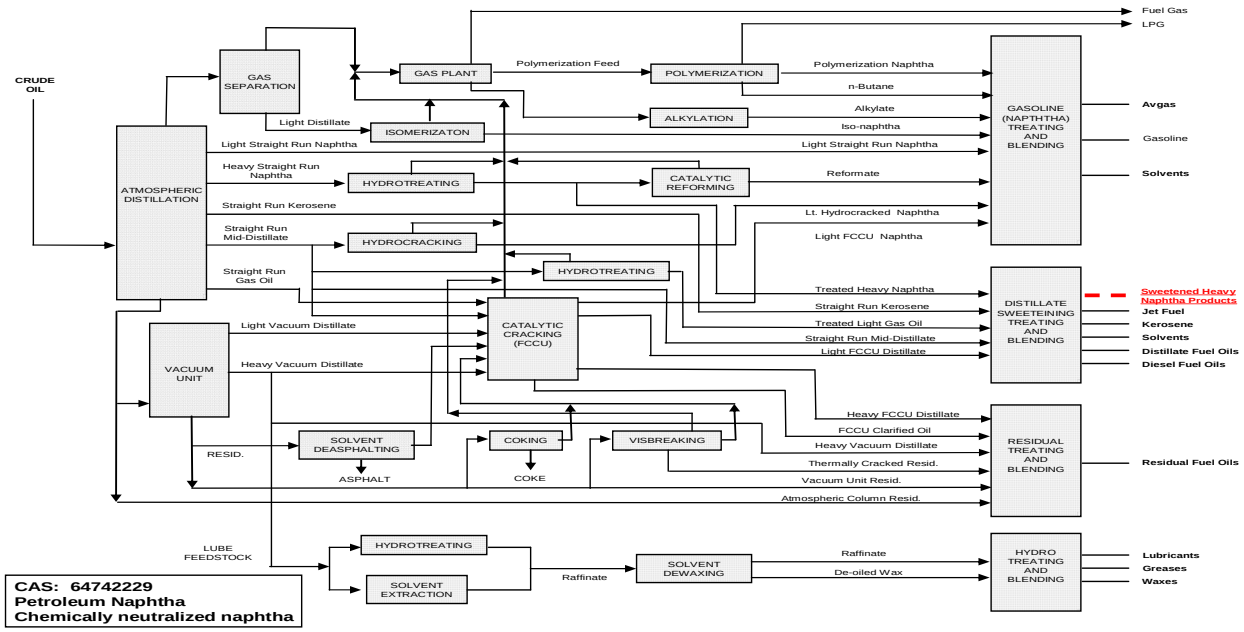


**Figure A2.5. Process flow diagram for CAS RN 64742-22-9 (Hopkinson 2008)**
CAS RN 64742-22-9 is shown to be formed after distillate sweetening (sulfur removal), treating and blending in a refinery to remove acids from heavy naphtha.

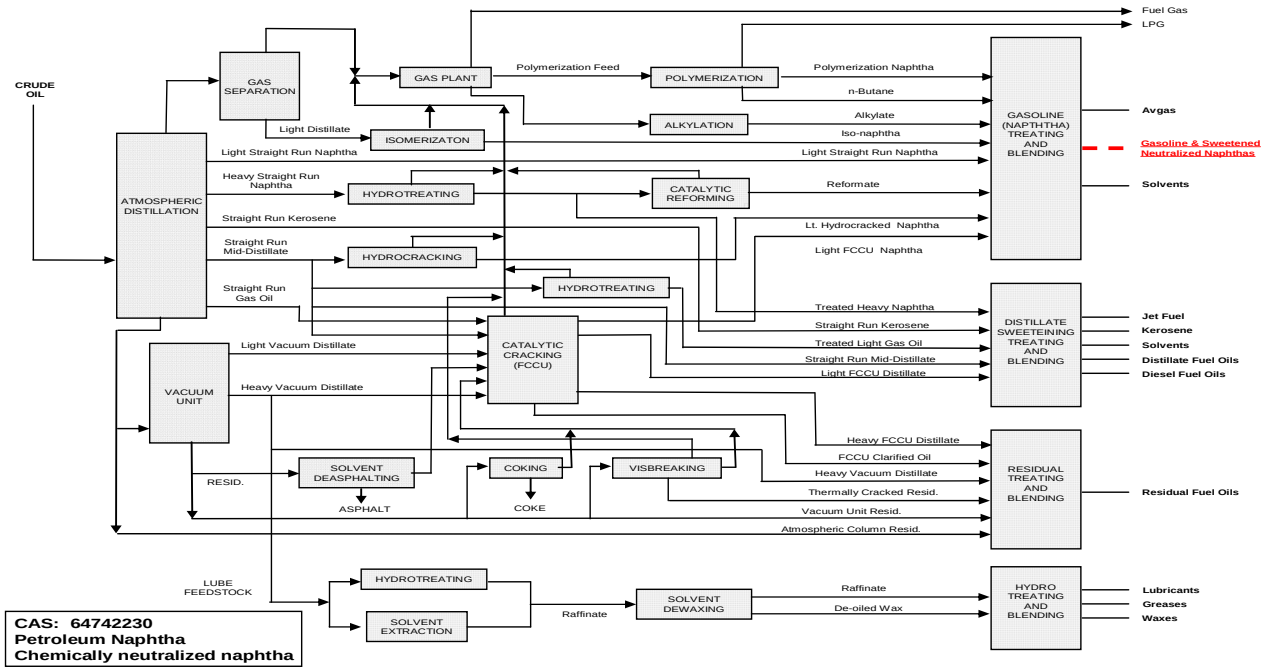


**Figure A2.6. Process flow diagram for CAS RN 64742-23-0 (Hopkinson 2008)**

CAS RN 64742-23-0 is shown to be formed after treating and blending in a refinery to remove acids from light naphtha.

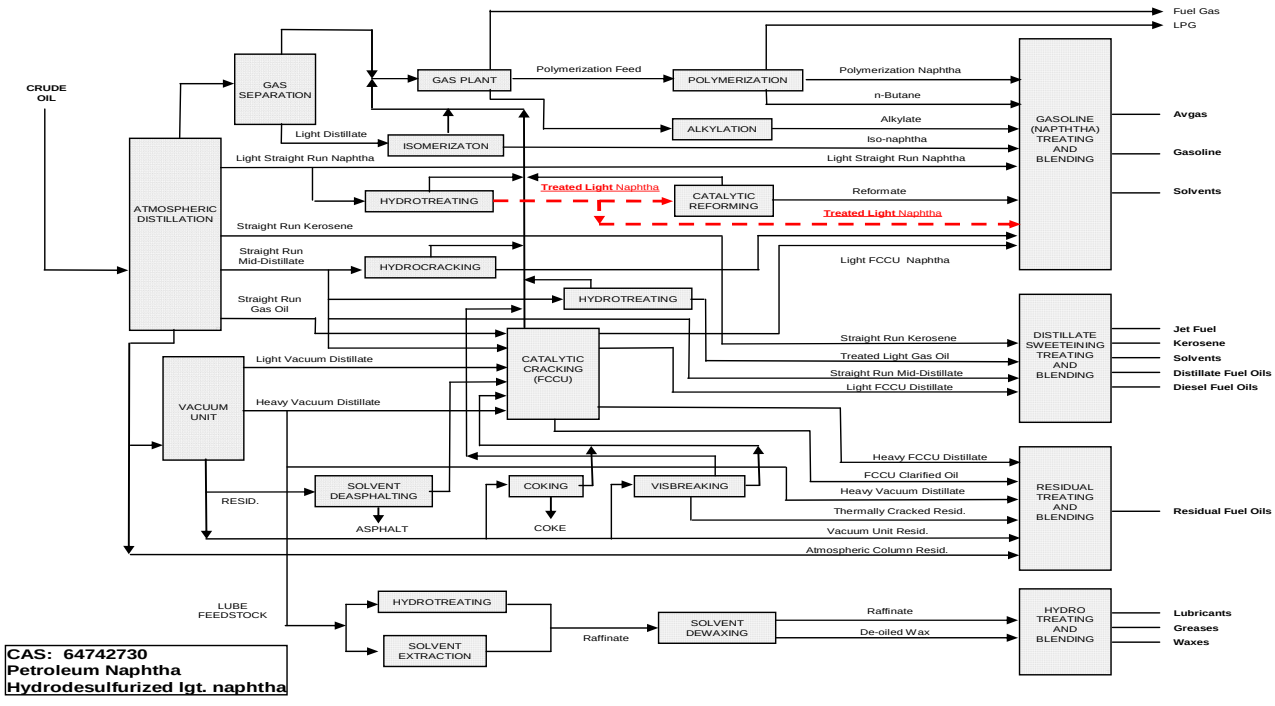


**Figure A2.7a. Process flow diagram for CAS RN 64742-73-0, refinery (Hopkinson 2008)**

CAS RN 64742-73-0 is shown to be a processing intermediate (bottom substance) formed after hydrotreating in a refinery.

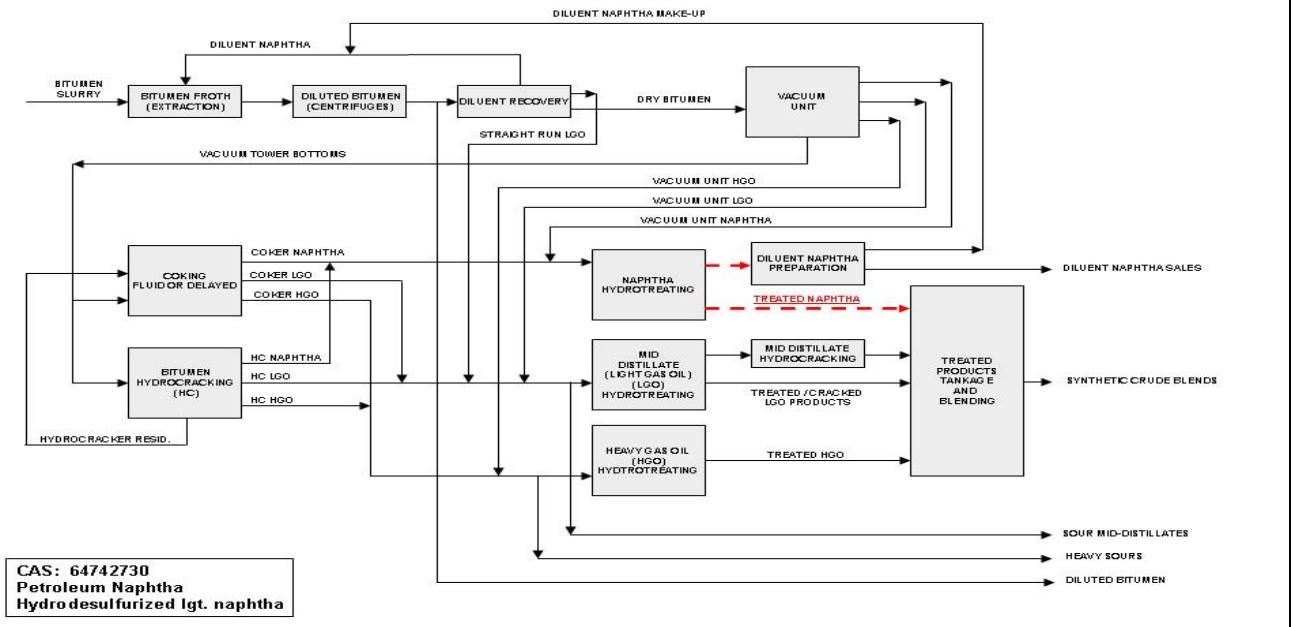


**Figure A2.7b. Process flow diagram for CAS RN 64742-73-0, upgrader (Hopkinson 2008)**
CAS RN 64742-73-0 is shown to be formed after hydrotreating in an upgrader.

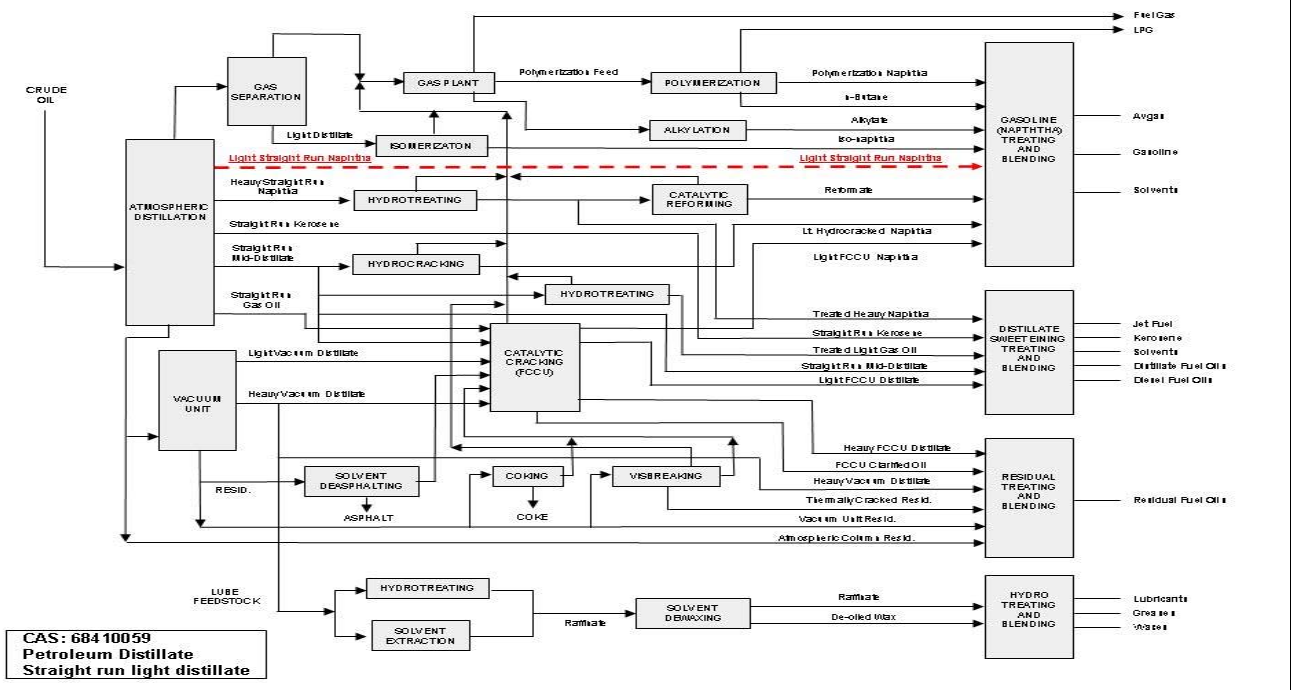


**Figure A2.8. Process flow diagram for CAS RN 68410-05-9 (Hopkinson 2008)**
CAS RN 68470-05-9 is a light product shown to be a processing intermediate formed after distillation in a refinery.

