HEAVY FUEL OILS CATEGORY
ANALYSIS AND HAZARD CHARACTERIZATION

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CONTENTS

EXECUTIVE SUMMARY

The Heavy Fuel Oils (HFOs) category includes two finished products (residual fuels) and the primary refinery streams from which they are blended. The residual fuels are primarily used in industrial boilers and other direct source heating applications (e.g., blast furnaces) and as a principal fuel in marine diesel applications. The residual fuels are products that consist primarily of the residuum from vacuum distillation and catalytic and thermal cracking processes. If necessary, gas oil or kerosene streams are blended to achieve the desired properties (i.e., viscosity) for various industrial applications. Physical-chemical properties, environmental fate, environmental effects and human health effects are summarized below and discussed in the body of the category analysis. The mammalian health effects data are derived primarily from dermal studies as this is the primary route of human contact.

Physical-Chemical Properties:

Substances in the Heavy Fuel Oil Category do not have sharply-defined melting points, but are viscous substances with pour points typically <30°C. Viscosity is the controlling product specification. The typical boiling range is generally between 350 to 650°C (CONCAWE, 1998) or by CAS definition 121 to 600°C (250 – 1112°F) [EPA, 2004] but higher and lower boiling blending components may be present depending on either the manufacturing processes or the technical requirements of the final product. Data from over 50 HFO samples submitted by US companies for the HPV Challenge program had boiling points ranging from 181 ≥ 1327^{0}F (83 ≥ 719^{0}C). Their individual constituents generally fall in the C20 to ≥C50 range, but this is influenced by refinery practices and the blending of these residual streams with gas oils or similar low viscosity fractions to enhance the flow characteristics. While the low-end molecular weight hydrocarbons have been reported as low as C7, flash point specification for heavy fuel oil products restricts the amount of C7 hydrocarbons. This practice of blending for performance enhancement influences the physical-chemical characteristics and creates a diverse group of petroleum products. The total vapor pressure of heavy fuel oils would normally be below measurable limits, but individual constituents representing the low molecular weight fractions may show measurable vapor pressures in their pure state. Partition coefficients representing the majority of compounds in the C20 to ≥C50 range are >6, but individual hydrocarbons representing the low-end molecular weight constituents may range from 1.7 to >6. Water solubility would be expected to be low for these substances, and studies have reported total dissolved hydrocarbons from <1 mg/L to approximately 6 mg/L in aqueous preparations of heavy fuel oils.

Environmental Fate:

When heavy fuel enters the environment the individual constituents will partition to various environmental compartments in accordance with their own physical-chemical properties. Low molecular weight fractions of heavy fuel may dissolve in water or evaporate to the atmosphere. The remaining constituents may float or sink depending on density relationships and become incorporated into soils/sediments. Some compounds may engage in direct photolytic reactions if they receive sufficient energy from sunlight to effect the chemical reactions. Others may undergo indirect photodegradation with photosensitized oxygen compounds in the troposphere. Photodegradation rates for volatile components may be rapid, and these constituents would not be expected to persist in the atmosphere. Components of heavy fuels are stable to hydrolysis and this process is not a fate pathway for dissolved fractions. However, the limited constituents of heavy

fuels that dissolve in water become available for biodegradation. Biodegradation rates are related to molecular weight and structural conformation, with the lower molecular weight fractions being first to be utilized by microbes due to their bioavailability. From spill events, biodegradation of the different molecular species follows a specific order and is influenced by temperature, dispersion, and available nutrients. Heavy fuel oils are not expected to be readily biodegradable.

Ecotoxicity:

When the acute aquatic toxicity values for heavy fuel oils were compared on the basis of the loading rates of water accommodated fractions, LL50 values for acute toxicity endpoints were always >100 mg/L. In some instances, no adverse effects were observed at the maximum loading rate of 1000 mg/L. Although the data for the category members are limited, algae appeared to be the most sensitive aquatic species. The lowest EL50 values for algae fell within the range of 10 to 30 mg/L when evaluated on the basis of growth biomass. In recognition that substances in the heavy fuel oil category are diverse materials that are commonly blended with lower molecular weight petroleum substances to meet technical requirements, ecotoxicity data from the gas oil and kerosene categories were used to assess potential adverse effects that could be attributed to constituents having carbon numbers as low as seven. Gas oil and kerosene streams typically show greater toxicity than heavy fuel oils due to the higher solubility of their constituent compounds. In general, toxicity values for gas oil and kerosene streams tend to fall within the range of 1 to 100 mg/L on the basis of loading rates. Using the range of 1 to 100 mg/L for read-across to all members of the heavy fuel oil category may overestimate the aquatic toxicity of the category members, but reflects a potential toxicity based on consideration of the variable nature of these substances. For chronic aquatic toxicity, test data on gas oils may be used as read-across for the heavy fuel oil category because the two finished fuels can be blended with middle distillates or by definition overlap with middle distillates at the low-end range of their molecular weight hydrocarbons. The lowest NOELR and LOELR were 0.05 mg/L and 0.10 mg/L, respectively, for a 21-day *D. magna* reproduction study.

Human Health Effects:

Substances in the Heavy Fuel Oil Category demonstrate low oral and dermal toxicity, minimal eye irritation, minimal to moderate skin irritation with single exposures and are not skin sensitizers. The other mammalian health effects of HFOs are dependent on their content of polycyclic aromatic compounds (PAC)

Repeated dose dermal studies indicate that toxicity induced by different HFO streams affected essentially the same organ systems (liver, spleen, thymus and bone marrow). Streams with higher aromatic content and broader aromatic ring distribution profiles tended to be more toxic with lower LOAEL and NOAEL values [e.g. CAS RN 64741-62-4 catalytic cracked clarified oil LOAEL = 5 to 10.6mg/kg ; NOAEL = 1.06 to < 8mg/kg] compared to the overall ranges of LOAELs 5 to 500mg/kg and NOAELs 1.06 to125mg/kg. There can be some overlap in toxicity values resulting from differences in feedstock and processing steps. Polycyclic aromatic compound (PAC) content and aromatic ring class distribution profiles are determined by crude oil stock and the nature and severity of processing. Toxicity levels for residual fuel oils blended from these streams may fall anywhere in that range of activity. Most studies from these streams did not report adverse histological changes in reproductive organs or when evaluated, effects on sperm number and morphology.

Genetic toxicity studies *in vitro* demonstrate that many streams in the heavy fuel oil category are gene mutagens. However the level of activity is related to PAC content over a continuum from low activity in streams containing less biologically active PAC to greater activity in streams with higher PAC content. Heavy fuel oils are expected to be positive for *in vitro* mutagenicity. Studies of chromosome damage or micronucleus formation indicate that in general heavy fuel oil streams are not clastogenic in animals regardless of the refinery process they are derived from.

Results of developmental toxicity studies from the Heavy Fuel Oil category indicate that the most severe adverse effects appear in CAS RN 64741-62-4, catalytic cracked clarified oils with NOAELs ranging from 0.05 to 10mg/kg compared to the overall range of LOAELs 1 to1000mg/kg and NOAELs 0.05 to 500mg/kg. In all cases where fetal toxicity is reported, the effects are accompanied by maternal toxicity.

Results from a reproductive function assay and evaluation of reproductive organs and sperm in 13 week studies demonstrate that these endpoints are generally not adversely affected by treatment with heavy fuel oil streams. Studies of several vacuum distillates in which females were treated prior to mating, through mating and gestation to GD20 demonstrated that exposure to high concentrations did not adversely affect mating and the ability to implant but did adversely affect successful completion of pregnancy and pup viability in a dose related manner at doses in the range of 250mg/kg – 1000mg/kg, doses at which maternal toxicity was also present. These values are higher than those seen in developmental studies. Since the most sensitive endpoints for developmental or reproductive toxicity are expected to be effects on fetal survival and growth resulting from *in utero* exposure, NOAELs for reproductive toxicity are not expected to be lower than the corresponding NOAELs for developmental toxicity.

Modeled data based on PAC aromatic ring distribution profile of streams has been developed for repeated dose and developmental toxicity evaluation. The PDR_{10} value is the dose level at which a 10% change in response from control value for a given endpoint is seen for a specific sample. For heavy fuel oils, the PDR10 values correlate reasonably well with the LOAEL and NOAEL derived from animal data and indicate that cracked stocks with higher 3-7 ring aromatic content have the greatest toxic potential. Use of this method can prove valuable in estimating potential and comparative biological activity for materials for which animal data are not available or where dose levels are very widely spaced. Toxic potency can be ranked based on aromatic ring profile within or across CAS numbers in this category.

Dermal carcinogenicity studies performed with catalytic cracked clarified oil [CAS RN 64741-62-4] demonstrated that materials with a high content of PACs are dermal carcinogens and act primarily by initiating tumor development. Read-across results from whole vacuum residual samples in the Asphalt Category Assessment Document indicated that similar materials with a different distribution of PAC were not dermal carcinogens. Thus, the content and analytical profiles of PACs play a significant role in skin cancer in mice.

Overall, the materials in the Heavy Fuel Oil Category are not acutely toxic but can induce levels of systemic and developmental toxicity with repeated doses that are linked to the concentration and distribution profiles of 1-7 ring polycyclic aromatic compounds but all materials comprise a single Heavy Fuel Oils category. The distributions and concentrations of PACs vary by crude oil basestocks and processing steps. Mammalian repeat dose and developmental toxicity of HFO members depends on their PAC profile. There is a recognizable distinction between straight-run and cracked HFOs in the amount of DMSO extractable PAC and toxicity values (NOAEL/PDR10s) with cracked HFOs generally showing greater toxicity. However there is no difference in the risk

management of HFOs based on PAC content. For EU global hazard communication purposes all CAS RNs in the Heavy Fuel Oil Components category carry the same hazardous classifications (EC 1272/2008, 2008; CONCAWE, 2012).

Human Exposure

Heavy fuel oils are mainly used as marine fuel for large diesel engines or boilers, for commercial and industrial heating, and in the production of steam and electricity in power plants. There is no direct consumer use of HFO or residual fuel oils and no anticipated exposure of children. Manufacture and transport of HFO and residual fuel oil products are done in closed systems and typically at elevated temperature thus limiting worker exposure. There are numerous laws and regulations limiting occupational exposure and environmental release of heavy fuel oil substances and residual fuel oil products and safe handling practices mandated within the petroleum industry.

Measurement of dermal exposure to neck, hands and forearms in occupational settings has demonstrated low dermal loads, likely due to high compliance of glove use by workers during HFO handling tasks and general avoidance of contact with HFO due to its high viscosity and maintenance at elevated temperatures during storage, transport and use. Storage of HFO in closed systems and elevated temperatures can result in formation and accumulation of hydrogen sulfide in the enclosed space. The 2011 OSHA occupational exposure limit for H2S is 20ppm (ceiling value) and 2010 ACGIH 8hr TLV = 1ppm with a 5ppm limit for 15 min short term exposure.

In conclusion, the information provided in this Heavy Fuel Oils Category Assessment Document is sufficient to characterize physicochemical properties and evaluate the environmental and human health hazards of heavy fuel oils and residual fuel oil products in accordance with EPA's Challenge Program.

1. DESCRIPTION OF HEAVY FUEL OILS CATEGORY

The Heavy Fuel Oils (HFOs) category includes two finished products (residual fuels) and the primary refinery streams from which they are blended. The residual fuels are primarily used in industrial boilers and other direct source heating applications (e.g., blast furnaces) and as a fuel for large marine diesel engines. The residual fuels are products that consist primarily of the residuum of the refining process after virtually all of the higher quality hydrocarbons have been removed from crude oil feedstock. Historically, fuel oils were based on residuals from atmospheric distillation. However, the increasing demand for transportation fuels such as gasoline, kerosene and diesel, and lubricants has led to an increased value for the atmospheric residuum as a feedstock for vacuum distillation and for cracking processes. As a consequence, most heavy fuel oils are currently based on vacuum residuum and residua from thermal and catalytic cracking operations (CONCAWE, 1998). These high viscosity residual streams may in turn be "cut" with lower quality, lighter weight distillates to produce a finished residual fuel of a specified viscosity. The choice of the distillate cutter stock is itself variable and largely a function of availability at any given time within the refinery and the viscosity specifications of the fuel being manufactured. While materials frequently used as cutter stocks are included in this category, other streams may be used, e.g., kerosene and gas oils. The properties of these other materials are described in other Petroleum HPV Category documents. The exact blend used for a specific residual fuel is determined largely by the desired viscosity of the finished fuel and applicable technical specifications. Some of the refinery streams in the heavy fuel oil category that have lower viscosities and lower polycyclic aromatic compound (PAC) levels have low-volume, specialty applications such as cutter stock in cutback asphalt, and carbon electrode production (ASTM, 2002)

Members of the heavy fuel oils category are a diverse group of substances that encompass hydrocarbons with a wide range of molecular weights, with carbon numbers ranging from C7 to ≥C50 and boiling points between 250 – 1112 °F (121 to 600 °C) (Concawe, 1998) but higher and lower boiling blending components may be present depending on either the manufacturing processes or the technical requirements of the final product. However, "typical" heavy fuel oils are C20 to ≥C50 with the low carbon numbers and boiling temperatures being associated with lighter weight "cutter" streams (CONCAWE, 1998). Data from over 50 HFO samples submitted by US companies for the HPV Challenge program had a boiling range from 152 ≥ 1327^{0}F (67 ≥ 719^{0}C). All the category members are complex substances, containing variable amounts of alkanes, cycloalkanes, aromatics, olefins, asphaltenes, and hetero-molecules containing sulfur, oxygen, nitrogen and organo-metals. Because they are complex substances composed of relatively high molecular weight compounds, the materials in this category are difficult to characterize in detail. Consequently, they are typically not defined by detailed compositional information but instead by process history, physical properties, and product use specifications (ASTM, 2003). Since viscosity and sulfur are often the controlling specifications, and other limiting requirements - notably boiling point ranges - are unspecified, there is significant variation in the chemical composition of the resulting commercial residual fuel products (IARC, 1989).

1.1 Production

1.1.1 Process Streams

All of the process streams and the two residual fuel oils comprise a single Heavy Fuel Oil category. The process history of a refinery stream determines its chemical composition and the carbon ranges for streams in this category are directly related to physical/chemical properties and the

potential for environmental effects. See Appendix A for a more detailed description of each of these streams. Knowledge of refining processes, in addition to carbon range and physical/chemical properties, coupled with tests of representative substances can be useful in evaluating human health effects. Figure 1 shows the major processes used to produce the refinery streams included in the heavy fuel oils category In the Heavy Fuel Oils category there are thirteen straight run refinery streams produced by atmospheric or vacuum distillation and eight refinery streams that are produced by cracking (five distillate and six residual streams), the process employing heat or heat plus a catalyst to break ("crack") the heavier, higher boiling petroleum streams produced by atmospheric or vacuum distillation into lighter molecular weight materials such as gasoline, diesel fuel, jet fuel and kerosene. Other substances in the HFO category are produced by catalytic reforming, a process that synthesizes aromatics from smaller paraffins, or are the results of further processing the straight-run or cracked streams by hydrotreating or solvent extraction. See Appendix A for a more detailed description of each of these streams.

Appendix B provides descriptions of these processes

1.1.2. Residual Fuel Oils

In addition to the process streams, the heavy fuel oil category also includes two blended residual fuel oils, Residual Fuel Oil (CAS 68476-33-5) and No. 6 Fuel Oil (CAS 68553-00-4). These two fuel oils are most often produced by blending any combination of the distillate and residual streams so that the finished fuel meets the appropriate product specifications. The residual fuels can also be blended with petroleum distillates (cutter stocks) covered in other API HPV Categories [e.g. kerosene, gas oils]. See Appendix A for a more detailed description of each of these two residual fuel oils.

In describing some of the SIDS endpoints for this category (e.g., particularly physical-chemical and environmental fate endpoints), data on Bunker C fuel oil has been cited and used as a supporting material that is representative of a No. 6 fuel oil. Bunker fuel gets its name from the containers on ships and in ports in which it is stored (i.e., "storage bunkers"). While there are several classes of bunker fuel (e.g., classes "A" and "B", etc.), Bunker C is a term that is commonly used as a synonym for residual fuel oil, No. 6 fuel oil, or heavy fuel oil (Irwin et al., 1997; CONCAWE, 1998). Therefore, the composition of Bunker C fuels is expected to be similar to other substances in this category, and any differences may be explained by the variability in the streams from which these products are made and the characteristics of the original crude oil. For this reason, Bunker C fuel oil is a valid supporting substance to this category that provides valuable data for characterizing SIDS endpoints. Furthermore, much of the data on the fate and effects of heavy fuel oils are derived from studies on oil spilled at sea, of which Bunker C fuel has been reported in a number of studies (Keizer et al., 1978; Jézéquel et al., 2003; Lee, et al., 2003).

Analytical data for representative materials in this category are shown in Table 1.

Table 1. Composition of Representative Samples of the HFO Category

Endpoint	Atmospheric Residual	Vacuum Distillate	Cracked Distillate	Cracked Residual	Fuel Oil No. 6 Oil (1)
CAS No.	64741-45-3	64741-57-7	64741-81-7	64741-62-4	68553-00-4
Specific gravity	0.9698	0.9285	0.9383	1.0725	0.9830
Refractive index	1.5132	1.515	1.5259	Too dark	ND
Distillation (°F)					
IBP	531	548	411	395	477

End point	1041	1131	831	952	1333
Non-aromatics	32.18	40.03	49.6	41.7	55
Aromatics (wt %)	67.82	59.97	50.4	58.3	44

(1) Also referred to as Bunker C fuel oil.
ND = No data.
API, 1987; CONSCI 1992a,b; DataChem 1990

1.2 Composition of Heavy Fuel Oil Blending Streams

While detailed compositional information is limited, general compositional information can be inferred from a refinery stream's physical properties and the type of processing it has undergone (Figure 1). However, these streams are not substantially different from one another as they all contain the same classes of hydrocarbon and heterocyclic compounds. The differences among the streams lie mostly in the proportions of these compounds in each stream. For instance, the higher the boiling temperature range of a stream, the higher the molecular weight of the oil's components, the higher the levels of PACs, polycycloparaffins and hetero-atoms (N, O, S, and metals) increase, and the lower the levels of paraffins (see Figure 2). Furthermore, since "cracking" raises the olefin and aromatic content of refinery streams, streams that have been "cracked" have higher olefin and aromatic hydrocarbon content than "straight run" streams that have undergone a limited amount of additional processing. For example, catalytically cracked clarified oil has been reported to contain as much as 58% three to five ring aromatic hydrocarbons (IARC, 1989). Thus, a residual fuel blended using primarily catalytically cracked or steam cracked components will have a higher PAC content (approaching 20 - 36%) than a fuel blended primarily of a non-cracked stream, i.e. heavy vacuum gas oil (CONCAWE, 1998). If on the other hand, the blending stocks are predominantly atmospheric or vacuum distillates or residuals, the concentration of three to seven ring aromatic hydrocarbons is likely to be of the order of 6-8% (IARC, 1989). The types and levels of PACs found in a specific fuel will depend on the processing the residual portion of the fuel has undergone, and the nature of the blending stream ("cutter" stock) that is used to adjust the viscosity of the finished fuel.