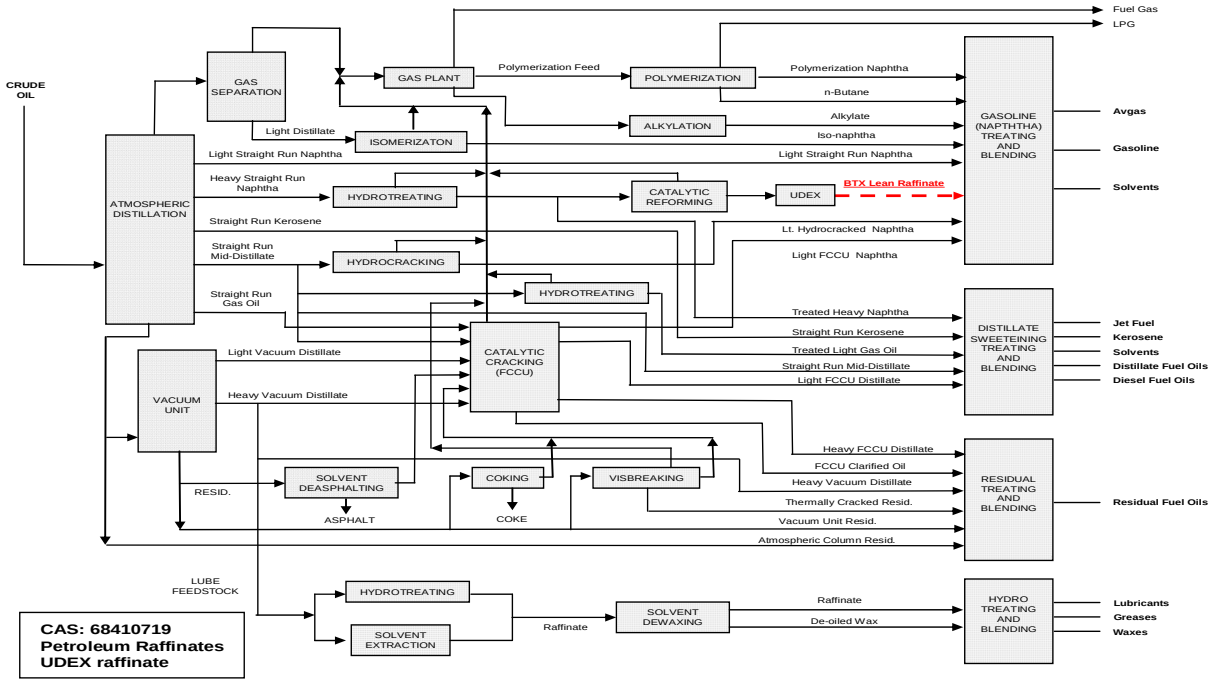


**Figure A2.9. Process flow diagram for CAS RN 68410-71-9 (Hopkinson 2008)**

CAS RN 68410-71-9 is shown to be a processing intermediate (raffinate) from an extraction column where aromatic compounds are removed from the product stream following catalytic reforming in a refinery.

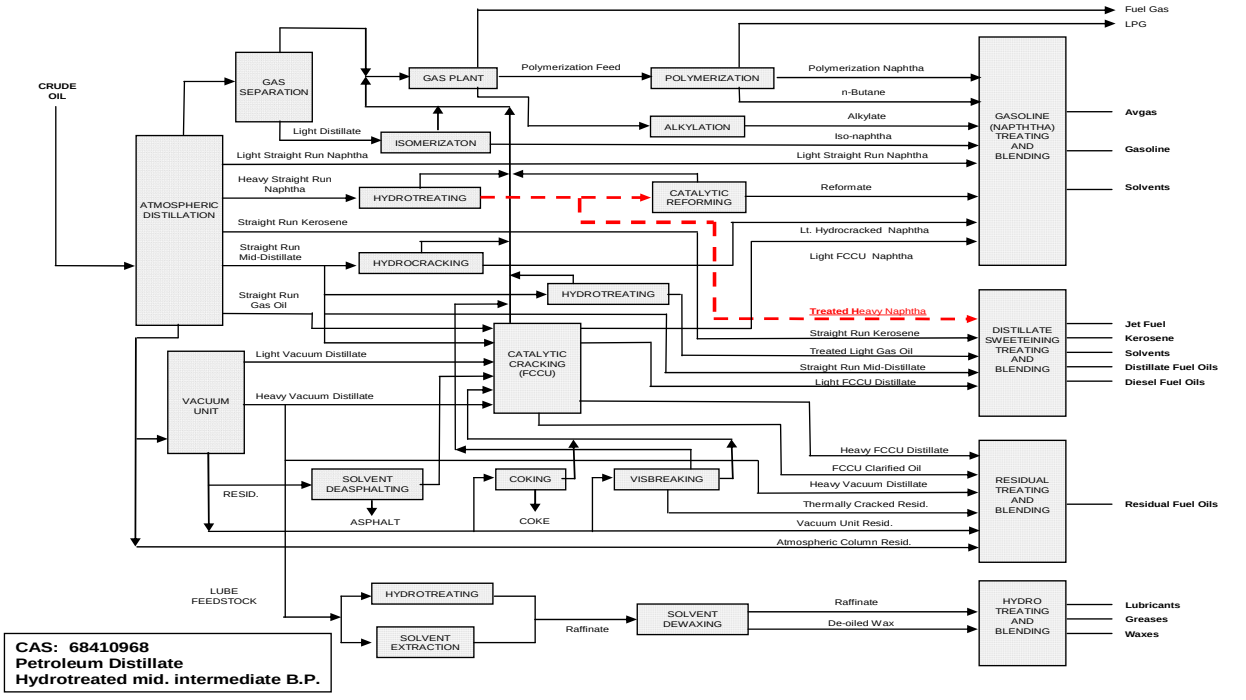


**Figure A2.10a. Process flow diagram for CAS RN 68410-96-8, refinery (Hopkinson 2008)**

CAS RN 68410-96-8 is shown to be a processing intermediate after hydrotreating heavy straight-run naphtha in a refinery.

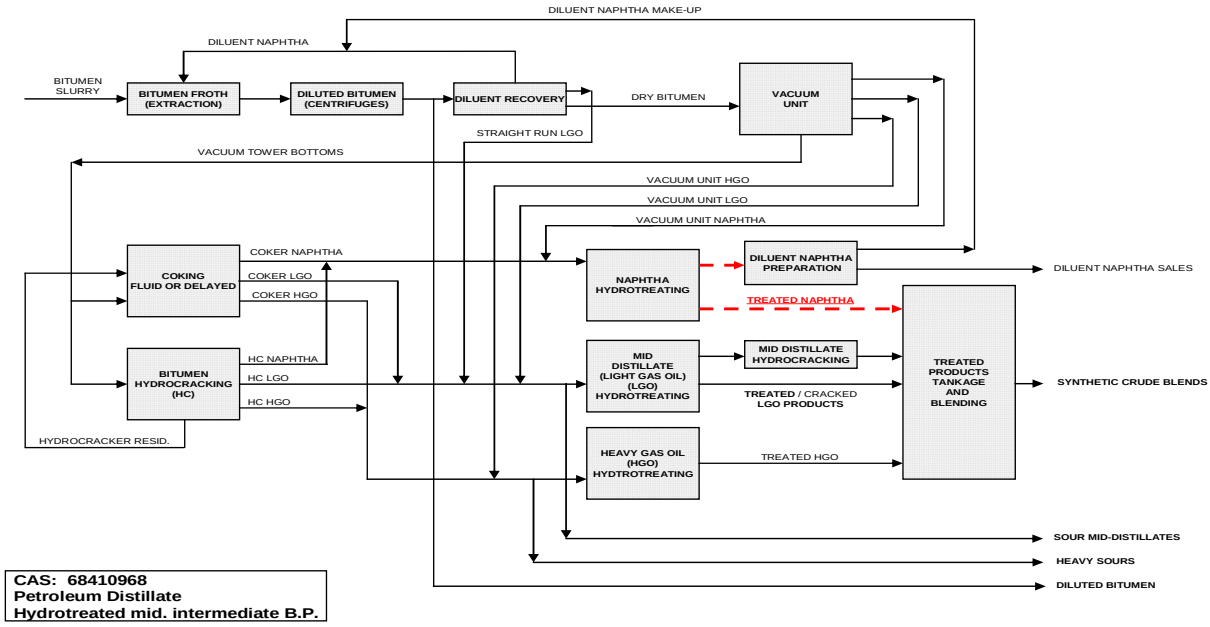


**Figure A2.10b. Process flow diagram for CAS RN 68410-96-8, upgrader (Hopkinson 2008)**
CAS RN 68410-96-8 is shown to be formed after hydrotreating heavy straight-run naphtha in an upgrader.

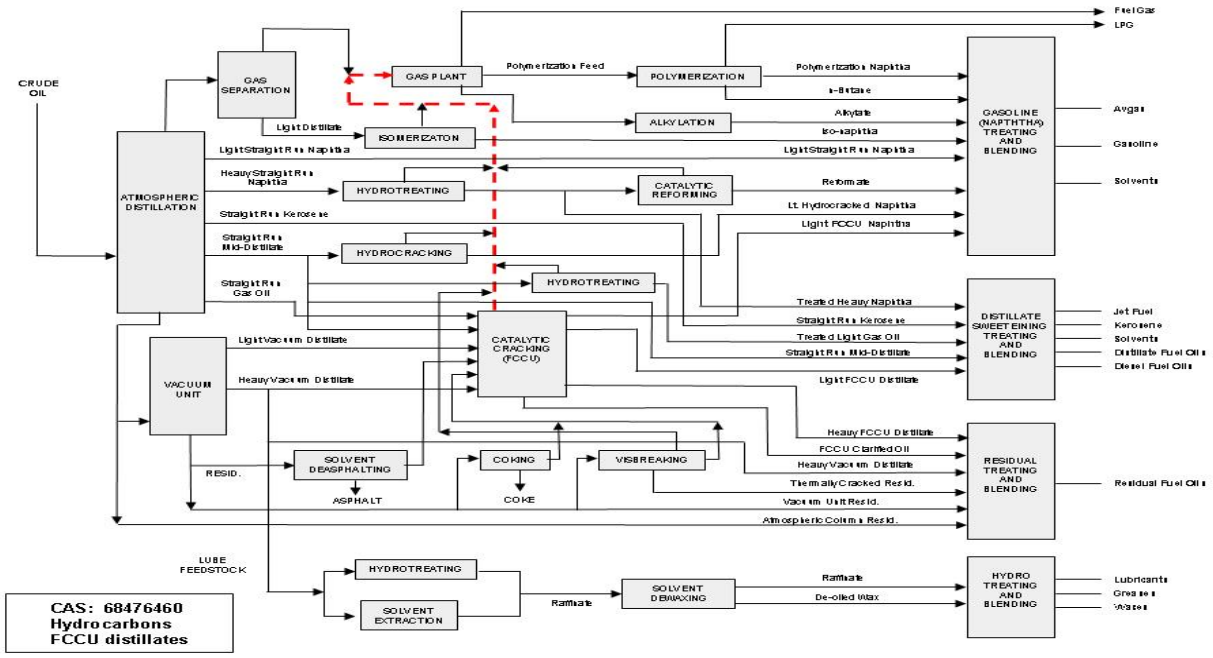


**Figure A2.11. Process flow diagram for CAS RN 68476-46-0 (Hopkinson 2008)**
CAS RN 68476-46-0 is shown to be a processing intermediate (distillate) formed after catalytic cracking in a refinery.

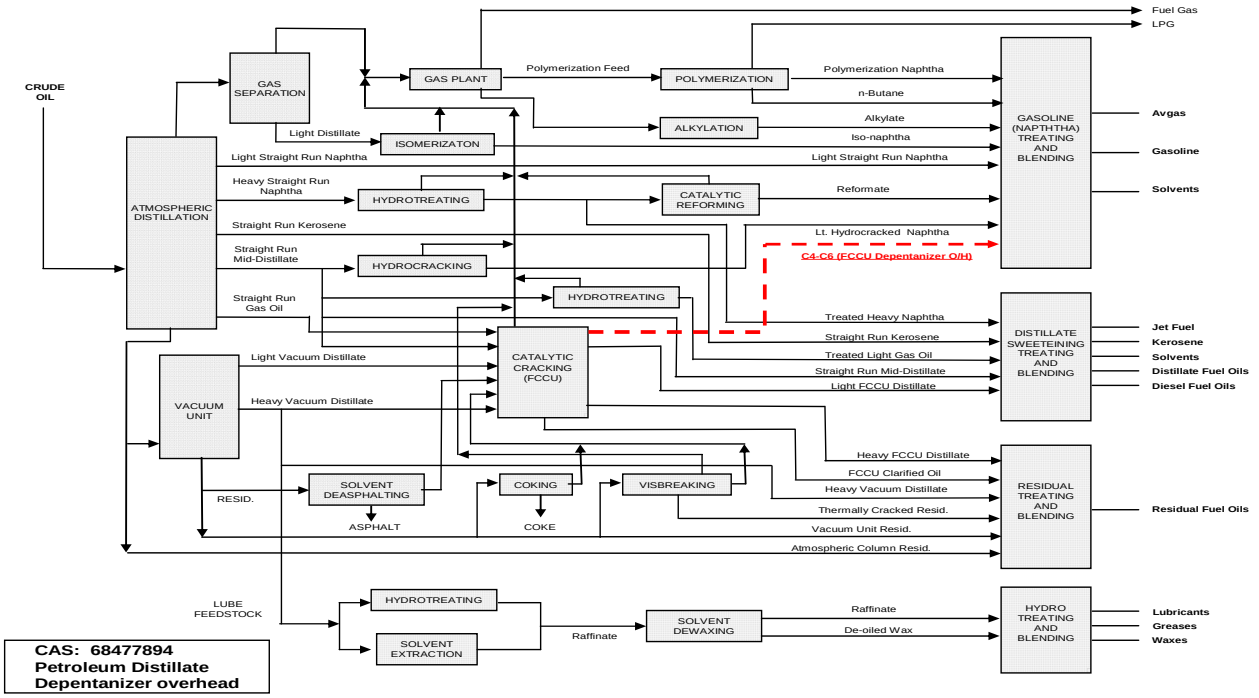


**Figure A2.12. Process flow diagram for CAS RN 68477-89-4 (Hopkinson 2008)**
CAS RN 68477-89-4 is shown to be a processing intermediate formed from a distillation column overhead product treated with a catalytic cracking process in a refinery.

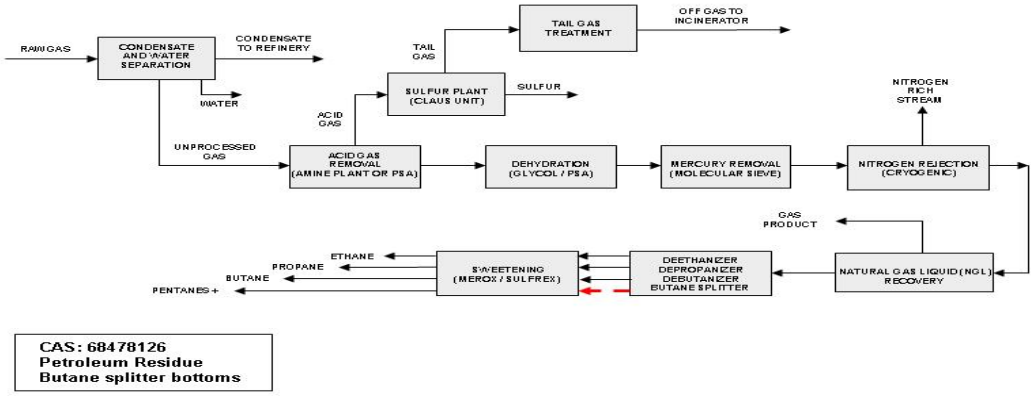


**Figure A2.13a. Process flow diagram for CAS RN 68478-12-6, gas plant (Hopkinson 2008)**
In a gas plant, distillation is not necessary due to the volatility of the compounds. CAS RN 68478-12-6 is shown to be formed after processing in the deethanizer/depropanizer/debutanizer to separate isobutene from heavier compounds.