Figure 1. HFO Process Diagram

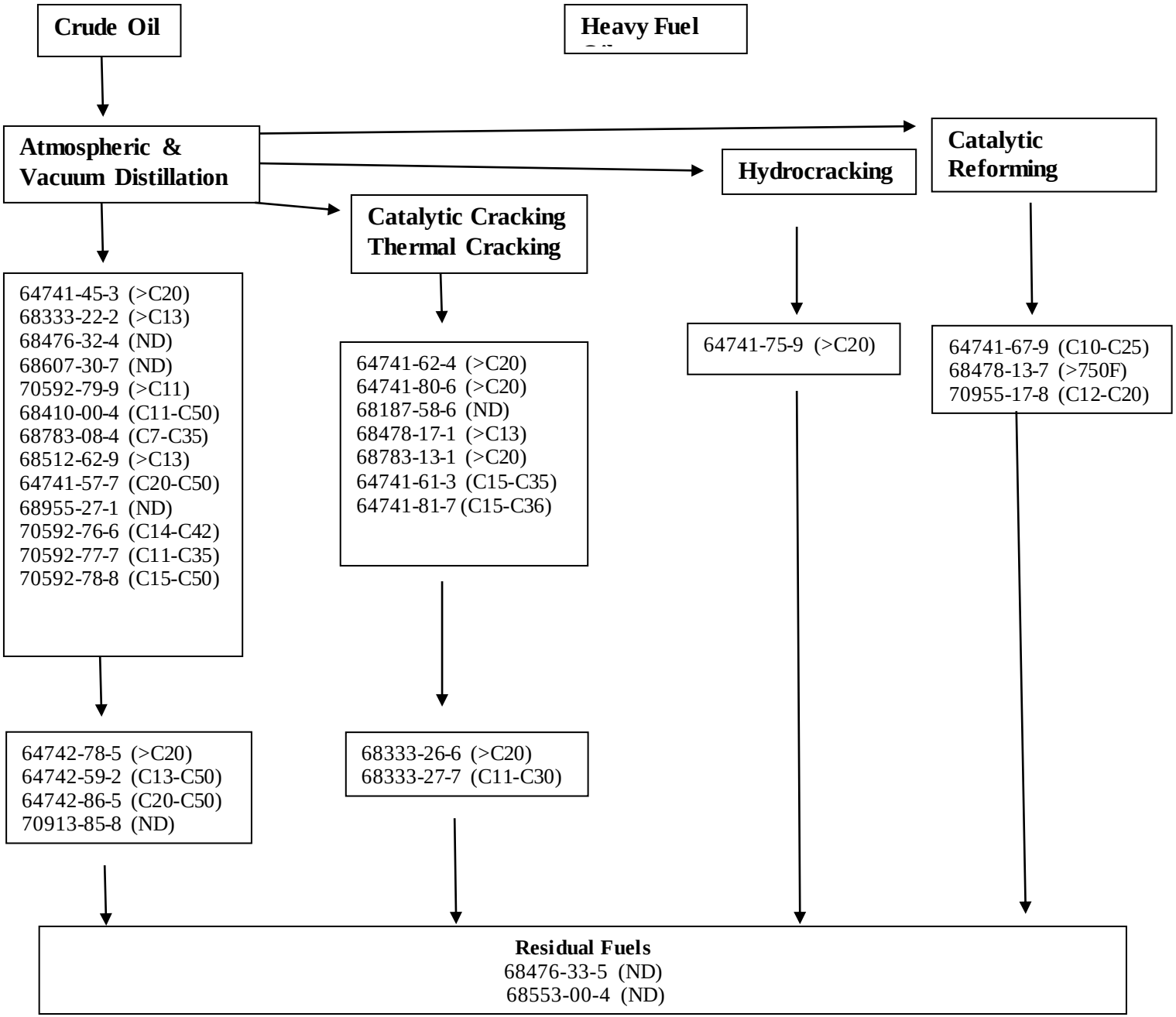
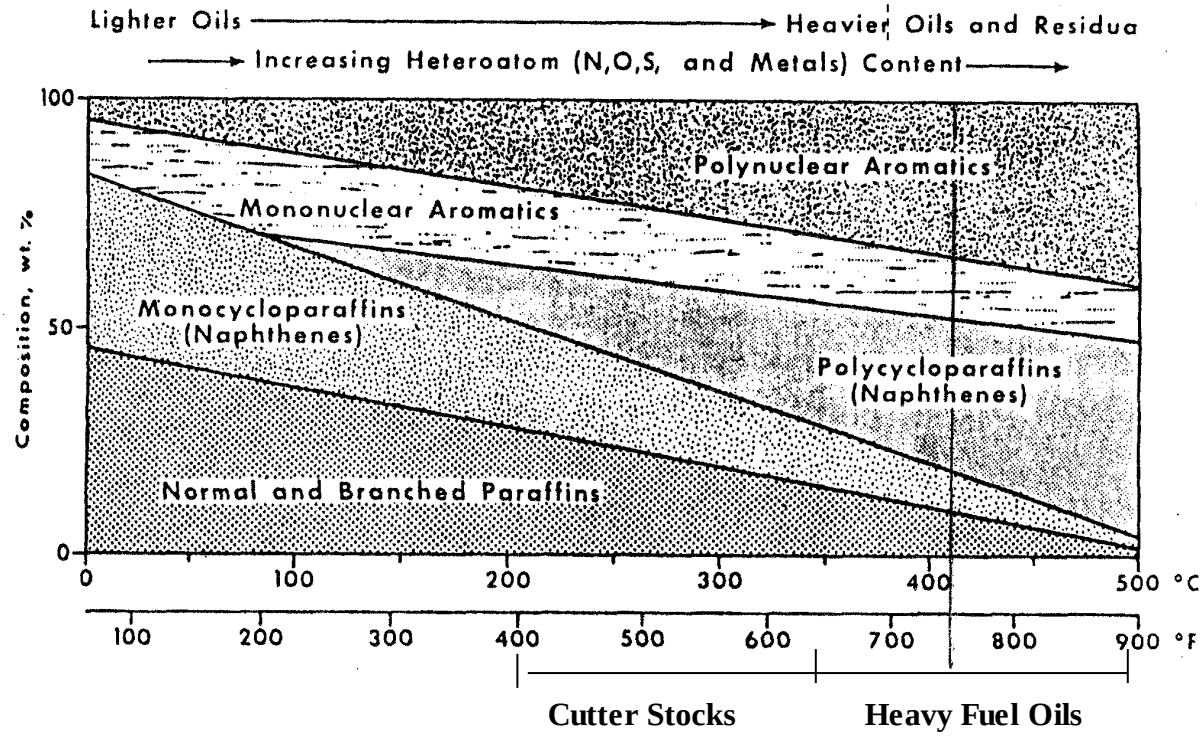


Figure 2. Refinery Stream Composition – Boiling Range vs. General Composition



[Speight, 1998]

Links to additional resources on refining processes and petroleum-related glossaries are presented in Appendix C.

2. CATEGORY DEFINITION AND JUSTIFICATION

The HFO Category includes finished products (residual fuels) and the primary refinery streams from which they can be blended. The category members are complex substances, containing variable amounts of alkanes, cycloalkanes, olefins, aromatics, asphaltenes, and hetero-molecules containing sulfur, oxygen, nitrogen and organo-metals. Because they are complex substances composed of relatively high molecular weight compounds, the materials in this category are difficult to characterize in detail. Consequently, they are typically not defined by compositional information but instead by process history, physical properties, and product use specifications (ASTM, 2003). The carbon number range of HFOs is primarily C20 to ≥C50 which determines the boiling range, volatility, water solubility, and viscosity of these substances. These properties in turn determine their environmental fate and potential ecotoxicity.

Because of the diversity of constituents in HFOs, it is not feasible to model the physicochemical endpoints for each one. Where modeling was necessary to fulfill an endpoint, such estimates were made for common hydrocarbon structures (e.g., saturated, aromatic, olefinic and heterocyclic hydrocarbons) and range of molecular weight hydrocarbons (i.e., number of carbon atoms) known

to be represented in HFO substances. Since molecular weight and structural conformation determine in large part many of the physico-chemical and fate processes, the modeled estimates for these isomeric structures are expected to represent potential ranges of values for all substances in the HFO Category.

The carbon number range was also used to predict the degree of ecotoxicity. This approach is valid and consistent with the current understanding of the mode of toxic action for non-polar organic molecules (such as petroleum hydrocarbons) to aquatic organisms (Peterson, 1994; van Wezel and Opperhuizen, 1995). Furthermore, the streams and products in the HFO Category are composed of constituent hydrocarbon compounds that also are represented in other petroleum product HPV categories that have measured ecotoxicity data. Therefore data from other categories was employed as read across to describe potential ecotoxicity for all substances in the HFO category.

The mammalian health effects of HFOs are dependent on their content of polycyclic aromatic compounds (which does not affect their low acute toxicity). PAC profiles of samples from 23 of 32 heavy fuel oil streams in this category analyzed by PAC Method II are provided in Table 12 in Section 6.1.2. In general terms, petroleum streams from thermal or catalytic cracking processes have higher PAC content than straight-run distillation fractions or streams derived from other non-cracking processes (i.e., hydrotreating). However this distinction may have no practical significance as the blending and co-mingling of residual fuels after leaving the refinery obscure any provenance.

When laboratory data were unavailable for mammalian endpoints, statistical modeling was employed using the PAC profile of representative samples. The association between PAC profile and certain repeat-dose, developmental, and genetic toxicity endpoints can be used to predict the toxicity of materials for which measured data are unavailable (API, 2008; Nicolich et al., 2010, 2012; Simpson et al., 2012). This association and the statistical models are described in Section 6.1.2 and Appendices D and E.

The blending of residual fuels may include gas oils or kerosene-range refinery streams. These supporting substances are covered in other Petroleum HPV Testing Group Categories.

3. PHYSICAL-CHEMICAL PROPERTIES

3.1 Physical-Chemical Screening Information Data Set (SIDS)

The substances covered under this HPV testing plan are substances of differing compositions. Because of the diversity of compounds encompassing heavy fuel oils, it is not feasible to model the physicochemical endpoints for each potential compound. Where modeling was necessary to fulfill an endpoint, such estimates were made for common hydrocarbon structures (e.g., saturated, aromatic, olefinic and heterocyclic hydrocarbons) and range of molecular weight hydrocarbons (i.e., number of carbon atoms) known to be represented in heavy fuel oil category. Since molecular weight and structural conformation determine in large part many of the physico-chemical and fate processes, the modeled estimates for these isomeric structures are expected to represent potential ranges of values for all substances in the heavy fuel oil category.

The physical-chemical endpoints in the HPV chemicals program include the following:

- Melting Point
- Boiling Point
- Vapor Pressure
- Octanol/Water Partition Coefficient
- Water Solubility

3.1.1 Melting Point

Heavy fuel oils and the streams from which they are produced are viscous substances without sharply defined melting points. They gradually become less viscous as the temperature rises. To better describe the physical phase or flow characteristics of these substances, the pour point is routinely used. The pour point is the lowest temperature at which movement of the test specimen is observed under prescribed conditions of the test (ASTM, 1999).

Measured pour points ranged from –2°C to 35°C (CONSCI, 1992a,b; CONSCI, 1993a-d; Jokuty et al., 2002; NIPER, 1993a,b). Those values are consistent with the review by CONCAWE (1998), which stated pour points for these products are typically <30°C. The differences in flow characteristics of heavy fuels are related to the composition of the crude oil from which they are produced, the variety of refining practices that result in streams that go into heavy fuels, and the practice of adding a lighter "cutter stock" to heavy fuel oils to improve their viscosity characteristics at low temperatures.

Based on the cited data, heavy fuel oil streams and products will exist at ambient temperatures as dense, viscous oils. Those category members with the highest pour points will be characteristically solid to semi-solid substances, while those with the lowest pour points will be more liquid.

Conclusion: Pour point values of heavy fuel oils cited in the robust summaries range from –2°C to 35°C. This is consistent with the review by CONCAWE (1998), which stated pour points for these products are typically <30°C.

3.1.2. Boiling Point

For complex petroleum substances, boiling points are expressed as ranges (i.e., distillation ranges) that are governed by the individual constituent hydrocarbons within the complex substance. Constituent molecules have individual boiling points, and boiling points increase as molecular weight increases. Substances within the Heavy Fuel Oil HPV category are highly diverse, and are produced from a variety of refining processes; processes including both atmospheric and vacuum distillation. Therefore, the boiling ranges of the substances also would be expected to vary widely. CONCAWE (1998) reported that heavy fuels have a typical carbon range from C20 to ≥ C50 and typical boiling ranges from 350 to 650°C, but the final boiling ranges are influenced by the refinery practices and the composition of the individual hydrocarbons in the substances. Affecting the variability for finished residual fuels is the practice of adding lower molecular weight cutter stocks to heavy fuels in order to meet density specifications and to improve the flow characteristics of finished residual fuel products. Based on the general CAS definitions for the refining streams in this category, boiling points can range from 121 to 600°C (EPA, 2004), but the initial and/or final boiling

points of constituent streams could be higher or lower than the typical range due to the manufacturing processes used. Measured boiling ranges for any of the heavy fuel oil streams will depend upon the source of the feedstocks and the refining processes from which they are derived. For example, the mean initial and final boiling points (± standard deviation) for 54 heavy fuel oil samples analyzed for the American Petroleum Institute were 237°C (±63°C) and 611°C (±68°C), respectively. The overall lowest and highest boiling points for HFO samples were 181-1327^{0}F (83 – 719^{0}C). These data are provided in the robust summary.

Conclusion: A boiling range of 350 to 650°C may be considered typical for heavy fuel oils having constituent compounds in the C20 to ≥C50 range (CONCAWE, 1998). By their CAS definitions, the boiling point distribution ranges from 121 to 600°C. The initial and/or final boiling points of constituent streams could be higher or lower than the typical range due to the manufacturing processes used.

3.1.3 Vapor Pressure

Referenced data characterizing the vapor pressure of heavy fuel oils generally were derived from company product safety bulletins (e.g., material safety data sheets). However, unless an independent evaluation of the methods used and details of the test substance can be made, these types of references can only be assigned a reliability of 4 "un-assignable" (OECD, 2007). Additionally, for most of the heavy fuel oil refinery streams in the category, company product data generally are lacking. Therefore, vapor pressures were calculated using the MPBPWIN subroutine of the EPI-Suite^{TM} computer model (EPA, 2001). This provided a range of vapor pressure estimates for various hydrocarbon and non-hydrocarbon compounds spanning the carbon number range and representing the general chemical structures of constituents expected to be present in all members of the heavy fuel oil category. These individual vapor pressures should be qualified as only representing a possible range of vapor pressures because heavy fuel oils contain thousands of different molecules. For these substances, the total vapor pressure of the substance is the sum of the partial pressures of the individual constituents, and the partial pressure of an individual constituent is a product of the vapor pressure of the pure substance times its mole fraction in the complex substance (Raoult's Law). Therefore, the contribution of an individual compound to the overall vapor pressure is quite low.

Heavy fuels oils by definition typically contain compounds having carbon numbers from 20 to ≥50 (CONCAWE, 1998). The practice of adding cutter stocks to improve the flow characteristics of the finished fuels lowers the molecular weight distribution so that a number of the category members have small amounts of low-end molecules containing 7 to 15 carbon atoms which are the most volatile and water-soluble. However, flash point specifications for heavy fuel oil products (>60°C or >140°F) would restrict the amount of C7 hydrocarbons. Vapor pressure estimates were calculated for compounds representing paraffinic, olefinic, naphthenic, aromatic, and polar/heterocyclic components in heavy fuel streams. The calculations included a range of molecular weight compounds to include the low molecular weight structures of the cutter stocks. As would be expected, the estimates show that the lowest molecular weight components have the greatest vapor pressure, and vapor pressure decreases with increasing molecular weight. For the range of molecular weights most prominent in heavy fuel oils (e.g., those having carbon numbers from C20 to ≥C50), estimated vapor pressures ranged from $1x10^{-8}$ kPa to $5x10^{-20}$ kPa. These are not measurable by standard guideline methods (OECD, 1995a). For the range of molecular weights representing potential cutter stocks (e.g., carbon numbers C7+), estimated vapor pressures for individual compounds representing constituents in heavy fuel oils ranged from 0.007 kPa to 9 kPa.

Vapor pressure values from company product literature sources were obtained for five CAS members of the heavy fuel oil category and reported in the robust summaries. For those measurements taken at 20 or 21°C, the minimum and maximum vapor pressures were <0.013 kPa and 2.0 kPa (Nova Chemicals, 2004; Valero, 2006; Houston Refining, 2006a,b).

Conclusion: Vapor pressures of individual constituent compounds in heavy fuel oils having carbon numbers from C20 to ≥C50 are extremely low and below measurable levels using standard guideline methods. Estimated vapor pressures that would be representative for compounds of those carbon chain lengths in heavy fuels ranged from $1x10^{-8}$ kPa to $5x10^{-20}$ kPa. Estimated vapor pressures of lower molecular weight compounds that are representative of potential cutter stock streams ranged from 0.007 kPa to 9 kPa. These estimates were similar to data reported in company product literature for finished fuels. Those data showed vapor pressures ranging from <0.013 to 2.0 kPa when measured at 20 or 21°C.

3.1.4 Partition Coefficient

In substances such as the heavy fuel oils, the percent distribution of the hydrocarbon groups (i.e., paraffins, naphthenes, olefins, aromatics, polar/heterocyclics) and the carbon chain lengths determines in-part the partitioning characteristics of the substance. Generally, hydrocarbons with fewer carbon atoms tend to have lower partition coefficients than those with higher carbon numbers (CONCAWE, 2001). Additionally, aromatic compounds also tend to have lower partition coefficients than other classes of hydrocarbons of similar molecular weight. However, due to their complex composition and limitations of analytical measurements of multi-component substances, unequivocal determination of the partition coefficient (i.e., log K_{ow}) of these substances cannot be made. Rather, partition coefficients of representative hydrocarbon types covering the range of carbon atoms found in substances in this category were modeled using the subroutine KOWWIN of the EPI-Suite™ computer model (EPA, 2001).

Standardized methods for measuring partition coefficient are analytically limited to substance up to log Kow ~4, or occasionally 5 (OECD, 1995b), while log Kow estimates up to 6 may be made by HPLC (OECD, 1989). Constituent compounds in heavy fuel oils typically have carbon chains ranging from C20 to C50 (CONCAWE, 1998), and log Kow values estimated by KOWWIN for these structures are generally >6, indicating that the partition coefficients of heavy fuel oils would not be measurable by standard guideline methods. However, cutter stocks added to heavy fuel oils to reduce viscosity may include very small amounts of compounds as low as C7.