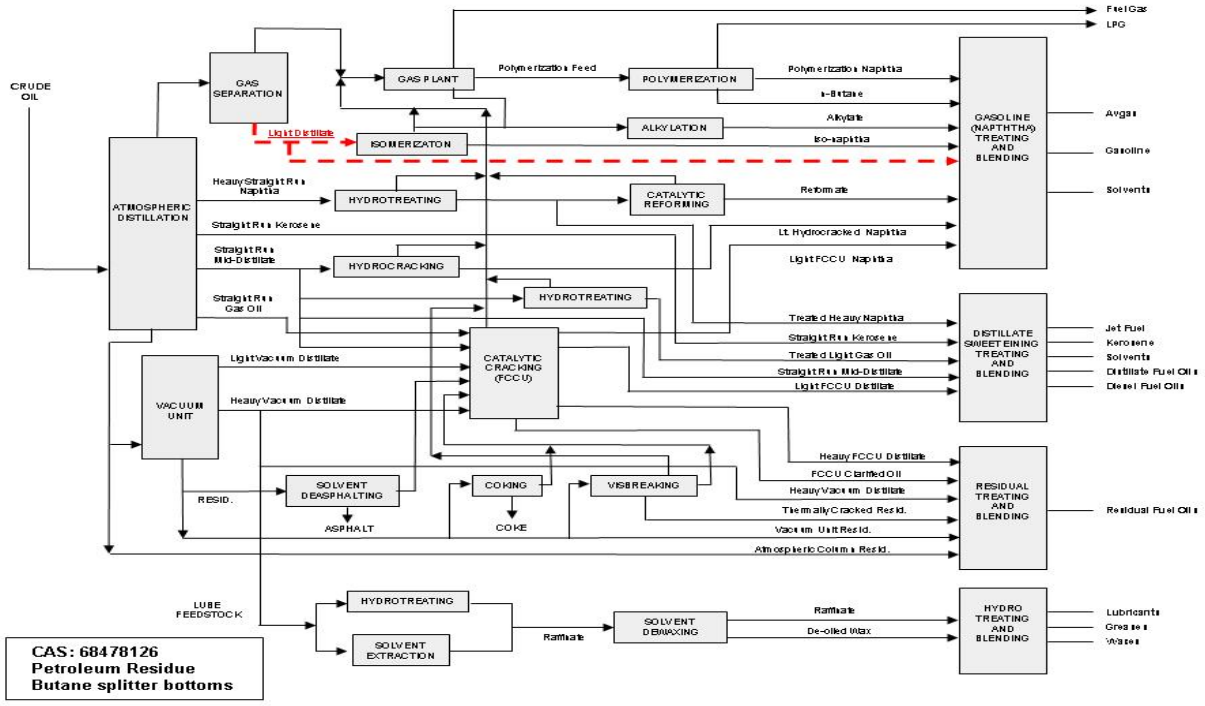


**Figure A2.13b. Process flow diagram for CAS RN 68478-12-6, refinery (Hopkinson 2008)**
CAS RN 68478-12-6 is shown to be a bottom product from a gas separation unit in a refinery.

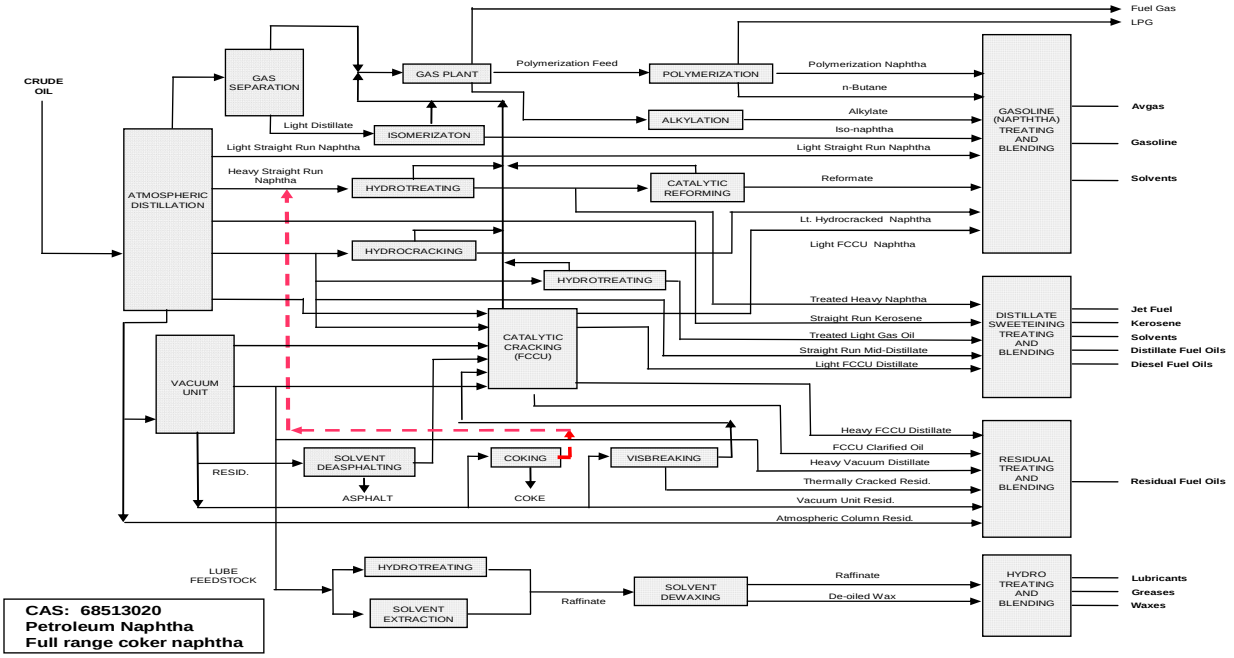


**Figure A2.14a. Process flow diagram for CAS RN 68513-02-0, refinery (Hopkinson 2008)**
CAS RN 68513-02-0 is shown to be a processing intermediate that represents an overhead distillate stream from a fractionation column in a coking unit.

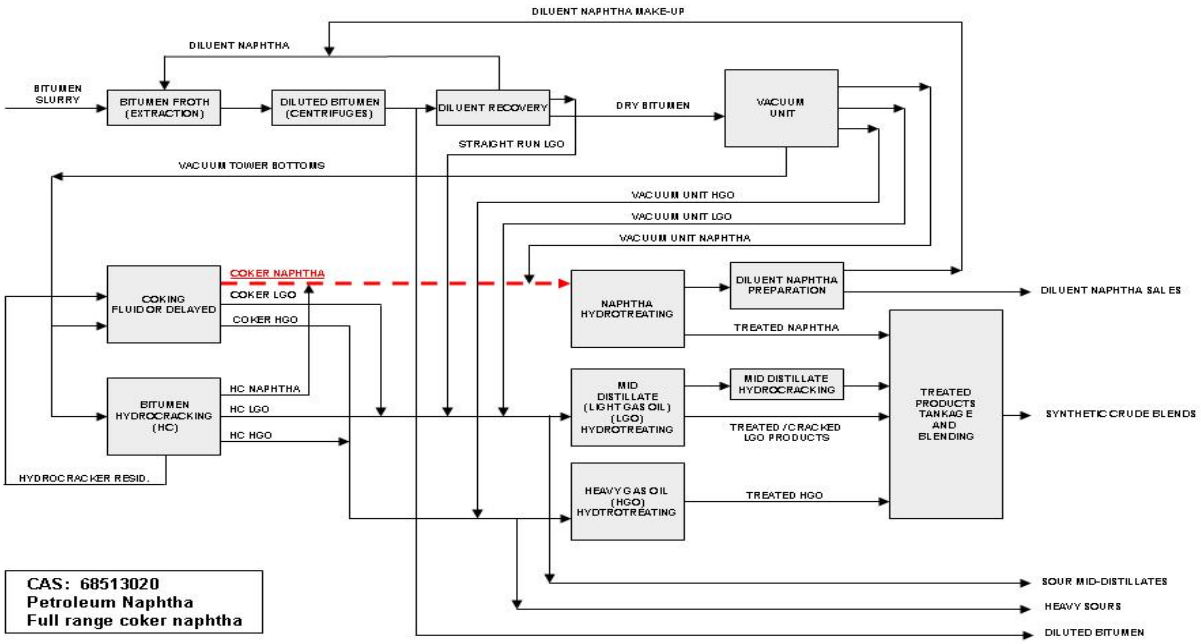


**Figure A2.14b. Process flow diagram for CAS RN 68513-02-0, upgrader (Hopkinson 2008)**
CAS RN 68513-02-0 is shown to be a processing intermediate formed after fractionation in a coking unit.

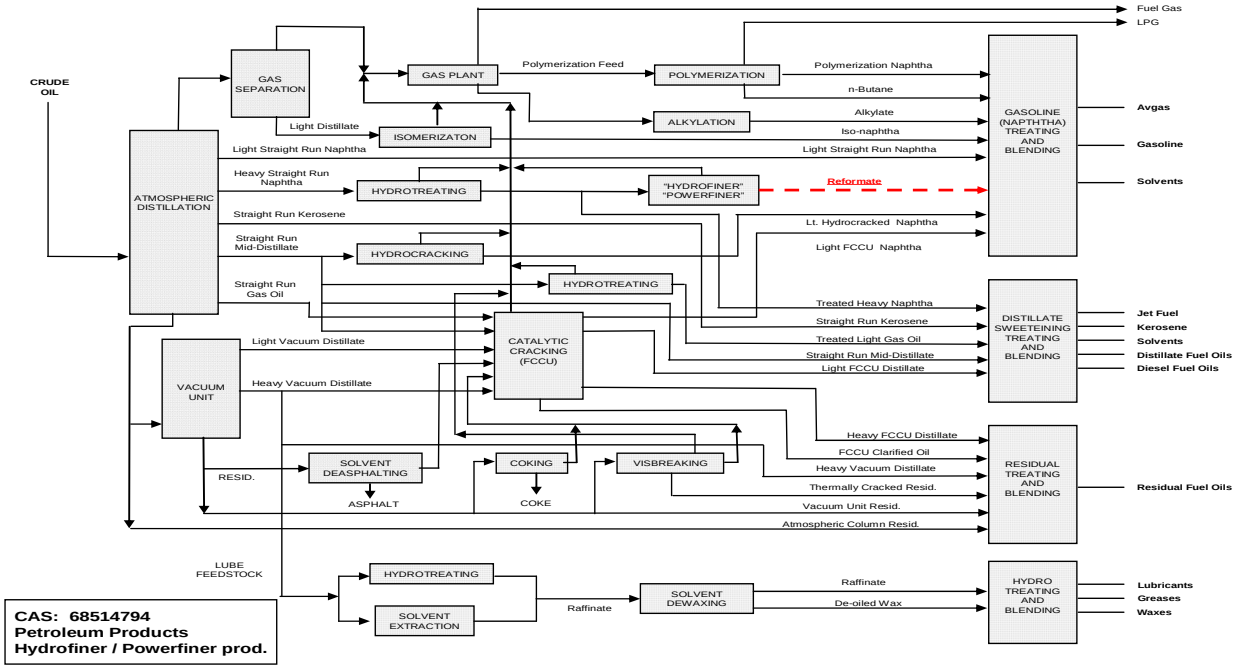


**Figure A2.15. Process flow diagram for CAS RN 68514-79-4 (Hopkinson 2008)**
CAS RN 68514-79-4 is shown to be a processing intermediate formed after hydrofining or powerfining in a refinery.

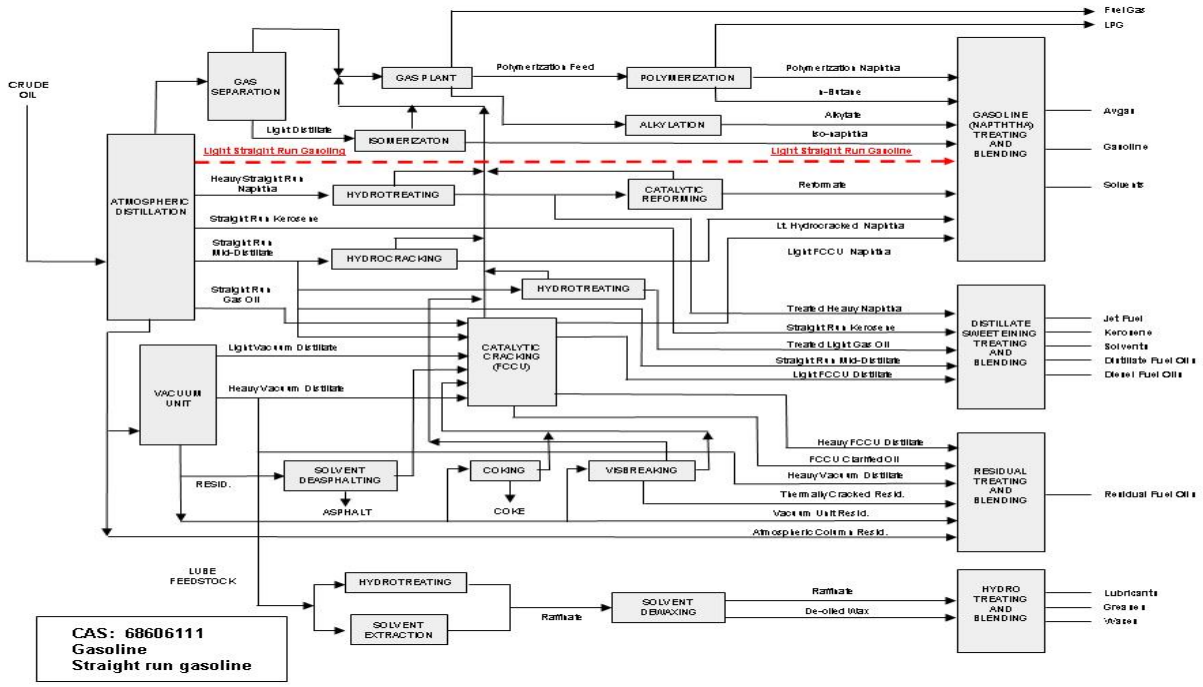


**Figure A2.16. Process flow diagram for CAS RN 68606-11-1 (Hopkinson 2008)**
CAS RN 68606-11-1 is shown to be a processing intermediate coming directly from the atmospheric distillation column in a refinery.

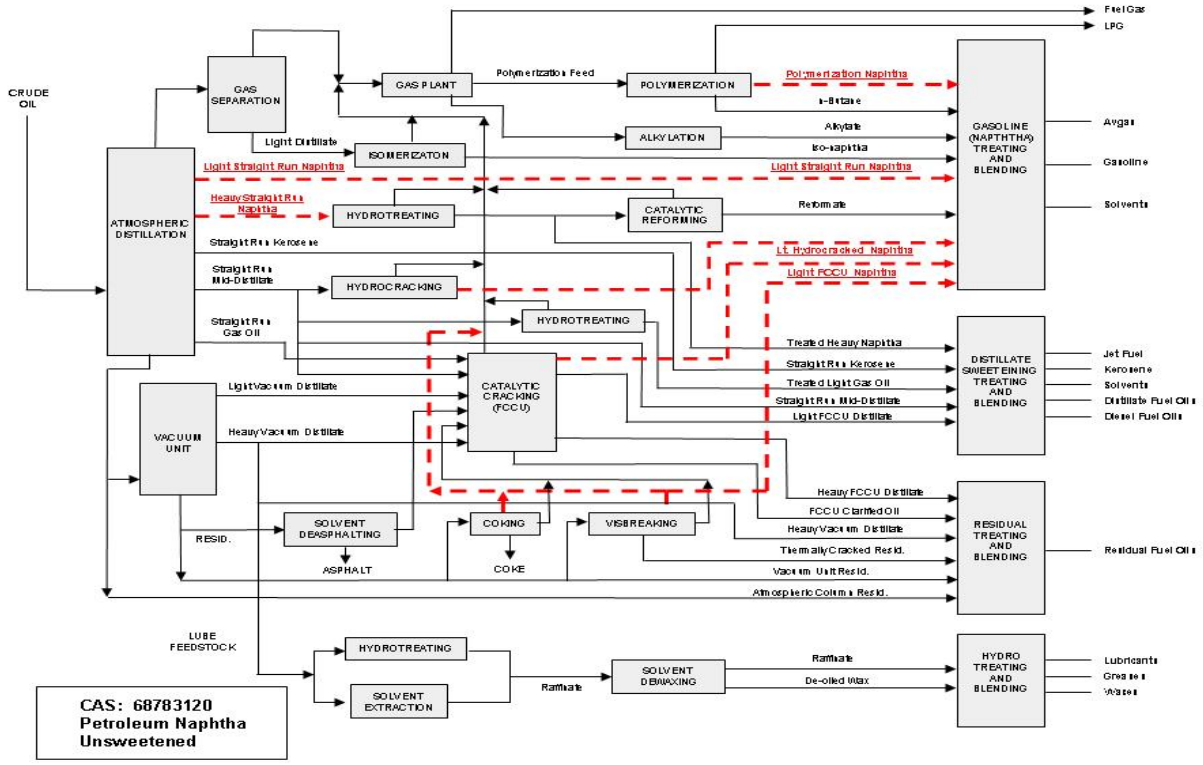


**Figure A2.17a. Process flow diagram for CAS RN 68783-12-0, refinery (Hopkinson 2008)**
CAS RN 68783-12-0 is shown to be a processing intermediate produced from various distillation processes in a refinery.