To show the potential range of partition coefficients that might exist based on constituent compounds in heavy fuel oils, KOWWIN estimates were made for a variety of hydrocarbon and non-hydrocarbon types (e.g., alkanes, olefins, naphthenes, aromatics, thiophenes, benzothiophenes, pyridines, etc.) covering molecular weights representing C7 to C50 chain lengths. These estimates show log K_{ow} values to range from 1.7 to 25. The modeled data represent a potential range of log Kow values for the constituent compounds expected to exist in heavy fuel oils.

Conclusion: Modeled estimates of log Kow values for carbon chain lengths of C7 to C50 covering representative structural hydrocarbon and non-hydrocarbon compounds expected to exist in heavy fuel oils fell within a range from 1.7 to 25. For typical heavy fuel oil constituents covering carbon numbers C20 to ≥C50, standard guidelines for measuring log Kow would not produce accurate measurements.

3.1.5 Water Solubility

When released to water, dissolution of the water-soluble constituents in heavy fuel oils will depend upon environmental factors affecting the mixing and weathering of the substance. The lowest molecular weight components in fuel oils have the highest solubility levels also have appreciable vapor pressures and thus would tend to both dissolve and volatilize from the surface. For this reason, measurements of aqueous-phase hydrocarbons taken during spill events do not provide accurate estimations of solubility. Solubility values determined in the laboratory under controlled conditions can still prove difficult and include experimental biases. This is because at any particular loading rate (i.e., weight of substance per unit volume of water), aqueous concentrations of each component are a function of relative volume of aqueous and petroleum phases, partition coefficient between phases, amount of component present and the maximum water solubility of each component. Initially as the petroleum substamce is added in amounts below the solubility limit of the least soluble component the aqueous concentration increases proportionally until the least soluble component reaches a saturation concentration, and only the more soluble components continue to dissolve, resulting in a two phase system. Further addition of the petroleum substance results in an aqueous concentration that is a non-linear function of the amount added. Shiu et al. (1990) demonstrated this effect and also documented that the ratio of oil:water required to maximize the amount of total hydrocarbons in the aqueous phase is different depending on the oil product. Thus, while an oil:water ratio of 1:80 or greater for a gasoline produced no substantial difference in concentrations of total dissolved hydrocarbons, the concentration of total dissolved hydrocarbons in water for a heavy fuel oil declines when the ratio is less than 1:10. This is important as the solubility studies cited in the robust summary employed several different oil:water ratios. Data presented by Shiu et al. (1990) indicates that the greatest concentration of hydrocarbons in the aqueous phase occurs when the oil:water ratio is 1:10 or greater.

The studies cited in the robust summaries demonstrate that measurements of total dissolved hydrocarbons in the aqueous phase of heavy fuel oil:water mixtures fall roughly in the range from <1 mg/L to approximately 6 mg/L. Under controlled conditions with minimal opportunity for volatilization, the total hydrocarbon concentration in distilled water from fuel oil no. 6 was 6.26 mg/L at 22°C (Shiu et al., 1990). This was measured by purge/trap GC/FID using an oil:water ratio of either 1:5 or 1:10, a stirring time of at least 24 hours and a settling time of at least 48 hours. Care was taken to mitigate oil/water emulsions by minimizing the turbulence below that necessary to separate oil droplets from the oil layer. This value was essentially identical to that measured by Anderson, et al. (1974) at an oil:water ratio of 1:9. They measured 6.3 mg/L total dissolved hydrocarbons at 20°C in seawater for a Bunker C fuel oil using an oil:water ratio of 1:9. In this study, analysis was by CCl_4-extraction and infrared spectrophotometry. In this study care was taken to avoid formation of oil:water emulsions and loss of potential volatile components. MacLean and Doe (1989) also measured the total dissolved hydrocarbon concentration in a water soluble fraction of Bunker C fuel oil. Using an oil:water ratio of 1:40, they obtained total dissolved hydrocarbon concentrations of 4.5 mg/L in freshwater and 2.3 mg/L in seawater, both at 20°C. Analysis of those samples was done by hexane extraction and fluorescence spectrophotometry. Also reported in an oil properties database (Jokuty et al. 2002) was a measured value of 0.4 mg/L for a water soluble fraction of Bunker C fuel oil (Suntio, 1986). However, the details of this measurement could not be reliably judged due to the lack of experimental details.

Because blended fuels are composed of the refining streams from which they are produced, the range of solubility values of <1 to approximately 6 mg/L as total dissolved petroleum hydrocarbons is expected to approximate the water solubility for all substances within the heavy fuel oil

subcategories. Specific solubility values for heavy fuels oils and the refining streams are dependent upon the composition of the crude oil, the refining process that it undergoes, and the practice of adding cutter stocks to enhance the flow characteristics of finished fuels.

Conclusion: A range of total dissolved hydrocarbons in the aqueous fraction of heavy fuel oil:water mixtures has been reported as <1 to approximately 6 mg/L. The dissolved hydrocarbon concentration is affected by the oil:water ratio, the carbon number distribution of the heavy fuel oil, and the composition of the hydrocarbons in the heavy fuel oil.

3.2 Assessment Summary for Physical-Chemical Endpoints

Members of the Heavy Fuel Oil Category originate as residuals from atmospheric and vacuum distillation. They do not have sharply-defined melting points, but are viscous substances with pour points typically <30°C. Their individual compounds generally fall in the C20 to ≥C50 range, but this is influenced by refinery practices and the blending of these residuals with gas oils or similar low viscosity fractions to enhance the flow characteristics. Therefore, small quantities of low-end molecular weight hydrocarbons for some category member have been reported as low as C7. However, flash point specifications for heavy fuel oil products (>60°C or >140°F) would restrict the amount of these C7 hydrocarbons. This blending practice influences the physical-chemical characteristics and creates a diverse group of petroleum streams. The total vapor pressure of heavy fuel oils would normally be below measurable limits, but individual constituents representing the low molecular weight fractions may show measurable vapor pressures in their pure state. Partition coefficients representing the majority of compounds in the C20 - C50 range are >6, but individual hydrocarbons representing the low-end molecular weight constituents may range from 1.7 to >6. Water solubility would be expected to be low for these substances, and studies have reported total dissolved hydrocarbons from <1 mg/L to approximately 6 mg/L in aqueous preparations of heavy fuel oils.

4. ENVIRONMENTAL FATE

4.1 Environmental Fate Endpoints

To assess the environmental fate properties for the HPV program, the U.S. EPA has selected important fate endpoints by which these substances may be characterized. Thus, environmental fate endpoints include the following**:**

- photodegradation,
- stability in water (hydrolysis),
- environmental distribution (fugacity), and
- biodegradation.

In determining these fate characteristics for constituents in heavy fuel oils, the USEPA's collection of physical-chemical and environmental fate models in EPI-Suite™ (EPA, 2000) were used to estimate the properties of photodegradation, stability in water, and environmental distribution. Measured data, when available, were included in the assessment. Biodegradation was examined for these substances in light of their physical-chemical properties and the capacities of the constituent compounds to undergo microbial metabolism.

4.1.1 Photodegradation

4.1.1.1 Direct

The direct photolysis of an organic molecule occurs when it absorbs sufficient light energy to result in a structural transformation. Only light energy at wavelengths between 290 and 750 nm can result in photochemical transformations in the environment, although absorption is not always sufficient for a chemical to undergo photochemical degradation. Saturated and one-ring aromatic hydrocarbons do not show absorbance in the 290 to 800 nm range and would not be expected to be directly photodegraded. Polycyclic aromatic hydrocarbons (PAHs), on the other hand, have shown absorbance of the 290 to 800 nm range of light energy and are capable of being degraded by ultraviolet radiation (Fasnacht and Blough, 2002). In laboratory experiments, ultraviolet illumination of thin films of heavy fuel oil led to disappearance of PAH and sulfur heterocyclic compounds (Garrett et al., 1998). The loss was more pronounced for larger polycyclic species and the more alkylated forms of the parent hydrocarbon. This pattern of loss also was demonstrated *in situ*, where disappearance of PAHs on painted granite panels placed in an intertidal marine location was greatest for larger and more alkylated species (Jezequel, et al. 2003). The degree and rate at which these compounds photo-degrade depends upon whether conditions allow penetration of light with sufficient energy to effect a change. Direct photodegradation of heavy fuel oils would not be anticipated to be a significant fate pathway due to the physical consistency limiting dispersion and the resistance of the saturated and single-ring aromatic fractions of these materials to undergo direct photolytic transformations.

4.1.1.2 Indirect

Constituents of heavy fuel oils that volatilize to the troposphere have the potential to undergo gas-phase oxidation reactions with photochemically produced hydroxyl radicals (OH), other oxygen containing radicals (e.g., NO_3) and ozone (O_3). Atmospheric oxidation as a result of these types of reactions is not direct photochemical degradation but rather indirect photodegradation (Schwarzenbach et al, 2003). The importance of the different atmospheric reactants to degradation depends on the structure of the compound. For example, Atkinson (1990) reported that reactions with OH and NO_3 radicals can be important for alkanes, whereas reactions with O_3 are negligible. Additionally, nighttime reactions with NO_3 radicals occur at rates approximately two orders of magnitude less than daytime OH radical reactions. Olefins may react with OH and NO_3 radicals and O_3, with OH and O_3 being the most important. Of the latter two, OH reaction rates are faster. For aromatic compounds, interaction with the OH radical is the only important removal process.

The potential to undergo indirect photodegradation was estimated using the atmospheric oxidation potential (AOP) model subroutine (AOPWIN V1.90) of the EPI-Suite™ computer models (EPA, 2001). This model calculates a chemical half-life and an overall OH radical reaction rate constant based on a 12-hour day and a given OH radical concentration. This program also estimates the reaction rates and half-lives for the reaction of olefins with O_3, but as described by Atkinson (1990), these rates tend to be substantially less than those for the OH radical. For this reason, only the half-lives for the reaction with the OH radical are reported for the series of olefinic hydrocarbons selected for the AOP model. It should be understood that these reactions have been worked out only for gaseous phase compounds in the troposphere. Reactions occurring for particulate, aerosol, and surface particle-adsorbed interactions are beyond the scope of the model. The half-life values estimated for the heterocyclic compounds should be qualified by adding that these substances have not been fully investigated as to their involvement in OH radical reactions. It is

presumed that these substances also undergo similar reactions since the aromatic structure is that which is susceptible to OH radical addition. The AOPWIN routine also provides reaction rate constants and half-life data for heterocyclic compounds.

Atmospheric oxidation half-lives were calculated by the AOPWIN model for the various molecular weight and isomeric structures representing constituent hydrocarbon (paraffins, naphthenes, olefins, aromatics) and heterocyclic compounds in heavy fuel oils. Structures and molecular weights of selected constituents were chosen on the basis of carbon number as identified in the description of the category substances and known hydrocarbon composition of heavy fuel oils. Therefore, the estimated values identify a potential range of half-lives for substances in the heavy fuel oil category. The half-lives for representative constituents of heavy fuel oils were determined to range from <0.1 days to approximately 5.2 days. This range spans isomeric structures for representative paraffinic, olefinic, naphthenic, aromatic, and heterocyclic compounds in heavy fuel oils that cover the molecular weights of C7 to C50 carbon chain lengths. For the majority of the thousands of compounds constituting heavy fuel oils, their low vapor pressures would preclude them from entering the troposphere where these reactions take place. However, the half-life values determined for these substances indicate that should any of the lighter fractions of these streams enter the atmosphere, they would degrade and not persist.

Conclusion: Substances in heavy fuel oil category would not persist in the atmosphere should conditions exist whereby they partition to the air. Reaction rates calculated for indirect photodegradation ranged from <0.1 days to approximately 5.2 days for a variety of hydrocarbon and heterocyclic compounds covering carbon numbers from C7 to C50.

4.1.2. Stability in Water

Hydrolysis is the transformation process in which a water molecule or hydroxide ion reacts to form a new carbon-oxygen bond. Chemicals that have the potential to hydrolyze include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters (Harris, 1982). The majority of the chemical constituents in heavy fuel oils are hydrocarbons, which are not included in these groups. Therefore, these substances are not subject to hydrolysis reactions with water.

Conclusion: Substances in the heavy fuel oil category will be stable and not react with water.

4.1.3. Transport between Environmental Compartments

Fugacity-based multimedia modeling provides basic information on the relative distribution of chemicals between selected environmental compartments (e.g., air, water, soil, sediment, suspended sediment and biota). The US EPA has agreed that computer-modeling techniques are an appropriate approach to estimating chemical partitioning (fugacity is a calculated, not measured endpoint). A widely used fugacity model is the EQC (Equilibrium Criterion) model (Trent University, 1999). The EQC model is a Level 1 (i.e., steady state, equilibrium, closed system and no degradation) model that utilizes the input of basic chemical properties including molecular weight, vapor pressure, and water solubility to calculate distribution within a standardized regional environment. EPA cites the use of this model in its document “Determining the Adequacy of Existing Data” that was prepared as guidance for the HPV chemicals program (EPA, 1999).

The range of properties of heavy fuel oils is such that they cannot be considered as a single group with respect to environmental distribution. Because of the varied properties of the individual

constituents, when a heavy fuel oil enters the environment, the individual constituents will distribute independently of one another according to their own physical-chemical characteristics. Therefore, it is useful to consider a representative range of molecular weight compounds and isomeric structures to assess how the various fractions of heavy fuel oil can potentially distribute. To gain an understanding of the potential distribution of the constituent compounds in heavy fuel oil, the EQC model was used to characterize the environmental distribution of representative hydrocarbon and heterocyclic compounds in heavy fuel oils for different molecular weight ranges and isomeric structures. Compounds selected for modeling were chosen on the basis of carbon number as identified in the description of the category substances and known and estimated hydrocarbon composition of heavy fuel oils (Potter and Simmons, 1998; Quann and Jaffe, 1992; Saeger and Jaffe, 2002). In so doing, an understanding of the potential environmental distribution of components in heavy fuel oil may be gained. Distribution patterns determined by the EQC model for the different constituents are shown in Table 2.

Table 2. Estimated Percent Distribution of Constituent Compounds Represented in Heavy Fuel Oil.

Compound Type/ Carbon Chain		Air	Water	Soil	Sediment	Suspended Sediment	Biota
n-alkanes							
	C7	100	<0.1	<0.1	<0.1	<0.1	<0.1
	C11	93	<0.1	7	<0.1	<0.1	<0.1
	C20	<0.1	<0.1	98	2	<0.1	<0.1
	C50	<0.1	<0.1	98	2	<0.1	<0.1
iso-alkanes							
	C7	100	<0.1	<0.1	<0.1	<0.1	<0.1
	C11	95	<0.1	5	<0.1	<0.1	<0.1
	C20	<0.1	<0.1	98	2	<0.1	<0.1
	C50	<0.1	<0.1	98	2	<0.1	<0.1
cycloalkanes	(1-ring)						
	C7	100	<0.1	<0.1	<0.1	<0.1	<0.1
	C11	99	<0.1	0.9	<0.1	<0.1	<0.1
	C20	<0.1	<0.1	98	2	<0.1	<0.1
	C50	<0.1	<0.1	98	2	<0.1	<0.1
	(2-ring)						
	C11	97	0.1	3	0.1	<0.1	<0.1
	C20	2	<0.1	96	2	<0.1	<0.1
	C50	<0.1	<0.1	98	2	<0.1	<0.1
	(3-ring)						
	C12	94	0.4	5	0.1	<0.1	<0.1
	C20	2	<0.1	96	2	<0.1	<0.1
	C50	<0.1	<0.1	98	2	<0.1	<0.1
olefins							
	C7	100	<0.1	0.1	<0.1	<0.1	<0.1
	C11	96	<0.1	4	<0.1	<0.1	<0.1
	C20	<0.1	<0.1	98	2	<0.1	<0.1
	C50	<0.1	<0.1	98	2	<0.1	<0.1
aromatics	(1-ring)						
	C7	99	0.8	0.4	<0.1	<0.1	<0.1
	C11	88	0.4	11	0.2	<0.1	<0.1
	C20	<0.1	<0.1	98	2	<0.1	<0.1
	C50	<0.1	<0.1	98	2	<0.1	<0.1
	(2-ring)						
	C11	53	6	40	0.9	<0.1	<0.1
	C20	<0.1	<0.1	98	2	<0.1	<0.1
	C50	<0.1	<0.1	98	2	<0.1	<0.1

(3-ring)						
C14	1	4	93	2	0.1	<0.1
C20	<0.1	<0.1	98	2	<0.1	<0.1
C50	<0.1	<0.1	98	2	<0.1	<0.1
heterocyclics (quinolines)						
C9	3	89	8	0.2	<0.1	<0.1
C14	5	2	91	2	<0.1	<0.1
C20	<0.1	<0.1	98	2	<0.1	<0.1
C50	<0.1	<0.1	98	2	<0.1	<0.1
(pyridines)						
C7	8	88	4	<0.1	<0.1	<0.1
C14	0.2	0.5	97	2	<0.1	<0.1
C20	<0.1	<0.1	98	2	<0.1	<0.1
C50	<0.1	<0.1	98	2	<0.1	<0.1
(naphthenic acids)						
C7	4	88	8	0.2	<0.1	<0.1
C11	0.5	30	68	1.5	<0.1	<0.1
C20	<0.1	<0.1	98	2	<0.1	<0.1
C50	<0.1	<0.1	98	2	<0.1	<0.1
(thiophene/dibenzothiophenes)						
C7	90	4	6	0.1	<0.1	<0.1
C12	3	4	91	2	<0.1	<0.1
C20	<0.1	<0.1	98	2	<0.1	<0.1
C50	<0.1	<0.1	98	2	<0.1	<0.1

As shown in Table 2 partitioning behavior of constituent molecules of heavy fuel oils depends largely on molecular weight, with smaller compounds (e.g., 7 to 12 carbon atoms) partitioning to the air or water according to their vapor pressure or water solubility properties. For some of the classes of heterocyclic compounds, the water solubility drives the partitioning to the water. As the chain lengths of the hydrocarbon and heterocyclic constituents approach a size of approximately 15 - 20 carbon atoms, their vapor pressure and water solubility become negligible, and partitioning to air or dissolving in water is unimportant. For those molecules that fall within the typical C20 to ≥C50 carbon chain lengths described by CONCAWE (1998), the partitioning to air or water is minimal.