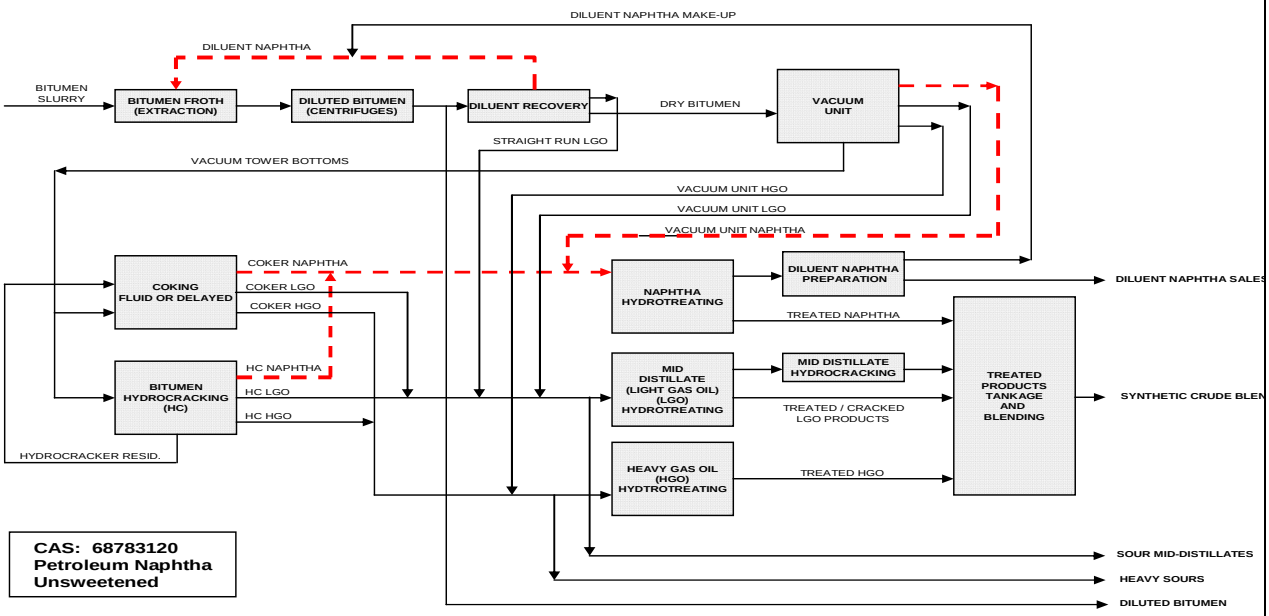


**Figure A2.17b. Process flow diagram for CAS RN 68783-12-0, upgrader (Hopkinson 2008)**
CAS RN 68783-12-0 is shown to be a processing intermediate that describes naphthas formed after various processes in an upgrader.

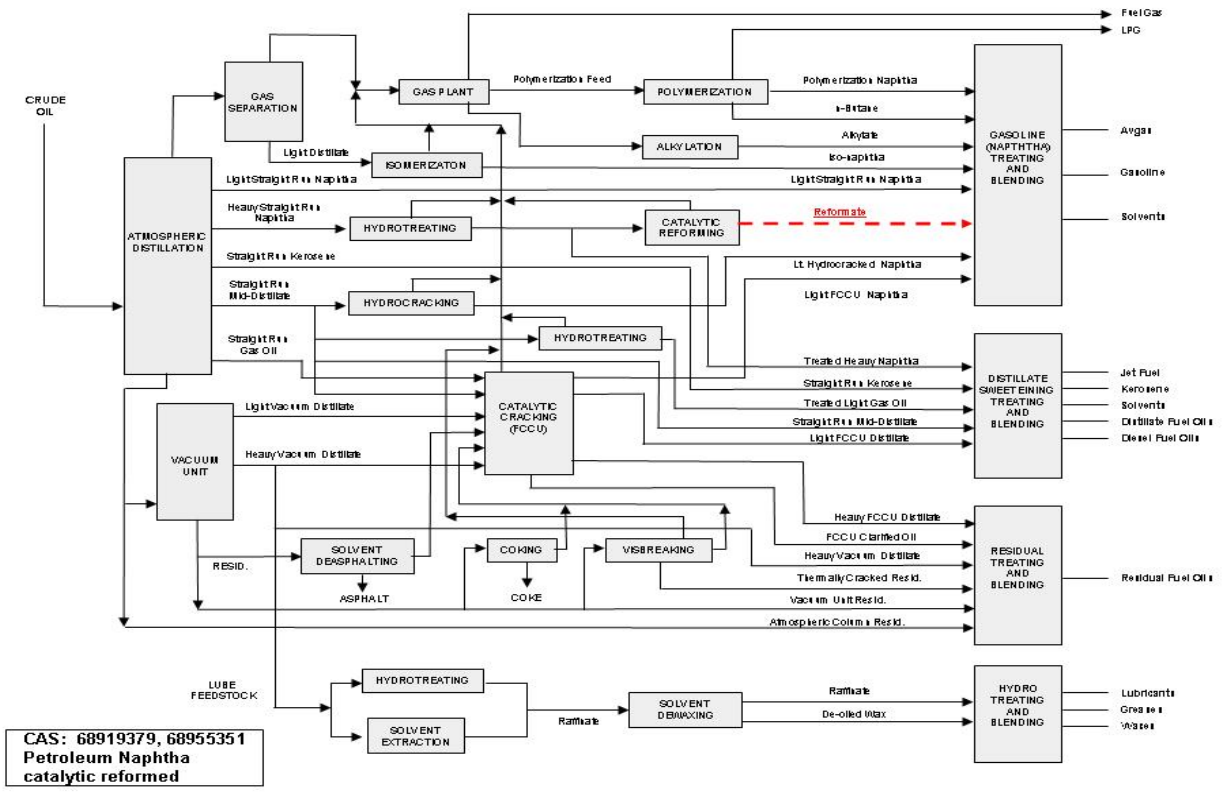


**Figure A2.18. Process flow diagram for CAS RN 68919-37-9 (Hopkinson 2008)**

CAS RN 68919-37-9 is shown to be a processing intermediate that is represented as a product of a distillation column fed with effluent from a catalytic reforming process.

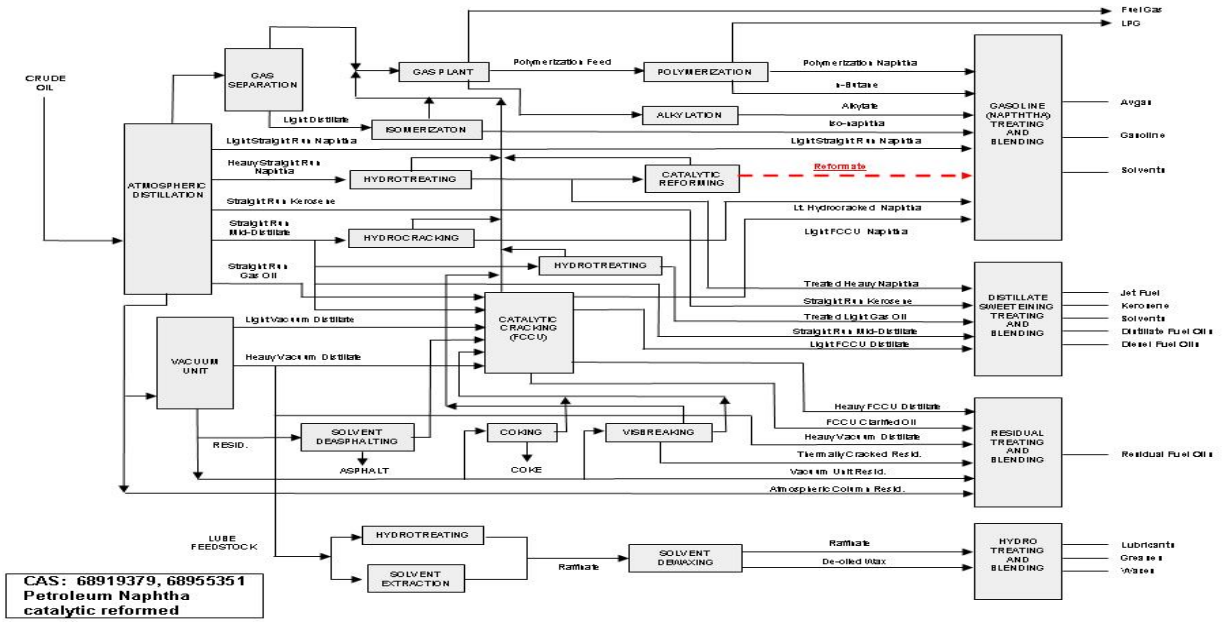


**Figure A2.19. Process flow diagram for CAS RN 68955-35-1 (Hopkinson 2008)**

CAS RN 68955-35-1 is shown to be a processing intermediate from a distillation column fed with effluent from a catalytic reforming process.

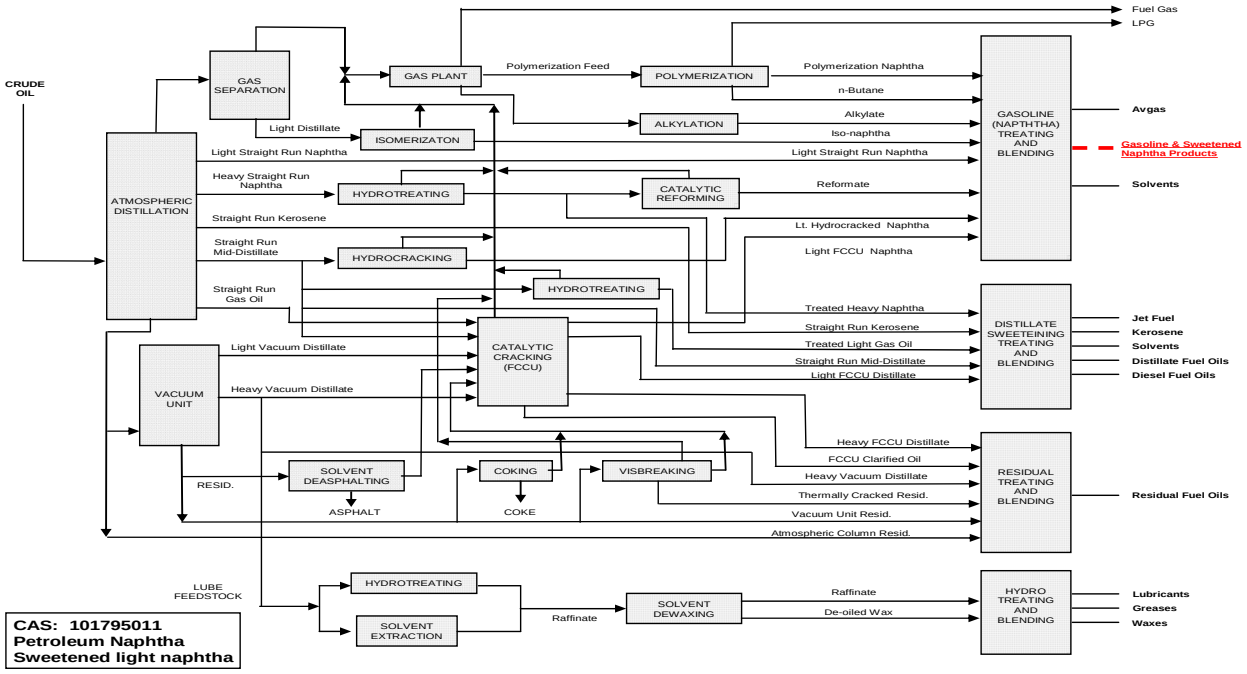


**Figure A2.20. Process flow diagram for CAS RN 101795-01-1 (Hopkinson 2008)**
CAS RN 101795-01-1 is formed after mercaptans and other acid compounds are removed through sweetening.

# Appendix 3: Data Tables for Site-restricted Low Boiling Point Naphthas

**Table A3.1. Detailed hydrocarbon analysis of CAS RN 68919-37-9 (API 2003a)**

| Carbon number | % | | | | |
|---|---|---|---|---|---|
| | **Alkanes** | **Isoalkanes** | **Cycloalkanes** | **Alkenes** | **Aromatics** |
| $C_4$ | 1.6 | 0.5 | 0.0 | 0.0 | 0.0 |
| $C_5$ | 3.3 | 6.1 | 0.1 | 0.7 | 0.0 |
| $C_6$ | 2.9 | 7.2 | 0.4 | 0.5 | 8.8 |
| $C_7$ | 1.2 | 4.5 | 0.2 | 0.3 | 22.7 |
| $C_8$ | 0.7 | 0.2 | 0.1 | 0.1 | 22.6 |
| $C_9$ | 0.0 | 0.1 | 0.2 | 0.0 | 8.8 |
| $C_{10}$ | 0.0 | 1.0 | 1.6 | 0.0 | 0.6 |
| Total | 9.4 | 20.8 | 2.7 | 1.6 | 63.8 |

**Table A3.2. Physical and chemical properties of representative structures contained in low boiling point naphthas[1,2]**

| Chemical class, name and CAS RN | Boiling point (°C) | Melting point (°C) | Vapour pressure (Pa) | Henry's Law constant (Pa·m$^3$/mol) | Log $K_{ow}$ | Log $K_{oc}$ | Aqueous solubility (mg/L at 25°C, unless otherwise stated) |
|---|---|---|---|---|---|---|---|
| **Alkanes** | | | | | | | |
| $C_4$ Butane (106-97-8) | −0.5 (e) | −138.2 (e) | $2.43 \times 10^5$ (e) | $9.63 \times 10^4$ (e) | 2.89[a] (e) | 3.00 | 61[b] |
| $C_6$ Hexane (110-54-3) | 68.7[c] | −95.3[c] (e) | $2.0 \times 10^4$ (e) | $1.8 \times 10^5$ | 3.90[a] (e) | 2.17 | 9.5[d]–13 (20°C) fresh; 75.5 (20°C) salt[c] |
| $C_9$ Nonane (111-84-2) | 150.8[b] (e) | −53.5[b] (e) | $5.93 \times 10^2$ (e) | $3.4 \times 10^5$ (e) | 5.65[b] (e) | 2.97 | 0.22 (e) |
| $C_{12}$ Dodecane (112-40-3) | 216.3[b] (e) | −9.6[b] (e) | 18[d] (e) | $8.29 \times 10^5$ (e) | 6.10[b] (e) | 3.77 | 0.0037[c] |
| **Isoalkanes** | | | | | | | |
| $C_4$ 2-Methyl propane (75-28-5) | −11.7[e] | −138.3 (e) | $3.48 \times 10^5$ (e) | $1.21 \times 10^5$ (e) | 2.76[e] | 1.55 | 49[b] |
| $C_6$ 2-Methyl pentane (43133-95-5) | 60.2[a] (e) | −153.7[a] (e) | $2.8 \times 10^4$ [a] (e) | $1.7 \times 10^5$ (e) | 3.21 | 2.10 | 14[a] (e) |
| $C_9$ 2,3-Dimethyl heptane (1071-26-7) | 133 (e) | −113[a] (e) | $1.4 \times 10^3$ | $6.4 \times 10^4$ | 4.61 | 2.85 | 0.700 |
| $C_{12}$ 2,3-Dimethyl decane (17312-44-6) | 181.36 | −43 | 165.3 | $2.5 \times 10^5$ | 6.09 | 3.64 | 0.113 |
| ***n*-Alkenes** | | | | | | | |
| $C_9$ Nonene (27215-95-8) | 149.5 | −56.7 | 500 (e) | $2.4 \times 10^4$ | 4.55 | 2.97 | 3.62 |
| $C_{12}$ 9-Methyl-1-undecene (74630-41-4) | 192.2 | −33 | 99.8 | $1.3 \times 10^5$ | 6 | 5.2 | 0.13 |
| **One-ring cycloalkanes** | | | | | | | |
| $C_6$ Cyclohexane (110-82-7) | 80.7[a] (e) | 6.6[a] (e) | $1.3 \times 10^4$ [a] (e) | $1.52 \times 10^4$ (e) | 3.44[e] | 2.22 | 55[a] (e) |
| $C_9$ 1,2,3-Trimethyl cyclohexane (1678-97-3) | 144[f] (e) | −66.9[f] (e) | 650 | $1.7 \times 10^4$ | 4.43 | 2.86 | 4.56 |
| $C_{12}$ Hexyl cyclohexane (4292-75-5) | 224[f] (e) | −43[f] (e) | 15.2[f] (e) | $2.9 \times 10^4$ | 6.05 | 3.77 | 0.12 |

| Chemical class, name and CAS RN | Boiling point (°C) | Melting point (°C) | Vapour pressure (Pa) | Henry's Law constant ($Pa \cdot m^3/mol$) | Log $K_{ow}$ | Log $K_{oc}$ | Aqueous solubility (mg/L at 25°C, unless otherwise stated) |
|---|---|---|---|---|---|---|---|
| **Two-ring cycloalkanes** | | | | | | | |
| $C_9$ *cis*-Bicyclo[4.3.0]nonane (4551-51-3) | 167[f] (e) | −53[f] (e) | 320 | $2.0 \times 10^3$ | 3.71 | 3.00 | 19.3 |
| $C_{12}$ 1,1-Bicyclohexyl (92-51-3) | 177.9[f] (e) | −51.4[f] (e) | 196[f] (e) | 20.4 (e) | 3.18[f] (e) | 3.00 | 109 (e) |
| **One-ring aromatics** | | | | | | | |
| $C_6$ Benzene (71-43-2) | 80[f] (e) | 5.5 (e) | $1.2 \times 10^4$ | 562 | 2.13[f] (e) | 2.22 | 1790[f] (e) |
| $C_9$ 1-Ethyl-2-methyl benzene (611-14-3) | 165.2[f] (e) | −80.8[f] (e) | 348 | 560 | 3.53[f] (e) | 2.93 | 74.6[f] (e) |
| $C_{12}$ 1,2,3-Triethylbenzene (42205-08-3) | 229.59 | 11.85 | 10.6 | 595.2 | 5.11 | 3.72 | 1.8 |
| **Two-ring aromatics** | | | | | | | |
| $C_{12}$ 1,1-Biphenyl (92-52-4) | 256.1[f] (e) | 69[f] (e) | 1.19 (e) | 31.2 (e) | 3.98[f] (e) | 3.8 | 6.94 (e) |

[1] All values are modelled unless marked with an (e), denoting experimental value. Models used were as follows: melting and boiling points and vapour pressure, MPBPWIN 2008; Henry's Law constant, HENRYWIN 2008; $K_{ow}$, KOWWIN 2008; $K_{oc}$, PCKOCWIN 2009; water solubility, WSKOWWIN 2008.

[2] References: [a] Daubert and Danner 1989; [b] McAuliffe 1963; [c] Verschueren 2001; [d] McAuliffe 1966; [e] Hansch et al. 1995; [f] EPIsuite 2008.

**Table A3.3. Primary degradation half-lives in soil of hydrocarbons from a formulated gasoline (Prince et al. 2007a, 2007b)**

| Class/compound | Median half-life (days) | Mean half-life (days) |
|---|---|---|
| ***n*-Alkanes** | | |
| Butane | 15.0 | 31.8 |
| Hexane | 6.5 | 10.2 |
| Nonane | 3.2 | 4.4 |
| Dodecane | 2.8 | 3.8 |
| **Isoalkanes** | | |
| 2-Methyl propane (isobutane) | 17.1 | 41.7 |
| 2-Methyl pentane | 10.4 | 16.7 |
| 3-Methyl pentane | 10.1 | 21.3 |
| 2-Methyl heptane | 4.8 | 6.0 |
| 4-Methyl nonane | 3.2 | 4.8 |
| **Alkenes** | | |
| *cis*-3-Hexene | 6.5 | 8.4 |
| **Cycloalkanes** | | |
| 1,1,3-Trimethyl cyclohexane | 8.5 | 14.2 |
| **Cycloalkenes** | | |
| Cyclopentene | 8.1 | 11.5 |
| 4-Methyl cyclopentene | 8.1 | 12.5 |
| **One-ring aromatics** | | |
| Benzene | 3.2 | 4.6 |
| 1-Methyl ethyl benzene | 3.2 | 5.2 |
| 2-Ethyl-1,3-dimethyl benzene | 3.2 | 4.9 |
| **Two-ring aromatics** | | |
| Naphthalene | 3.2 | 4.4 |

**Table A3.4. Modelled data for primary (BIOHCWIN 2008)[1], ultimate (BIOWIN 2009) biodegradation of representative structures of low boiling point naphthas**

| Class/compound | Primary half-life (days) (BioHCWIN) | Ultimate biodegradation result (BioWin) | Half-life compared to criteria (days) |
|---|---|---|---|
| **Alkanes** | | | |
| $C_4$ Butane | 3.5 | Days–weeks | < 182 |
| $C_6$ Hexane | 4.7 | Days–weeks | < 182 |
| $C_9$ Nonane | 7.4 | Days–weeks | < 182 |
| $C_{12}$ Dodecane | 11.8 | Days–weeks | < 182 |
| **Isoalkanes** | | | |
| $C_4$ Isobutane | 3.1 | Weeks | < 182 |
| $C_6$ 2-Methyl pentane | 4.2 | Weeks | < 182 |
| $C_9$ 2,3-Dimethyl heptane | 7.7 | Weeks | < 182 |
| $C_{12}$ 2,3-Dimethyl decane | 12.1 | Weeks | < 182 |
| ***n*-Alkenes** | | | |
| $C_9$ Nonene | 4.1 | Days–weeks | < 182 |
| $C_{12}$ 9-Methyl-1-undecene | 10.8 | Weeks | < 182 |
| **One-ring cycloalkanes** | | | |
| $C_6$ Cyclohexane | 55.4 (28–182)[3] | Weeks | < 182 |
| $C_9$ 1,2,3-Trimethyl cyclohexane | 3.5 | Weeks | < 182 |
| $C_{12}$ *n*-Hexyl cyclohexane | 15.7 | Weeks | < 182 |
| **Two-ring cycloalkanes** | | | |
| $C_9$ *cis*-Bicyclo[4.3.0]nonane | 55.9 | Weeks | < 182 |
| $C_{12}$ 1,1-Bicyclohexyl | 27 | Weeks–months | < 182 |
| **One-ring aromatics** | | | |
| $C_6$ Benzene | 4.6 (5–16)[3] | Weeks–months | < 182 |
| $C_9$ 1-Methyl-2-ethylbenzene | 4.9 | Weeks | < 182 |
| $C_{12}$ 1,2,3-Triethyl benzene | 4.9 | Weeks–months | < 182 |
| **Two-ring aromatics** | | | |
| $C_{12}$ Biphenyl | 31.0 (1.5–7)[3] | Weeks | < 182 |

[1] Primary half-life estimations are for non-specific media (i.e., water).

[2] A probability greater than or equal to 0.5 indicates "biodegrades fast." A probability less than 0.5 indicates "does NOT biodegrade fast"—from BIOWIN submodel 7 (Anaerobic Linear Biodegradation Probability) (BIOWIN 2009).
[3] Howard et al. 1991.

**Table A3.5a. Empirical data for photodegradation of components of low boiling point naphthas in air (Atkinson 1990)**

| Substance | Half-life (days) |
|---|---|
| Butane | 3.4 |
| 2-Methyl propane | 3.2 |
| Pentane | 2.0 |
| Isopentane | 2.0 |

**Table A3.5b. Atmospheric degradation of representative structures for low boiling point naphthas (AOPWIN 2008)**

| Class/compound | Half-lives (days) | |
|---|---|---|
| | Oxidation | Ozone[1] |
| **Alkanes** | | |
| $C_4$ Butane | 4.1 | NA |
| $C_6$ Hexane | 2 | NA |
| $C_9$ Nonane | 1.1 | NA |
| $C_{12}$ Dodecane | 0.8 | NA |
| **Isoalkanes** | | |
| $C_4$ 2-Methyl propane | 4.4 | NA |
| $C_6$ Methyl pentane | 2 | NA |
| $C_9$ 2,3-Dimethyl heptane | 1.1 | NA |
| $C_{12}$ 2,3-Dimethyl decane | 0.8 | NA |
| ***n*-Alkenes** | | |
| $C_9$ Nonene | 0.1 | 0.1 |
| $C_{12}$ 9-Methyl-1-undecene | 0.28 | 0.96 |
| **One-ring cycloalkanes** | | |
| $C_6$ Cyclohexane | 1.3 | NA |
| $C_9$ 1,2,3-Trimethyl cyclohexane | 0.8 | NA |
| $C_{12}$ *n*-Hexyl cyclohexane | 0.6 | NA |
| **Two-ring complex rings** | | |
| $C_9$ *cis*-Bicyclo[4.3.0]nonane | 0.8 | NA |
| $C_{12}$ 1,1-Bicyclohexyl | 1.3 | NA |
| **One-ring aromatics** | | |
| $C_6$ Benzene | 5.5 (2–20)[1] | NA |
| $C_9$ 1-Methyl-2-ethylbenzene | 1.4 | NA |
| $C_{12}$ 1,2,3-Triethyl benzene | 0.6 | NA |
| **Two-ring aromatics** | | |
| $C_{12}$ Biphenyl | 1.6 | NA |

Abbreviation: NA, not available.
[1] Howard et al. 1991.

**Table A3.6. Potential presence of representative structures for low boiling point naphthas that are persistent in air**

**(a)**

| | **64741-74-8** | **64742-22-9** | **64742-23-0** | **64742-73-0** | **68410-71-9** | **68476-46-0** | **68477-89-4** |
|---|---|---|---|---|---|---|---|
| **Carbon range** | 4–8 | 6–12 | 4–11 | 4–11 | 6–9 | 3–11[1] | 4–6[2] |
| **Boiling point range (°C)** | −10 to 130 | 65–230 | −20 to 190 | 155–217 | 20–130 | 27–204 | 25–200 |
| **Alkanes (%)** | 60 | 70 | 80 | 85 | 90 | 86 | 100 |
| **$C_4$** | Yes | | Yes | Yes | | | |
| **$C_5$** | Yes | | Yes | Yes | | Yes | Yes |
| **$C_6$** | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| **Isoalkanes** | | | | | | | |
| **$C_4$** | Yes | | Yes | Yes | | Yes | Yes |
| **$C_5$** | Yes | | Yes | Yes | | Yes | Yes |
| **$C_6$** | Yes | | Yes | Yes | Yes | | |
| **Aromatics (%)** | 40 | 30 | 20 | 15 | 10 | 14 | 0 |
| **$C_6$** | Yes | Yes | Yes | Yes | Yes | Yes | |

**(b)**

| | **68478-12-6** | **68513-02-0** | **68514-79-4** | **68606-11-1** | **68783-12-0** | **68919-37-9** | **68955-35-1** | **101795-01-1** |
|---|---|---|---|---|---|---|---|---|
| **Carbon range** | 4–6 | 4–15 | 5–12 | 5–9 | 5–12 | 5–12<br>4–10 | 4–12 | 5–8 |
| **Boiling point range (°C)** | 25–200 | −35 to 275 | 27–210 | 30–177 | 0–230 | 35–230 | 30–220 | 20–130 |
| **Alkanes (%)** | 100 | 70 | 35 | 80 | 80 | 35 | 37 | 80 |
| **$C_4$** | | Yes | | | | No/Yes | | |
| **$C_5$** | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| **$C_6$** | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| **Isoalkanes** | | | | | | | | |
| **$C_4$** | | Yes | | | | No/Yes | | |
| **$C_5$** | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| **$C_6$** | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| **Aromatics (%)** | 0 | 30 | 65 | 20 | 20 | 65 | 63 | 20 |
| **$C_6$** | | Yes | Yes | Yes | Yes | Yes | Yes | Yes |

[1] The carbon number range is 5–11 based on boiling points.
[2] The carbon number range is 5–6 based on boiling points.

**(c)**

| | **64741-54-4** | **64741-55-5** | **64741-64-6** | **68410-05-9** | **68410-96-8** |
|---|---|---|---|---|---|
| **Carbon range** | 4–10 | 4–10 | 4–11 | ND | ND |
| **Boiling point range (°C)** | 48–249 | 27–238 | 40–168 | ND | ND |
| **Alkanes (%)** | | 86 | | | |
| **$C_4$** | | | | | |
| **$C_5$** | Yes | Yes | Yes | | |
| **$C_6$** | Yes | Yes | Yes | | |
| **Isoalkanes** | | | | | |
| **$C_4$** | | | | | |
| **$C_5$** | Yes | Yes | Yes | | |
| **$C_6$** | Yes | Yes | Yes | | |
| **Aromatics (%)** | | 14 | | | |
| **$C_6$** | Yes | Yes | Yes | | |

ND – No data

**Table A3.7. Fish BAF and BCF predictions for low boiling point naphthas using the Arnot-Gobas kinetic model (BCFBAF 2008) with corrections for metabolism**

| | Log $K_{ow}$[b] | $k_M$ (per day)[c] | BCF (L/kg) | BAF (L/kg) |
|---|---|---|---|---|
| **Alkanes** | | | | |
| $C_4$ Butane | 2.9 | 1.2 | 46 | 46 |
| $C_6$ Hexane | 3.9 | 0.6 | 299 | 301 |
| $C_9$ Nonane | 5.7 | 0.07 (e)[d] | 1905[e] | 3890[e] |
| $C_{12}$ Dodecane | 6.1 | 0.38 (e) | 1642[e]<br>240 (e) | 6681[e] |
| **Isoalkanes** | | | | |
| $C_4$ Isobutane | 2.8 | 1.4 | 35 | 35 |
| $C_6$ 2-Methyl pentane | 3.2 | 1 | 87 | 86 |
| $C_9$ 2,3-Dimethyl heptane | 4.6 | 0.04 (e) | 2140 | 2974 |
| $C_{12}$ 2,3-Dimethyl decane | 6.1 | 0.16 (e) | 1910 | 8232 |
| ***n*-Alkenes** | | | | |
| $C_9$ Nonene | 4.6 | 0.27 | 910 | 964 |
| $C_{12}$ 9-Methyl-1-undecene | 6.0 | 0.16 | 1966 | 7630 |
| **One-ring cycloalkanes** | | | | |
| $C_6$ Cyclohexane | 3.0 | 3.2 (e) | 97[e] | 97[e] |
| $C_9$ 1,2,3-Trimethyl cyclohexane | 4.4 | 0.19 | 1862[e] | 1026 |
| $C_{12}$ *n*-Hexyl cyclohexane | 6.1 | 0.14 (e) | 2180 | 9605 |
| **Two-ring cycloalkanes** | | | | |
| $C_9$ *cis*-Bicyclo[4.3.0]nonane | 3.7 | 0.16 | 303 | 307 |
| $C_{12}$ 1,1-Bicyclohexyl | 5.9 | 0.29 (e) | 1160 | 2463 |
| **One-ring aromatics** | | | | |
| $C_6$ Benzene | 2.2 | 0.45 | 10 | 10 |
| $C_9$ 1-Methyl-2-ethylbenzene | 2.9 | 0.57 | 191[e] | 191[e] |
| $C_{12}$ 1,2,3-Triethylbenzene | 3.7 | 0.39 | 891 | 1024 |
| **Two-ring aromatics** | | | | |
| $C_{12}$ Biphenyl | 3.8 | 0.42 | 386 | 390 |

[a] Arnot and Gobas (2003) – inputs used for the model were log $K_{ow}$ values provided by EPIsuite (2008)
[b] EPIsuite (2008)
[c] Value for a 10-g fish
[d] (e) – experimental half-life used
[e] BAF and BCF values adjusted based on experimental BCF-generated biotransformation rates, provided structures and log $K_{ow}$s were similar.