Much information on oil dispersion has been gained from studies of heavy fuel oil spills (Fuel oil #6 or Bunker C). These oils which are utilized as fuels by cargo ships are the most frequently spilled oils (Jézèquel et al. 2003). When spilled on water, heavy fuel oil usually spreads into thick, dark colored slicks that will often breakup into discrete patches and tar balls (NOAA, 2004). Only the lowest molecular weight fractions would be expected to disperse into the water column, and 5-10% of the material is expected to evaporate within the first few hours of a spill. The specific gravity of a particular fuel oil may vary from 0.95 to 1.03; thus, spilled oil can float, suspend, or sink (NOAA, 2004). Small changes in water density may dictate whether the oil will sink or float. With time and the effects of weathering, heavy fuel oil attains a tar-like consistency, and these tar balls will become incorporated into soil or bottom sediments where they will undergo slow to moderate biodegradation.

Conclusion: When a heavy fuel oil enters the environment, the individual compounds of the substance will partition in accordance with their own physical-chemical properties. For the low molecular weight hydrocarbon fractions of heavy fuel oil, the atmosphere is the principal environmental compartment to which they will partition. Some of the heterocyclic compounds that have significant water solubility values will partition to the water. As the molecular weights of the individual components increase to the range considered typical of heavy fuel oil (i.e., C20 to ≥C50),

the low volatility and low water solubility prevent these constituents from entering the atmosphere or dissolving in water at greater than minimal levels.

4.1.4. Biodegradation

No studies were located that described the biodegradation characteristics of the streams or finished fuels in the heavy fuel oil category oil when these properties were examined using standardized guideline testing methods. Therefore, this biodegradability assessment relies on information from other petroleum streams (e.g., gasoline naphthas, kerosene, gas oils, etc.), various laboratory investigations describing the microbial utilization of petroleum substances, and field studies undertaken in response to heavy fuel oil spill events.

Biodegradability Characteristics of Various Petroleum HPV Categories
As part of other HPV test plans and analysis documents, the biodegradability of the different distillation fractions of crude oil has been described (API, 2003a-d; API, 2008; API, 2010). When viewed together, these data show a continuum of molecular weight fractions and the biodegradability characteristics of those fractions. Heavy fuel oils are substances composed of the same constituents as described for the other petroleum fractions, with the fundamental difference being in the proportion of those constituents making up the substance. Based on chemical analyses, heavy fuel oils fall within the molecular weight continuum of the series of petroleum fractions presented in Table 3, and thus the biodegradability potential shown by those fractions can be applied to the category members of heavy fuel oils. Biodegradation data cited for several distillation fractions of crude oil that would be expected to cover the molecular weight range of heavy fuel oils is presented in Table 3. For the sake of comparison, the data presented are from standard "ready" biodegradability studies whenever possible.

Table 3. Representative Biodegradation Data for Distillation Fractions of Crude Oil.

Petroleum Substance	Principal Carbon Range	Test Type	Biodegradation (% degraded)	Reference
Gasoline blending streams	C4 – C12	OECD 301F	77% "readily biodegradable"	API (2008)
Kerosene	C9 – C16	OECD 301F	58.6%; "not readily biodegradable"	API (2010)
Gas Oils	C9 – C25	OECD 301F	60%; "not readily biodegradable"	API (2012b)
Lubricating base oils	C15 – C50	OECD 301F	38%; "not readily biodegradable"	API (2011a)
Aromatic extracts	C15 – C54	OECD 301D	0%; "not readily biodegradable"	API (2012a)
Waxes and related materials	C20 – C50	OECD 301F	40%; "not readily biodegradable"	API (2011b)

The data cited above are representative biodegradation rates for their respective category streams and were selected because most were run under a similar guideline protocol. However, biodegradation rates vary and other values are reported in the cited references. Regardless, these data provide the basis for a general conclusion that biodegradation can be extensive for the

fractions most soluble and available for microbial utilization. Heavy fuel oils, with their principal constituents covering the C20 to ≥C50 range, would not be readily biodegradable. This was demonstrated by Walker et al. (1976), who reported 11% biodegradation of a commercial Bunker C fuel oil, probably the lighter fractions (e.g., <C20) present in this oil. The lighter fractions associated with these streams would be expected to show appreciable biodegradation rates, as shown by the biodegradation of kerosene and gas oils in Table 3.

Biodegradability of Compound Groups in Heavy Fuel Oil

It is generally recognized that most hydrocarbons in crude and refined oils are biodegradable (Prince et al., 2003; Prince, 2002). Furthermore, the sequence of hydrocarbon utilization by microbes following a spill is sequential, generally following in the order from easiest to the most recalcitrant as alkanes>isoalkanes>alkenes>alkylbenzenes>polyaromatic hydrocarbons>high molecular weight cycloalkanes (Bartha and Atlas, 1977). However, there is much overlap as this sequence is influenced by factors such as molecular weight, hydrocarbon branching, and degree of alkylation. Thus for alkanes, biodegradation is relatively rapid for those having ≤12 carbon atoms (Prince, 2002), and simple branched hydrocarbons are preferentially degraded before the highly branched forms. Simple aromatic molecules may be degraded similarly to alkanes, but biodegradation decreases with added ring structures and number and length of alkyl side chains. For polyaromatic hydrocarbons the parent structure is preferentially degraded over those with added alkyl groups. Prince et al. (2003) showed this relationship for unsubstituted and C1 – C3 phenanthrenes and chrysenes.

In addition to the saturated and aromatic hydrocarbons fractions, heavy fuel oils may contain considerable amounts of compounds containing the heteroatoms, oxygen, nitrogen, sulfur, and some heavy metals (most abundant being vanadium and nickel) (Tissot and Welte, 1984). Sulfur is the third most abundant atomic constituent in crude oils, following carbon and hydrogen, and may be present in the medium as well as heavy fractions (Tissot and Welte, 1984). These sulfur species are dominated by derivatives of thiophene, namely benzothiophene, dibenzothiophene, and benzonaphthothiophenes, and their alkylated forms. While thiophene itself is rare, the other forms can be important constituents in high sulfur crude oils. Typically, the parent molecule is less abundant than the alkylated derivatives. The degree of alkylation of the parent form is important to biodegradation, and these sulfur compounds behave similarly to polyaromatic hydrocarbons in that increasing alkylation decreases the rate of biodegradation. Prince et al (2003) showed that the dibenzothiophenes and phenanthrenes are degraded at approximately the same rate. Nitrogen and oxygen heteroatoms exist at much lower concentrations as sulfur compounds, and at least for nitrogen species, tend to exist in the heaviest fractions of petroleum (Tissot and Welte, 1984). Even so, some of the simpler nitrogen- (e.g., indoles, carbazoles, quinolines) and oxygen-containing compounds (e.g., naphthenic acids) have some capacity to be biodegraded (Sugaya, et al., 2001; Herman et al., 1994).

The heaviest fractions of constituents in heavy fuel oil are the resins and asphaltenes. These are high molecular weight complex arrangements of polycyclic aromatic or naphthenoaromatic nuclei with chains and heteroatoms (oxygen, nitrogen, sulfur, and metals) substituting for carbon atoms in the cyclic structures (Tissot and Welte, 1984). Many of these have molecular weights of 2000 to 5000 and show little degradation; hence they can persistent in the environment for a long time (Prince, 2002; Prince et al., 2003).

Field Studies of Petroleum Spills

Extensive research on oil degradation in marine environments indicates that virtually all kinds of oils are susceptible to microbial oxidation. When a heavy fuel oil is spilled, shoreline microbial

communities respond quickly to the oiling, with numbers of hydrocarbon-degrading microbes and mineralization potentials increasing after exposure (Leahy and Colwell, 1990). The rate of mineralization is influenced by microbial characteristics (e.g., species composition), and environmental factors such as available nutrients, oxygen, temperature and degree of dispersion (Mulkins-Phillips and Stewart, 1974; Rashid, 1974; Prince, 2002; Garrett, et al., 2003). In marine systems, degradation is most enhanced by the addition of nutrients (nitrogen and phosphorus), as these are considered most limiting in seawater (Richmond et al., 2001). In general, due to the high viscosity of heavy fuels, their tendency to slowly weather into discrete tar balls, and the eventual incorporation of those substances into soil/sediment can physically isolate and prevent dispersion and microbial attack (Richmond et al., 2001; Prince et al., 2003). However, over time, component hydrocarbons are depleted through selective biodegradation (Lee, et al. 2003).

Conclusion: Heavy fuel oils would not be expected to pass the criteria for ready biodegradability when assessed using standard guideline protocols. However, hydrocarbon and many heterocyclic compounds have been shown to be utilized by microbial communities as an energy source. These constituents in heavy fuel oils may be considered inherently biodegradable. Their rates of consumption by microbes depend upon physical factors associated with weathering to aid in dispersion as well as the availability of nutrients and oxygen for the microbial communities.

4.2. Assessment Summary for Environmental Fate

When heavy fuel enters the environment the individual constituents partition to various environmental compartments in accordance with their own physical-chemical properties. As described above, fractions of heavy fuel < C20 may dissolve in water or evaporate to the atmosphere. Heaviest fractions may float or sink depending on density relationships, and become incorporated into soils/sediments. Some compounds may engage in direct photolytic reactions if they receive sufficient energy from sunlight to effect the chemical reactions. Others may undergo indirect photodegradation with photosensitized oxygen compounds in the troposphere. Photodegradation rates for volatile components may be rapid, and these constituents would not be expected to persist in the atmosphere. Components of heavy fuels are stable to hydrolysis and this reaction is not a fate pathway for dissolved fractions. However, constituents of heavy fuels that dissolve become available for biodegradation. Biodegradation rates are related to molecular weight and structural conformation, with the lower fractions being first to be utilized by microbes due to their bioavailability. From spill events, biodegradation of the different molecular species follows a specific order and is influenced by temperature, dispersion, and available nutrients.