**Table A3.8. Comparisons of experimental BAFs and modelled BAFs (BCFBAF 2008) for selected aromatic hydrocarbons**

| | Reference; Study Design | Log $K_{ow}$ | BAF[a] Measured (L/kg) | BAF[b] Modelled (L/kg) |
|---|---|---|---|---|
| **One-ring aromatics*** | | | | |
| $C_6$ Benzene | Zhou et al. 1997 Atlantic salmon (white muscle); 96 h (WSF of crude oil) | 2.13 (e) | 4 | 8.9 |
| $C_7$ Toluene | Zhou et al. 1997 Atlantic salmon (white muscle); 96 h (WSF of crude oil) | 2.73 (e) | 11 | 27.6 |
| $C_8$ Ethyl benzene | Zhou et al. 1997 Atlantic salmon (white muscle); 96 h (WSF of crude oil) | 3.15 (e) | 26 | 61.5 |
| $C_8$ Xylenes | Zhou et al. 1997 Atlantic salmon (white muscle); 96 h (WSF of crude oil) | 3.12 (e) | 47 | 70.2 |
| $C_9$ Isopropyl benzene | Zhou et al. 1997 Atlantic salmon (white muscle); 96 h (WSF of crude oil) | 3.66 (e) | 20 | 162 |
| $C_9$ Propyl benzene | Zhou et al. 1997 Atlantic salmon (white muscle); 96 h (WSF of crude oil) | 3.69 (e) | 36 | 155 |
| $C_9$ Ethyl methyl benzene | Zhou et al. 1997 Atlantic salmon (white muscle); 96 h (WSF of crude oil) | 3.98 (e) | 51 | 374 |
| $C_9$ Trimethyl benzene | Zhou et al. 1997 Atlantic salmon (white muscle); 96 h (WSF of crude oil) | 3.66 (e) | 74 | 161 |
| **Two-ring aromatics*** | | | | Lower trophic[c] |
| $C_{10}$ Naphthalene | Neff et al. 1976 Clam; 24 h (oil-in-water dispersion of No. 2 fuel oil) lab study | 3.30 (e) | 2.3 | 113 |
| $C_{11}$ Methyl naphthalenes | Zhou et al. 1997 Atlantic salmon (white muscle); 96 h (WSF of crude oil) lab study | 3.87 (e) | 230 | 379 |
| $C_{11}$ 1-Methyl naphthalene | Neff et al. 1976 Clam; 24 h (oil-in-water dispersion of No. 2 fuel oil) lab study | 3.87 (e) | 8.5 | 379 |
| $C_{11}$ 2-Methyl naphthalene | Neff et al. 1976 Clam; 24 h (oil-in-water dispersion of No. 2 fuel oil) lab study | 3.86 (e) | 8.1 | 429 |
| $C_{12}$ Dimethyl naphthalene | Neff et al. 1976 Clam; 24 h (oil-in-water dispersion of No. 2 fuel oil) lab study | 4.31 (e) | 17.1 | 784 |

[a] BCFBAF (2008)
[b] Arnot and Gobas (2003); (BCFBAF 2008)
[c] BAFs of lower trophic level were used for comparison
Abbreviation: WSF – water-soluble fraction

**Table A3.9. Comparisons of experimental BCFs and modelled BCFs (BCFBAF 2008) on some representative structures of gas oils**

| | Reference; Species tested | Log $K_{ow}$ | BCF[a] Measured (L/kg) | BCF[b] Modelled (L/kg) |
|---|---|---|---|---|
| **Alkanes*** | | | | |
| $C_8$ *n*-alkanes Octane | JNITE 2010; Carp | 5.18 (e) | 530 | 1480 |
| $C_{12}$ *n*-alkanes *n*-Dodecane | Tolls and v Dijk 2002 unpublished; Fathead minnow | 6.10 (e) | 400 | 901 |
| **One-ring cycloalkanes*** | | | | |
| $C_6$ Cyclohexane | JNITE 2010; Carp | 3.44 (e) | 77 | 76 |
| $C_7$ 1-Methyl cyclohexane | JNITE 2010; Carp | 3.61 (e) | 240 | 220 |
| $C_8$ Ethyl cyclohexane | JNITE 2010; Carp | 4.56 (e) | 2529 | 839 |
| **Two-ring cycloalkanes*** | | | | |
| $C_{10}$ *Trans*-decalin | JNITE 2010; Carp | 4.20 | 2200 | 884 |
| $C_{10}$ *Cis*-decalin | JNITE 2010; Carp | 4.20 | 2500 | 884 |
| **One-ring aromatics*** | | | | |
| $C_9$ 1,2,3-Trimethyl benzene | JNITE 2010; Carp | 3.66 (e) | 125–141 | 159 |
| $C_{10}$ 1,2-Diethyl benzene | JNITE 2010; Carp | 3.72 (e) | 478–556 | 221 |
| $C_{11}$ 1-Methyl-4-tert-butyl benzene | JNITE 2010; Carp | 3.66 (e) | < 1.0 | 890 |
| **Cycloalkanes monoaromatic*** | | | | |
| $C_{10}$ Tetralin | JNITE 2010; Carp | 3.49 (e) | 230 | 176 |
| **Two-ring aromatics*** | | | | |
| $C_{10}$ Naphthalene | JNITE 2010; Carp | 3.30 (e) | 94 | 112 |
| | | | | |
| $C_{11}$ 2-Methyl naphthalene | Jonsson et al. 2004; Sheepshead minnow | 3.86 (e) | 1871 | 405 |
| $C_{12}$ 1,3-Dimethyl naphthalene | Jonsson et al. 2004; Sheepshead minnow | 4.42 (e) | 2051 | 1021 |

[a] Experimental BCFs from various sources.
[b] Modelled BCFs using BCFBAF (2008); BCFs of a lower trophic fish were chosen to match the lipid content of fish in the Japanese database.

**Table A3.10. Empirical data for aquatic toxicity of low boiling point naphthas**

| Test organism | Common name | Type of test | Endpoint | Comment | Value (mg/L) | Reference |
|---|---|---|---|---|---|---|
| *Oncorhynchus mykiss* | Rainbow trout | 96 h acute | $LL_{50}$ | Closed system WAF; six studies | 10–18 | CONCAWE 1996 |
| *Oncorhynchus mykiss* | Rainbow trout | 96 h acute | $LL_{50}$<br>NOAEC | Closed system WAF | 12<br>4.5 | ECB 2000g |
| *Pimephales promelas* | Fathead minnow | 96 h acute | $LL_{50}$ | Closed system WAF | 8.3 | PPSC 1995a |
| *Pimephales promelas* | Fathead minnow | 96 h acute | $LC_{50}$ | $C_9$–$C_{12}$ isoalkanes | 2600 | ECB 2000k |
| *Daphnia magna* | Water flea | 48 h acute | $EL_{50}$ | Closed system WAF; eight studies | 4.5–32 | Adema et al. 1986 |
| *Pseudokirchneriella subcapitata* | Green alga | 72 h growth rate | $EC_{50}$ | Catalytically cracked naphtha | 880 | ECB 2000i |
| | | | NOAEL | | 0.1 | |
| *Mysidopsis bahia* | Mysid shrimp | 96 h acute | $EL_{50}$ | Closed system WAF | 13.8 | PPSC 1995b |
| *Crangon crangon* | Brown shrimp | 96 h acute | $LC_{50}$ | Closed system whole product 64742-73-0 | 4.3 | ECB 2000h |
| *Chaetogammarus marinus* | Marine gammarid | 96 h acute | $LC_{50}$ | Closed system whole product 64742-73-0 | 2.6 | ECB 2000h |
| *Chaetogammarus marinus* | Marine gammarid | 96 h acute | NOAEC | WAF Isopar G; $C_9$–$C_{12}$ isoalkanes | 100% WAF | ECB 2000k |
| *Leuciscus idus* | Golden orfe | 48 h acute | NOAEC | WAF Isopar J; $C_9$–$C_{12}$ isoalkanes | 100% WAF | ECB 2000k |
| *Xenopus* sp. | Frog | 96 h acute | $LC_{50}$ | 7% mortality; *n*-dodecane | 500 | Buryskova et al. 2006 |
| | | 96 h acute | $EC_{50}$ terato-genesis | 18% teratogenicity; *n*-dodecane | 50 | |

Abbreviations: $EC_{50}$, the concentration of a substance that is estimated to cause a defined effect on 50% of the test organisms; $EL_{50}$, the loading concentration of a substance that is estimated to cause some toxic effect on 50% of the test organisms; $LC_{50}$, the concentration of a substance that is estimated to be lethal to 50% of the test organisms; $LL_{50}$, the loading concentration of a substance that is estimated to be lethal to 50% of the test organisms; NOAEC/L, no-observed-adverse-effect concentration/loading; WAF, water accommodated fraction.

**Table A3.11. Modelled data for toxicity of low boiling point naphthas to aquatic organisms (PetroTox 2009)**

**(a)**

| Organism | Acute $LL_{50}$ (mg/L) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | **68514-79-4** | **68919-37-9[1]** | **68955-35-1** | **64741-74-8** | **64742-73-0** | **68410-96-8** | **64742-22-9** | **64742-23-0** |
| *Daphnia magna* | 7.5 | 18.5 | 7.5 | 21.9 | 4.6 | 4.8 | 2.1 | 4.8 |
| *Oncorhynchus mykiss* | 2.9 | 7.8 | 2.9 | 12.5 | 2.7 | 2.7 | 1.1 | 2.8 |
| *Pseudokirchneriella subcapitata*[2] | 2.2 | 6.5 | 2.2 | 9.3 | 2.3 | 2.2 | 1.1 | 2.4 |
| *Rhepoxynius abronius* | 1.1 | 3.7 | 1.1 | 5.9 | 1.3 | 1.3 | 0.5 | 1.3 |
| *Palaemonetes pugio* | 2.4 | 6.7 | 2.4 | 10.9 | 2.3 | 2.4 | 0.9 | 2.4 |
| *Menidia beryllina* | 105 | 148 | 105 | 83 | 12 | 22.4 | 10.7 | 12.3 |

**(b)**

| Organism | Acute $LL_{50}$ (mg/L) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | **68410-71-9** | **68478-12-6** | **68477-89-4** | **68513-02-0** | **68606-11-1** | **68783-12-0** | **101795-01-1** | **64741-64-6** | **68476-46-0** |
| *Daphnia magna* | 7.9 | 60.9 | 60.9 | 5.3 | 10.2 | 2.8 | 17.6 | 3.2 | 5.3 |
| *Oncorhynchus mykiss* | 4.5 | 34.9 | 34.9 | 2 | 5.8 | 1.6 | 10.1 | 1.8 | 3.1 |
| *Pseudokirchneriella subcapitata*[2] | 3.4 | 25.7 | 25.7 | 2.6 | 4.4 | 1.6 | 7.5 | 3 | 2.5 |
| *Rhepoxynius abronius* | 2.1 | 16.5 | 16.5 | 0.5 | 2.8 | 0.8 | 4.78 | 0.9 | 1.4 |
| *Palaemonetes pugio* | 3.9 | 30.3 | 30.3 | 1.5 | 5.1 | 1.4 | 8.8 | 1.6 | 2.6 |
| *Menidia beryllina* | 19.9 | 154 | 154 | 36.5 | 31.6 | 9.7 | 58 | 8 | 30 |

[1] Data from Table A2.1 used in calculations.

[2] Default particulate organic carbon concentration for algae: 2.0 mg/L.

# Appendix 4: Summary of Health Effects Information from Pooled Toxicological Data for LBPNs

| Toxicity type | CAS RN/ specific substance[1] | Effect levels[2]/results |
|---|---|---|
| Acute toxicity (oral) | Gasoline[3] | $LD_{50}$ = > 2000 mg/kg-bw (rat) (Rodriguez and Dalbey 1994a, 1994b). |
| | **68955-35-1** | $LD_{50}$ = 3500 mg/kg-bw (rat) (API 2008a). |
| Acute toxicity (inhalation) | 8 CAS RNs | $LC_{50}$ = > 5 mg/L (> 5000 mg/m$^3$)[4] (rat) (CONCAWE 1992; API 2008a). |
| | 8032-32-4 | $LC_{50}$ = 3400 ppm (9025 mg/m$^3$)[5,6] (rat) (RTECS 2008b). |
| Acute toxicity (dermal) | 9 CAS RNs | $LD_{50}$ = > 2000 mg/kg-bw (rabbit) (CONCAWE 1992; API 2008a; Rodriguez and Dalbey 1994c, 1994d). |
| Short-term and subchronic toxicity | | **INHALATION EXPOSURE** |
| | **64741-55-5** | **LOAEC for site-restricted LBPNs =** 1510 ppm (5475 mg/m$^3$) for increased liver weight. Concentrations of 0, 1510, 2610 or 4520 ppm (0, 5475, 9500 or 16 425 mg/m$^3$) were administered to male and female rats for 13 weeks.<br>*All doses*: Dose-related increases in liver weight (both sexes) and kidney weight (males at all doses, females at middle and high dose).<br>*16 425 mg/m$^3$*: Trace centrilobular hepatocellular hypertrophy; decreased mean body weight (male), proteinaceous casts within tubules in outer zone of medulla, degeneration and regeneration of tubular epithelium and chronic interstitial inflammation in kidneys (males) (API 1987a).<br><br>**LOAEC** = 2512 ppm (9041 mg/m$^3$) for nasal irritation. Concentrations of 0, 752, 2512 or 7518 ppm (0, 2707, 9041 or 27 059 mg/m$^3$) were administered to Sprague-Dawley rats (10 per dose), 6 h/day, 7 days/week. Parental females were exposed from 2 weeks prior to mating through to gestational day 19. Unmated females and parental males were exposed from 2 weeks prior to mating for 51 consecutive days.<br>*9041 mg/m$^3$* (females): Red staining on snout (nasal irritation).<br>*27 059 mg/m$^3$*: Increased spleen weights (relative and absolute) (females). Increased liver (relative) and kidney weights (relative and absolute) (males). Authors noted that increased kidney weight is male-rat-specific nephropathy and is not relevant to humans. Red staining on snout (nasal irritation; no histological changes).<br>*NOAEC*: 9041 mg/m$^3$ for systemic toxicity (Schreiner et al. 1999; API 2008a). |
| | 64742-95-6 | **LOAEC** = 500 ppm (1327 mg/m$^3$) for decreased growth rate. Concentrations of 0, 102, 500, 1514 ppm (0, 271, 1327 or 4019 mg/m$^3$)[5,7] were administered to pregnant CD-1 mice (30/dose), 6 h/day, from gestational days (GD) 6–15; |

| Toxicity type | CAS RN/ specific substance[1] | Effect levels[2]/results |
|---|---|---|
| | | surviving females sacrificed on GD 18 [systemic effects of developmental toxicity study described below].<br>≥ *1327 mg/m$^3$*: significant decrease in body weight gain; one unexplained mortality.<br>*4019 mg/m$^3$*: Maternal mortality (44%). Decreased percent haematocrit and mean corpuscular volume. Abnormal gait, laboured breathing, hunched posture, weakness, inadequate grooming, circling and ataxia (McKee et al. 1990).<br><br>**LOAEC** = 1800 mg/m$^3$ for hematological changes. Concentrations of 0, 1800, 3700 or 7400 mg/m$^3$ were administered to rats for 13 weeks.<br>≥ *1800 mg/m$^3$*: Low-grade anemia (females).<br>≥ *3700 mg/m$^3$*: Increased liver and kidney weights (females) (Shell Research Ltd. 1980). |
| | 64742-48-9 | **LOAEC** = 800 ppm (4679 mg/m$^3$) for hepatic effects. Concentrations of 0, 400 or 800 ppm (0, 2339 or 4679 mg/m$^3$) were administered to male Wistar rats (28 per dose), 6 h/day, 7 days/week, for 3 weeks.<br>*All doses*: Increased glutathione levels in the hemisphere (brain). Mucous membrane irritation. Increased relative kidney weight (dose-dependent) and body weight.<br>*4679 mg/m$^3$:* Oxidative stress induction in the brain, kidney and liver. Reactive oxygen species increased in the liver and hippocampus, but decreased in the kidney. Decreased hepatic glutamine synthetase activity. Decreased food consumption and increased water consumption (Lam et al. 1994).<br><br>**LOAEC** = 575 mg/m$^3$ for biochemical changes. Concentrations of 0, 575, 2875 or 5750 mg/m$^3$ were administered to male Wistar rats (20 per dose), 6 h/day, 5 days/week, for 4, 8, 12 or 17 weeks.<br>≥*575 mg/m$^3$*: Decreased serum creatine kinase at 17 weeks. Decreased cerebellar succinate dehydrogenase activity from weeks 8 to 17 (dose-dependent).<br>≥*2875 mg/m$^3$*: Changes in cerebellar glutathione levels and creatine kinase activity. Muscle membrane effects were suggested, as muscle membrane sialic and uronic acid residue levels were decreased (Savolainen and Pfaffli 1982). |
| | Gasoline[3] | **LOAEC** = 500 ppm (1327 mg/m$^3$) for changes in brain enzyme levels. Concentrations of 0 or 500 ppm (0 or 1327 mg/m$^3$)[5,8] were administered to male and female Sprague-Dawley rats (15 per sex per dose), 6 h/day, 5 days/week, for 4 weeks. Included are five per sex per dose that were allowed 4 weeks' recovery.<br>Increased kidney weight and hepatic ethoxyresorufin *O*-deethylase activity (males). Elevated lymphocyte counts |

| Toxicity type | CAS RN/ specific substance[1] | Effect levels[2]/results |
|---|---|---|
| | | and serum phosphate (males). Increased heart weight and glucose levels (females). Decreased hemoglobin levels (females). Altered brain biogenic amine levels (dependent on brain region and sex). Increased urinary ascorbic and hippuric acid levels. Most effects returned to control levels after recovery (Chu et al. 2005). |
| | 8052-41-3 | **LOAEC** = 363 mg/m$^3$ for increased mortality. Concentrations of 114–1271 mg/m$^3$ administered to Long-Evans rats ($n$ = 133), Sprague-Dawley rats ($n$ = 18), guinea pigs ($n$ = 262), albino New Zealand rabbits ($n$ = 29), male squirrel monkeys ($n$ = 27) and male beagle dogs ($n$ = 18), continuously for 90 days.<br>≥ *363 mg/m$^3$*: Mortality in guinea pigs (4/15, most susceptible).<br>*1271 mg/m$^3$*: Congested lungs, bronchitis and mixed inflammatory cell infiltration in the lungs of all species (Rector et al. 1966).<br><br>**LOAEC** = 214 mg/m$^3$ for an inflammatory response of the respiratory tract. Concentrations of 0 or 214 mg/m$^3$ were administered to female CD-1 rats (six per dose) by head-only exposure, 4 h/day for 4 consecutive days.<br>*214 mg/m$^3$*: Inflammatory cell infiltrate in nasal cavity, trachea and larynx; loss of cilia, hyperplasia of basal cells and squamous metaplasia of trachea and nasal cavity (Riley et al. 1984). |
| | Gasoline[3] | **LOAEC** = 300 mg/m$^3$ for structural changes of the respiratory tract. A concentration of 300 mg/m$^3$ was administered to female rats (20 per dose), 8 h/day, 5 days/week, for 15 days or 12 weeks.<br>*15 days*: Reduced levels of pulmonary surfactants.<br>*12 weeks*: Incidence of lung parenchymal changes (interstitial fibrosis and alveolar collapse) (Lykke and Stewart 1978; Stewart et al. 1979). |
| | | **ORAL EXPOSURE** |
| | 64742-95-6 | **LOAEL** = 500 mg/kg-bw per day for biochemical changes (both sexes) and decreased growth rate (males). Doses of 500, 750 or 1250 mg/kg-bw per day were administered to male and female rats (10 per sex per dose) for 3 months.<br>≥ *500 mg/kg-bw per day*: Decreased body weight (males). Dose-related increases in liver and kidney weights and relative weights, as well as increased serum glutamic pyruvic transaminase (males and females).<br>*1250 mg/kg-bw per day*: Increased alkaline phosphatase (males) (Bio/Dynamics Inc. 1991a).<br><br>**LOAEL** = 500 mg/kg per day for hematological changes. |

| Toxicity type | CAS RN/ specific substance[1] | Effect levels[2]/results |
|---|---|---|
| | | Doses of 125, 250 or 500 mg/kg per day were administered to male and female beagle dogs (four per sex per dose), 7 days/week for 90 days.<br>*500 mg/kg per day*: Borderline anemia (Bio/Dynamics Inc. 1991b). |
| | | **DERMAL EXPOSURE** |
| | **64741-54-4** | **LOAEL** = 200 mg/kg-bw for decreased growth rate. Doses of 200, 1000 or 2000 mg/kg-bw were applied to the shaven skin of male and female rabbits, 3 times/week for 28 days (12 applications total).<br>*200 mg/kg-bw*: Slight to moderate and slight skin irritation in males and females, respectively; reduced growth rate (males).<br>*1000 mg/kg-bw*: Moderate skin irritation; reduced growth rate.<br>*2000 mg/kg-bw*: Moderate skin irritation; weight loss (females), before reduced growth weight (males) (API 1986g). |
| | 64742-48-9 | **LOAEL** = 500 mg/kg-bw per day for hematological and 1500 mg/kg-bw per day for biochemical changes. Doses of 0, 500, 1000 or 1500 mg/kg-bw per day were administered to male and female F344 rats (10 per sex per group), 6 h/day, 5 days/week, for 4 weeks.<br>*500 mg/kg-bw per day*: Dose-dependent increase in white blood cells (due to increase in neutrophils and lymphocytes) in males.<br>*1000 mg/kg-bw per day*: Significant decrease in food consumption (females).<br>*1500 mg/kg-bw per day*: Severe erythema, moderate eschar formation, dose-dependent increase in white blood cells (due to increase in neutrophils and lymphocytes) in females, significant decrease in food consumption (males), mild anemia, decreased serum albumin (9–25%), total serum protein (10–13%) and blood urea nitrogen (9–25%) and increased platelet counts (10–20%) (Zellers 1985). |
| | **64741-55-5** | **LOAEL** = 30 mg/kg-bw per day for skin irritation. Doses of 0, 30, 125 or 3000 mg/kg-bw per day were applied to the clipped backs of male and female Sprague-Dawley rats (15 per sex per dose), 5 days/week for 90 days.<br>*All doses*: Dose-related increase in skin irritation, erythema and edema at treated sites and histopathological correlates of hyperplasia, inflammation and ulceration. No other effects reported (Mobil 1988a). |
| | **68955-35-1** | **LOAEL** = 1000 mg/kg-bw per day for increased mortality. Doses of 200, 1000 or 2000 mg/kg-bw per day applied to shaven skin of male and female rabbits, 3 times/week for 28 days (12 applications total). |

| Toxicity type | CAS RN/ specific substance[1] | Effect levels[2]/results |
|---|---|---|
| | | *200 mg/kg-bw per day*: Moderate skin irritation.<br>*1000 mg/kg-bw per day*: Moderate skin irritation; mortality in 1/5 males.<br>*2000 mg/kg-bw per day*: Severe skin irritation; decreased body weight gain and body weight; mortality in 2/5 males with tubular degeneration; granulopoiesis of bone marrow (API 1986h). |
| Chronic toxicity (non-cancer) | Gasoline[3] | **LOAEC** = 67 ppm (200 mg/m$^3$). Male and female B6C3F1 mice and Fischer 344 albino rats (approximately 6 weeks of age; 100 mice or rats per sex per group) exposed to 0, 67, 292 or 2056 ppm (0, 200, 870 or 6170 mg/m$^3$; as cited in IARC [1989a]) of the test substance (containing 2% benzene) via inhalation, 6 h/day, 5 days/week, for 103–113 weeks.<br>*All doses*: Lower survival rates (male rats). Ocular discharge and irritation (rats).<br>*870 mg/m$^3$*: Increased kidney weight (male rats).<br>*6170 mg/m$^3$*: Lower survival rates (male mice). Decreased body weight (rats and male mice). Decreased heart weight (rats) (MacFarland et al. 1984). |
| | 8030-30-6 | **LOAEL** = 25 mg (neat) (714 mg/kg-bw). Male and female C3H/HeN mice (25 per sex) exposed to 25 mg (714 mg/kg-bw)[9,10] of the test substance (neat), applied to the shaved skin of the dorsal thoracic region, 3 times/week for 105 weeks.<br>Dermal irritation after 10–15 days. Inflammatory and degenerative skin changes after 6 months (Clark et al. 1988). |
| Reproductive and developmental toxicity | | **INHALATION EXPOSURE** |
| | 64742-48-9 | **LOAEC** = 800 ppm (4679 mg/m$^3$). Pregnant Wistar rats exposed to 800 ppm (4679 mg/m$^3$)[5,11] of the test substance, via inhalation, 6 h/day from gestational days 7 to 20.<br>*4679 mg/m$^3$*: Decreased number of pups per litter and higher frequency of post-implantation loss. Increased birth weight of pups.<br>*4679 mg/m$^3$*: Decreased motor activity (non-significant). No effect observed for neuromotor activity. For learning ability, exposed rats showed behaviour comparable to that of controls at 1 month of age. At 2 months of age, impaired cognitive function (females) and impaired memory (males) were observed. At 5 months of age, learning and memory deficits were observed in both sexes.<br>*LOAEC*: 4679 mg/m$^3$ for reproductive, developmental and developmental neurotoxicity (Hass et al. 2001). |
| | 64741-63-5 | **NOAEC** = 7480 ppm (27 687 mg/m$^3$). Female Sprague-Dawley rats (10 per dose) exposed to 0, 750, 2490 or 7480 ppm (0, 2776, 9217 or 27 687 mg/m$^3$) of the test substance via inhalation, 6 h/day, 7 days/week, from 2 weeks prior to mating through to gestational day 19; and male Sprague-Dawley rats (10 per dose) exposed to same doses, |

| Toxicity type | CAS RN/ specific substance[1] | Effect levels[2]/results |
|---|---|---|
| | | 6 h/day, 7 days/week, from 2 weeks prior to mating for 46 consecutive days. Rats sacrificed on postnatal day 4.<br>*All doses*: No effect on reproductive organs (testes, epididymides, ovaries), reproductive performance or fetal development.<br>*NOAEC*: 27 687 mg/m$^3$ for developmental and reproductive toxicity (Schreiner et al. 2000b; API 2008a). |
| | 8052-41-3 | **NOAEC:** 300 ppm (1701 mg/m$^3$). 100 or 300 ppm (567 or 1701 mg/m$^3$) of test substance administered to pregnant rats via inhalation for 6 hours/day from gestational days 6-15 and 100 or 300 ppm (557 or 1701 mg/m$^3$) administered to male rats, 6 hours/day, 5 days/week for 8 consecutive weeks prior to mating.<br>*NOAEL* – 300 ppm for developmental and reproductive toxicity (Phillips and Egan 1981 as cited in US EPA 1998). |
| | | **ORAL EXPOSURE** |
| | 64742-95-6 | **LOAEL** = 1250 mg/kg-bw per day. Pregnant Sprague-Dawley CD rats (24 per dose) exposed to 0, 125, 625 or 1250 mg/kg-bw per day of the test substance, via gavage, from gestational days 6 to 15. Rats sacrificed on gestational day 20.<br>*1250 mg/kg-bw per day*: Reduced fetal body weight and increased incidence of ossification variations. Retardation in ossification of vertebral elements and sternebrae.<br>*LOAEL*: 1250 mg/kg-bw per day for developmental toxicity (Bio/Dynamics Inc. 1991c). |
| | **64741-55-5** | **NOAEL** = 2000 mg/kg. Pregnant Sprague-Dawley rats exposed to 2000 mg/kg of the test substance, via oral exposure, on gestational day 13 (other refinery streams also tested in separate experiments) to identify and compare any potential direct teratogenic effects that might be obscured by maternal or fetal toxicity resulting from repetitive exposure. Moderate to severe toxicity observed in the first rats treated (although none perished, fetal viability may have been compromised); thus, the test group was limited to five animals. Cesarean sections performed on gestational day 20.<br>*NOAEL*: 2000 mg/kg for reproductive toxicity and teratogenicity (Stonybrook Laboratories, Inc. 1995). |
| | **64741-74-8** | 0, 10, 25 or 50 mg/kg-bw per day of the test substance administered, via oral gavage, to pregnant New Zealand white rabbits (16 per dose) from gestational days 6 to 28.<br>*All doses*: No significant differences in fetal malformations or genetic or developmental variations.<br>*50 mg/kg-bw per day*: One rabbit aborted on gestational day 19.<br>*NOAEL*: 50 mg/kg-bw per day for reproductive and developmental toxicity (Miller and Schardein 1981). |

| Toxicity type | CAS RN/ specific substance[1] | Effect levels[2]/results |
|---|---|---|
| | | **DERMAL EXPOSURE** |
| | **68513-02-0** | **NOAEL =** 1000 mg/kg-bw per day. Pregnant Sprague-Dawley rats (12 per dose; 15 for control) exposed to 0, 100, 500 or 1000 mg/kg-bw per day of the test substance (neat), applied to the shaved skin of the back (not occluded) from gestational days 0 to 20. Observation until lactation day 4.<br>*NOAEL*: 1000 mg/kg-bw per day for reproductive and developmental toxicity (ARCO 1994). |
| | 8030-30-6 | **NOAEL:** 25 mg (714 mg/kg-bw per day). Male and female C3H/HeN mice (25 per sex) exposed to 25 mg (714 mg/kg-bw per day)[9,10] of the test substance (neat), applied to the shaved skin of the dorsal thoracic region, 3 times/week for 105 weeks.<br>No effects observed in gonads.<br>*NOAEL*: 714 mg/kg-bw per day for reproductive toxicity (Clark et al. 1988). |
| Carcinogenicity | | **DERMAL EXPOSURE (chronic)** |
| | 8030-30-6 | **Dermal carcinogenicity in mice**. Male and female C3H/HeN mice (42–50 days of age; 25 per sex) were exposed to 25 mg (694 mg/kg-bw per day)[9,10] of the test substance (neat) applied to the shaved skin of the dorsal thoracic region, 3 times/week for up to 105 weeks. Increased incidence of skin tumours (21%). Tumour incidence: 10/47 in test group (3 squamous cell carcinomas and 7 fibrosarcomas); 0/46 in the negative control group; 49/49 in the positive control group (49 squamous cell carcinomas). Tumours appeared after 94 weeks in the test group and 28 weeks in the positive control group (Clark et al. 1988). |
| | 64741-46-4 | **Dermal carcinogenicity in mice**. 50 male C3H/HeJ mice (6–8 weeks of age) were exposed to 50 mg (1351 mg/kg-bw per day)[9,10] of the test substance (neat) applied to the shaved skin of the interscapular region of the back, 2 times/week, until a papilloma > 1 $mm^3$ appeared. Increased incidence of skin tumours. Tumour incidence: 11/44 in the test group; 0/50 in the negative control group; 46/48 in the positive control group. Tumours appeared after 85 weeks in the test group and after 46 weeks in the positive control group (Blackburn et al. 1986). |
| | Gasoline[3] | **Dermal carcinogenicity in mice**. Male and female C3H/HeJ mice (15 per sex) were exposed to 50 µL (1000 mg/kg-bw per day)[10,12,13] of the test substance (API 81-24) (neat) applied to the clipped skin of the intrascapular region of the back (at least 1 $cm^2$), 2 times/week for 12 months. Insignificant increase in skin tumour incidence: 1/13 females (papilloma) and 0/15 males in the test group; 0/29 in the negative control group (API 1986o). |
| | | **DERMAL EXPOSURE (initiation/promotion)** |

| Toxicity type | CAS RN/ specific substance[1] | Effect levels[2]/results |
|---|---|---|
| | 64741-87-3 | **Initiation:** 30 male CD-1 mice (7–9 weeks of age) administered 50 µL (917 mg/kg-bw per day)[10,12,14] of the test substance (neat) for five consecutive days. After a 2-week rest period, 50 µL of the promoter phorbol-12-myristate-13-acetate (PMA) was administered 2 times/week for 25 weeks. Both substances applied to the shaved dorsal intrascapular skin. Insignificant increase in skin tumours. Tumour incidence: 3/29 in the test group (squamous cell papillomas); 3/30 in the negative control group; 30/30 in the positive control group. Tumours appeared after 20 weeks in the test group and 16 weeks in the negative control group.<br>**Promotion:** 30 male CD-1 mice (7–9 weeks of age) administered 50 µL of 7,12-dimethyl benzanthracene (DMBA) as a single dose. After a 2-week rest period, 50 µL (917 mg/kg-bw per day)[10,12,14] of the test substance was administered, 2 times/week, for 25 weeks. Both substances applied to the shaved dorsal intrascapular skin. No increase in skin tumours. Tumour incidence: 0% in the test and negative control groups; 30/30 in the positive control group (Skisak et al. 1994). |
| | | **INHALATION EXPOSURE (chronic)** |
| | Gasoline[3] | 0, 67, 292 or 2056 ppm (0, 200, 870 or 6170 mg/m$^3$; as cited in IARC 1989a) of the test substance (containing 2% benzene content) administered to male and female B6C3F1 mice and Fischer 344 albino rats (approximately 6 weeks of age; 100 mice or rats per sex per group), via inhalation, 6 h/day, 5 days/week, for 103–113 weeks. Increased incidence of hepatocellular tumours (adenomas and carcinomas) in female mice (14%, 19%, 21% and 48%, respectively; final group was statistically different from controls). Increased incidence of renal tumours in female mice (2/100 at the highest concentration). Concentration-related increased incidence of primary renal neoplasms in male rats (0, 1, 5 and 7, respectively). Appearance of tumours not considered statistically significant in male mice and female rats, and renal tumours not considered relevant to humans (MacFarland et al. 1984).<br><br>0, 10, 69 or 298 ppm (0, 27, 183 or 791 mg/m$^3$)[5,8] of the test substance (PS-6 blend) administered to F344 rats (31 rats per sex per group) or to a positive control (50 ppm 2,2,4-trimethyl pentane [TMP]), via inhalation, 6 h/day, 5 days/week, until sacrifice at 65–67 weeks. No renal cell tumour incidence observed in any exposure group. *Part of the initiation/promotion study mentioned below* (Short et al. 1989). |
| | | **INHALATION EXPOSURE (initiation/promotion)** |

| Toxicity type | CAS RN/ specific substance[1] | Effect levels[2]/results |
|---|---|---|
| | Gasoline[3] | ***Sequence reversal study (initiation)*:** Male F344 rats (8–9 weeks of age; 30 rats per group) exposed to 10, 69 or 298 ppm (27, 183 or 791 mg/m$^3$)[5,8] of the test substance (PS-6 blend) or to a positive control (50 ppm TMP), via inhalation, 6 h/day, 5 days/week, for 24 weeks. After a 4-week rest period, the promoter *N*-ethyl-*N*-hydroxyethylnitrosamine (EHEN) was administered at 170 ppm in drinking water for 2 weeks. Rats were sacrificed at 65–67 weeks. Appropriate controls present. Insignificant renal cell tumour incidence observed in all exposure groups (0, 1, 0 and 0 developed tumours, respectively).<br>***Sequence reversal study (promotion)*:** Male F344 rats (8–9 weeks of age; 30 rats per group) administered 170 ppm EHEN in drinking water for 2 weeks. After a 4-week rest period, 10, 69 or 298 ppm (27, 183 or 791 mg/m$^3$)[5,8] of the test substance (PS-6 blend) or a positive control (50 ppm TMP) was administered, via inhalation, 6 h/day, 5 days/week, for 24 weeks. Rats were sacrificed at 65–67 weeks. Appropriate controls present. Significant linear trend in the incidence of renal cell tumours observed (1, 1, 1 and 4 developed tumours, respectively) (Short et al. 1989).<br><br>***Promotion*:** 36 female B6C3F1 mice (12 days of age; 12 mice per concentration) administered DEN at 5 mg/kg-bw, via intraperitoneal injection. At 5–7 weeks of age, mice then exposed to the test substance (PS-6 blend), via inhalation, at concentrations of 0, 283 or 2038 ppm (0, 751 or 5410 mg/m$^3$)[5,8], 6 h/day, 5 days/week, for 16 weeks. Alternatively, the test substance was administered to initiated mice at 2038 ppm (5410 mg/m$^3$) in addition to 1 ppm of ethinyl estradiol (EE2) in the diet. Significant increase in the incidence of macroscopic hepatic neoplasms observed in mice exposed to 2038 ppm of the test substance alone, and also with co-exposure to EE2 (10.3-fold and 60-fold increase, respectively, over the proper controls) (Standeven et al. 1994). |
| Genotoxicity (*in vivo*) | | **INHALATION EXPOSURE** |
| | 8052-41-3 | **Negative for micronuclei induction:** Four male BALB/c mice exposed to 50 g/m$^3$ (50 000 mg/m$^3$) of white spirit, via inhalation, for 5 minutes, every 5 minutes. No induction of micronuclei in the polychromatic erythrocytes from bone marrow cells in mice (Gochet et al. 1984). |
| | **64741-55-5** | **Negative for chromosomal aberrations:** Rats (sex/number/strain not specified) exposed to 63, 297 or 2046 ppm (194, 915 or 6301 mg/m$^3$)[5,15] of the test substance (API 81-03), via inhalation, 6 h/day for 5 days. No induction of chromosomal aberrations (API 1985d). |

| Toxicity type | CAS RN/ specific substance[1] | Effect levels[2]/results |
|---|---|---|
| | Gasoline[3] | **Positive for atypical cell foci (*Sequence Reversal Study (Promotion)*).** Male F344 rats (8–9 weeks of age; 30 animals per group) administered 170 ppm EHEN in drinking water for 2 weeks. After a 4-week rest period, 10, 69 or 298 ppm (27, 183 or 791 mg/m$^3$)[5,8] of the test substance (PS-6 blend) was administered, via inhalation, 6 h/day, 5 days/week for 24 weeks. Rats were sacrificed at 65–67 weeks. Appropriate controls present. Observed significant linear trend for atypical cell foci and renal cell tumours (Short et al. 1989). |
| | | **Positive for RDS:** Male and female Fischer 344 rats (3 per sex per group) exposed to 2000 ppm (5309 mg/m$^3$)[5,8] of the test substance (PS-6 containing 2% benzene), via inhalation, 6 h/day for 4 and 18 days (male) or 18 days (female). Induction of RDS in kidney cells after 18 days (males only; changes in females not statistically significant) (Loury et al. 1987). |
| | | **Negative for UDS:** Male and female Fischer 344 rats (3 per sex per group) exposed to 0 or 2000 ppm (5309 mg/m$^3$)[5,8] of the test substance (PS-6), via inhalation, 6 h/day for 4 and 18 days (male) or 18 days (female). No induction of UDS in kidney cells (Loury et al. 1987). |
| | | **ORAL EXPOSURE** |
| | 64742-48-9 | **Negative for micronuclei induction:** Male and female Crl:CD-1 (ICR) BR Swiss mice (10-15 per sex per group) exposed to 0, 625, 1250 or 2500 mg/kg-bw per day (daily for 2 days) or 2500 mg/kg-bw (for 1 day) of the test substance, via oral gavage. No induction of micronucleated polychromatic erythrocytes (PCEs) and no significant change in the ratio of PCEs to normochromatic erythrocytes (NORMs) of mice. No induction of cytogenic damage (Khan and Goode 1984). |
| | Gasoline[3] | **Positive for RDS:** Male and female Fischer 344 rats (3 per sex per group) exposed to 200 mg/kg-bw per day (for 4 days) or 135 mg/kg-bw per day (for 18 days) of the test substance (PS-6 containing 2% benzene), via oral gavage. Induction of RDS in kidney cells after 4 and 18 days (males only; changes in females not statistically significant) (Loury et al. 1987). |
| | | **Positive for UDS:** Male and female B6C3F1 mice (3–4 per sex) exposed to 2000 mg/kg-bw of the test substance (PS-6 containing 2% benzene), as a single dose, via oral gavage. Hepatocytes isolated 2 hours (three mice) or 12 hours (four mice) after exposure. Induction of UDS in hepatocytes after 12 hours of exposure (confirmed by significant increase in percentage of cells in repair) (Loury et al. 1986). |
| | | **Negative for chromosomal aberrations:** Five male Sprague-Dawley rats exposed to 500, 750 or 1000 mg/kg per day of the test substance (PS-6), via oral administration, for 5 days |

| Toxicity type | CAS RN/ specific substance[1] | Effect levels[2]/results |
|---|---|---|
| | | (cells harvested 6 hours after final exposure). No induction of chromosomal aberrations in bone marrow cells of rats (Dooley et al. 1988). |
| | | **INTRAPERITONEAL EXPOSURE** |
| | 8052-41-3 | **Negative for micronuclei induction:** Male and female BALB/c mice (5 per sex per group) administered 0.01, 0.05 or 0.1 ml (371, 1855 or 3710 mg/kg-bw)[10,12,16] of white spirit, as a single dose, via intraperitoneal (i.p.) injection (sacrificed after 30 hours). No induction of micronuclei in the polychromatic erythrocytes from bone marrow cells in mice (Gochet et al. 1984). |
| | **64741-55-5** | **Negative for chromosomal aberrations**: Male and female Sprague-Dawley rats (15 per sex per group) were administered 0.3, 1.0 or 3.0 g/kg (300, 1000 or 3000 mg/kg-bw) of the test substance (API 81-04), as a single dose via i.p. injection (5 per sex per dose were sacrificed at 6, 24 and 48 hours after exposure). No induction of chromosomal aberrations, rearrangements or cell cycle disruption in bone marrow cells of rats (API 1985f). |
| **Genotoxicity (*in vitro*)[17]** | 68410-97-9 | **Negative for mutagenicity (reverse mutations; Ames):** *Salmonella typhimurium* TA98, TA100, TA1535 and TA1537 and *Escherichia coli* WP2(uvrA) were exposed to the test substance (hydrogenated pyrolysis gasoline) at concentrations of 0, 33, 100, 333, 1000, 3333 or 10 000 µg/plate, with and without exogenous metabolic activation (male Sprague-Dawley rat liver S9) (3 plates per concentration ± S9), using the Ames assay (Riccio and Stewart 1991).<br><br>**Negative for UDS:** Primary rat hepatocyte cultures derived from male Fischer 344 rats (10 weeks old) exposed to the test substance (hydrogenated pyrolysis gasoline) at doses of 8, 16, 32, 64, 128, 256, 512 or 1024 µg/ml for 18 hours, without exogenous metabolic activation. Toxicity observed at 512 and 1024 µg/ml (insufficient cells for UDS analysis); UDS not evident at lower doses (Brecher 1984a).<br><br>**Positive for cell transformation:** BALB/3T3-A31-1-1 mouse embryo cells exposed to the test substance (hydrogenated pyrolysis gasoline) at doses of 100, 250, 500 and 1500 µg/ml (15 cultures per dose) for 2 days, without exogenous metabolic activation. Toxicity seen at all dose levels (cloning efficiencies of 53.7% at 100 µg/ml to 0% at 1500 µg/ml). Transformation observed at 1500 µg/ml (frequency of 0.36) (Brecher 1984b). |
| | 64741-46-4 | **Negative for mutagenicity (reverse mutations; modified Ames):** *S. typhimurium* TA98 exposed to DMSO extracts of the test substance at doses of 0-50 µl/plate, with and without |

| Toxicity type | CAS RN/ specific substance[1] | Effect levels[2]/results |
|---|---|---|
| | | exogenous metabolic activation (Blackburn et al. 1986). |
| | **64741-55-5** | **Negative/equivocal for sister chromatid exchange:** *Negative:* Chinese hamster ovary cells exposed to the test substance (API 81-03) at doses of 0.05, 0.1, 0.2 or 0.3 µl/ml, without exogenous metabolic activation (rat liver S9). *Equivocal*: Chinese hamster ovary cells exposed to the test substance (API 81-03) at doses of 0.03, 0.05, 0.1 or 0.2 µl/ml, with exogenous metabolic activation. 2 intermediate doses induced small but statistically significant increases in SCE (API 1988b). |
| | 64742-48-9 | **Negative for cell transformation:** BALB/3T3-A31-1-1 mouse embryo cells exposed to the test substance at doses of 16, 32, 64 or 200 µg/ml (15 cultures per dose) for 2 days, without exogenous metabolic activation (S9). Toxicity seen at ≥32 µg/ml (cloning efficiencies of 67.2% at 32 µg/ml to 28.8% at 200 µg/ml) (Brecher and Goode 1984b). |
| | **68955-35-1** | **Positive for mutagenicity with activation (forward mutations; mouse lymphoma assay):** *Positive*: L5178Y $TK^{+/-}$ mouse lymphoma cells exposed to the test substance (API 83-05) at concentrations of 3.13-400 µl/ml, for 4 h, with exogenous metabolic activation (rat liver S9), using the mouse lymphoma assay. Response was concentration-related. *Negative*: L5178Y $TK^{+/-}$ mouse lymphoma cells exposed to the test substance (API 83-05) at concentrations of 6.25-500 µl/ml, for 4 h, without exogenous metabolic activation (rat liver S9), using the mouse lymphoma assay (API 1985p). |
| | **64741-74-8** | **Positive for mutagenicity without activation (forward mutations; mouse lymphoma assay):** *Positive*: L5178Y $TK^{+/-}$ mouse lymphoma cells exposed to the test substance (rerun tower overheads) at concentrations of 0, 0.013, 0.018, 0.024, 0.032, 0.042, 0.056, 0.075 or 0.10 µl/ml, without exogenous metabolic activation (rat liver S9), using the mouse lymphoma assay. Weak induction of forward mutations observed at the two highest doses. No dose–response trend was observed at the six lower doses. *Negative*: L5178Y $TK^{+/-}$ mouse lymphoma cells exposed to the test substance (rerun tower overheads) at concentrations of 0, 0.013, 0.018, 0.024, 0.032, 0.042, 0.056, 0.075 or 0.10 µl/ml, with exogenous metabolic activation (rat liver S9), using the mouse lymphoma assay. No induction of forward mutations observed at any dose (Kirby et al. 1979). |
| | Gasoline[3] | **Positive for UDS:** Hepatocytes derived from three male Fischer 344 rats, two male B6C3F1 mice and one human were exposed to the test substance (PS-6 containing 2% benzene) at doses of 0.01–0.33% by volume (rats) and |

| Toxicity type | CAS RN/ specific substance[1] | Effect levels[2]/results |
|---|---|---|
| | | 0.01-0.05% by volume (mice and humans). Maximum induction of UDS occurred at 0.10% by volume for rats (dose-dependent) (cytotoxicity occurred at higher doses). Induction of UDS occurred at 0.01% by volume for mice and humans (cytotoxicity occurred at higher doses; thus, a dose-response trend could not be established) (Loury et al. 1986).<br><br>**Negative for UDS:** Primary kidney cell cultures derived from two Fischer 344 rats exposed to the test substance (PS-6) at doses of 0.005, 0.010, 0.050 and 0.1% v/v. No induction of UDS observed at 0.005 and 0.010% v/v. Cytotoxicity occurred at higher doses (Loury et al. 1987). |

[1] Site-restricted LBPN substances are indicated in bold.
[2] Abbreviations: $LC_{50}$, median lethal concentration; $LD_{50}$, median lethal dose; LOAEC, lowest-observed-adverse-effect concentration; LOAEL, lowest-observed-adverse-effect level; NOAEC, no-observed-adverse-effect concentration.
[3] Gasoline captures the following CAS RNs: 8006-61-9 and 86290-81-5.
[4] 1 $m^3$ = 1000 L.
[5] The following formula was used for conversion of provided values into mg/$m^3$: (*x* ppm × Molar Mass (MM))/24.45.
[6] The molar mass (MM) of CAS RN 8032-32-4 was not available; therefore a MM of 64.9 g/mol (gasoline) was used (Roberts et al. 2001).
[7] The MM of CAS RN 64742-95-6 was not available; therefore a MM of 64.9 g/mol (gasoline) was used (Roberts et al. 2001).
[8] MM of gasoline reported to be 64.9 g/mol (Roberts et al. 2001).
[9] The following formula was used for conversion of provided values into mg/kg-bw: *x* mg/bw.
[10] Body weight (bw) not provided; thus, laboratory standards from Salem and Katz (2006) were used.
[11] MM of CAS RN 64742-48-9 reported to be 143 g/mol (Hass et al. 2001).
[12] The following formula was used for conversion of provided values into mg/kg-bw: *x* ml/kg-bw × ρ.
[13] Density (ρ) of gasoline reported to be 720 mg/ml (CONCAWE 1992).
[14] Density (ρ) of CAS RN 64741-87-3 reported to be 678.2 mg/ml (API 2003d).
[15] MM of CAS RN 64741-55-5 reported to be 75.3 g/mol (Lapin et al. 2001).
[16] Density (ρ) of CAS RN 8052-41-3 reported to be 779 mg/ml (Gochet et al. 1984).
[17] Negative result studies described in table correspond to studies with the highest dose used.