5. ENVIRONMENTAL EFFECTS

5.1. Aquatic Toxicity

For the assessment of the ecotoxicity of heavy fuel oils, the category substances are considered as a single group. This is valid because petroleum hydrocarbons elicit effects through non-polar narcosis, for which the mechanism of action is disruption of biological membrane function (Peterson, 1994; van Wezel and Opperhuizen, 1995). For this reason, heavy fuel oils share a common mode of action, and their acute toxicity would be expected to fall within a relatively narrow range. The potential for any category member to elicit adverse effects in aquatic organisms is attributed to the soluble fraction of constituents produced by that member. Substances composed of hydrocarbons with molecular weights predominately higher than the solubility “cut-off” for acute

toxicity show no measurable acute toxicity (CONCAWE, 2001). The solubility cut-off varies with the hydrocarbon structure; thus, for paraffinic hydrocarbons the solubility cut-off occurs at about C10, while for alkylbenzenes it is about C14 (CONCAWE, 2001).

Substances in the heavy fuel oil category generally consist of hydrocarbon molecules having 20 to ≥ 50 carbon atoms, although some streams in this category have low-end carbon atoms from 7 to 15. Heavy fuel oils also may be blended with gas oils or similar low viscosity fuels to meet market specifications. This makes a highly heterogeneous group of petroleum substances that spans a wide range of molecular weight fractions. The limited ecotoxicity data available for heavy fuel oils may not represent the hazard of all category members and particularly those that contain a relatively high proportion of hydrocarbons below the solubility cut-off for acute toxicity. For this reason, ecotoxicity data from the Kerosene/Jet Fuel and Gas Oils categories were included in this assessment to represent the potential toxicity of the low-end molecular weight fractions in heavy fuel oils (API, 2003a;b, API, 2010, 2012b). This is supported by the common mode of toxicity of petroleum hydrocarbons and the similar types of hydrocarbon constituents as found in heavy fuel oils. Kerosenes and gas oils are composed of saturated and aromatic hydrocarbon compounds having hydrocarbon structures and molecular weights similar to the light-end components in heavy fuel oils. Hence, the ecotoxicity of those substances provides conservative estimates of the ecotoxicity of the heavy fuel members having low initial boiling points and low-end carbon numbers of 7 to 15.

Heavy fuel oils also contain heterocyclic compounds that show solubility and molecular weight relationships similar to other hydrocarbons (i.e., solubility decreases with increasing molecular weight). These are typically aromatic or naphthoaromatic structures containing nitrogen, sulfur, and/or oxygen atoms. Because sulfur is the third most abundant element in crude oil, it occurs in more forms and molecular weight fractions than other heteroatoms (Tissot and Welte, 1984). Both oxygen and nitrogen are less abundant, and nitrogen heterocycles are likely to be found in the heavier fractions of petroleum substances. Examples of S-, O-, and N- heterocyclic compounds include thiophenes, pyridines, quinolines, naphthenic acids, and their alkylated homologs. In the heavier components of petroleum, these heteroatoms commonly occur together in the resin and asphaltene fractions (Tissot and Welte, 1984).

The contribution of these heterocyclic compounds to aquatic toxicity is not expected to be significant or measurable as part of the water soluble fraction of heavy fuel oil. Measured toxicity of several organosulfur compounds ranged from 1.2 mg/L (3-methylbenzothiophene) to 70 mg/L (benzothiophene), and no toxicity was observed at the solubility limit of dibenzothiophene (Seymour et al., 1997). As individual constituents in water soluble fractions, these are not expected to appear in concentrations high enough to elicit toxicity. As an example, Anderson, et al. (1974) measured 0.001 mg/L of dibenzothiophene in the aqueous fraction of a 10% oil-in-water bunker C fuel oil. While these organosulfur compounds may contribute to aquatic toxicity, their contribution would be integrated in the general hazard characteristics shown by the existing heavy fuel oil dataset.

When all ecotoxicity data sets presented below are considered, the ranges of endpoint values are expected to cover the potential ecotoxicity of all members of the heavy fuel oil category that contain various fractions of saturated, aromatic, and heterocyclic compounds.

The environmental effects endpoints in the HPV Challenge program include:

- Acute Toxicity to Fish,

- Acute toxicity to Aquatic Invertebrates, and
- Toxicity to Algae (Growth Inhibition).

For the assessment of ecotoxicity of poorly water soluble substaces as found in petroleum products, the generally accepted procedure is to report results expressed in terms of the "loading rate" (OECD, 2000). The loading rate is defined as the amount of the product that is equilibrated with the aqueous test medium, and the aqueous phase at equilibrium is termed the water-accommodated fraction (WAF) for the specific loading rate. Toxicological endpoints such as the LL50 or EL50 define the loading rate of the test substance lethal to or producing a specific effect in 50% of the test organisms. Test samples may be prepared as oil-water dispersions (OWDs), where the insoluble petroleum fractions remain in the exposure solutions. This method also results in an expression of the concentration of the applied substance (i.e., mg test substance/l), but the methodology does not prevent potential adverse effects to the organisms due to physical entrapment. Water-soluble fractions (WSFs) and their dilutions also may be reported in ecotoxicity studies. These preparations are expressed in terms of the percent dilution of a WSF. Occasionally, the measured concentrations of hydrocarbons in solution may be reported. Expressing toxicity as water soluble fractions has fallen out of favor because this practice does not allow the ecotoxicity of the substance to be expressed in terms of the amount of that substance required to produce a particular effect (OECD 2000). Such results are not comparable to results obtained under WAF or OWD preparation methods. Ecotoxicity data for some heavy fuel oils using different test methodologies have been reported and reviewed by CONCAWE (1998).

The data cited here include studies using WAFs and OWDs, since these methods provide a consistent basis on which to express the relative exposures of test organisms to these substances. Robust summaries for kerosene and gas oils ecotoxicity data cited below may be found in the in the HPV submissions for Kerosene/Jet Fuel Category Assessment Document (API, 2010) and Gas Oils Category Assessment Document (API, 2012b). These are included here to represent the potential toxicity of the types of hydrocarbons that may be used as cutter stocks in heavy fuel oils.

5.1.1 Acute toxicity to Fish

Data for heavy fuel oils showed slight or no acute toxicity to fish when tested as either WAFs or OWDs. Shell (1997a,b) tested WAFs of a “light” and a “heavy” residual fuel oil (CAS No. 68476-33-5) and found the 96-hour LL50s for exposures to rainbow trout (*Oncorhynchus mykiss*) to be between 100 mg/l and 1000 mg/l for the “heavy” residual fuel oil and >1000 mg/l for the “light” residual fuel oil. Mobil (1987a) obtained a 96-hour LL50 of >10,000 mg/l when bluegill (*Lepomis macrochirus*) were exposed to OWDs of No. 6 fuel oil.

Fish LL50 values for kerosene/jet fuel tested as WAFs were between 10 mg/l and 100 mg/l (API, 2010). LL50 values for distillate fuels cited in the gas oil HPV test plan ranged from 3.2 to 65 mg/l (API, 2012b). These data represent the potential toxicity of substances used as cutter stocks in heavy fuel oils.

5.1.2 Acute toxicity to Aquatic Invertebrates

Data for invertebrates (*Daphnia magna*) showed a similar range of sensitivities as fish. In testing WAFs of the “light” and “heavy” residual fuels, Shell (1997c,d) found the EL50 of the “light” to be >1000 mg/l while that of the “heavy” to between 220 mg/l and 460 mg/l. Mobil (1987b) exposed

daphnids to solutions in which oil was coated on the inside surface of the test vessels. The maximum loading rate of 10,000 mg/l in this study resulted in no immobilized daphnids.

Invertebrate EL50 values for kerosene/jet fuel tested as WAFs ranged from 1.4 mg/l to <89 mg/l (API, 2010). EL50 values for distillate fuels cited in the gas oil HPV Category assessment document ranged from 2.0 to <300 mg/l (API, 2012b). This range reflects the potential toxicity of substances used as cutter stocks in heavy fuel oils.

5.1.3 Toxicity to Algae (Growth Inhibition)

Shell (1997e,f) reported the EL50 values based on growth rate and biomass for 72-hour exposures of *Raphidocelis subcapitata* to a "light" and a "heavy" residual fuel oil. Tests were run in sealed vessels without headspace. For the "light" material, the EL_r50 (rate-based) was concluded to lie between 100 mg/l and 300 mg/l while the EL_b50 (biomass-based) was between 3 mg/l and 10 mg/l. This contrasted somewhat with toxicity endpoints for the "heavy" residual fuel oil which gave EL_r50 and EL_b50 values of between 30 mg/l and 100 mg/l. Mobil (1987c) coated the surface of test flasks with No. 6 fuel oil and measured algal (*R. subcapitata*) biomass over 96 hours. Test vessels were plugged with cotton which allowed air exchange. Growth inhibition at the maximum loading rate of 10,000 mg/l was 47.5%, but the authors concluded that the EL_b50 was >5,000 mg/l. Inhibition of 22% to 27% occurred in the lowest three test levels, but the authors suggested physical obstruction of light penetration may have affected cell growth.

In 96-hour exposures using WAFs of kerosene, EL50 values ranged from 5.0 to 6.2 mg/l when based on inhibition of growth rate, and ranged from 5.9 mg/l to 11 mg/l when based on biomass (API, 2010). In 72-hour WAF exposures, EL50 values based on growth rate and biomass fell within the range of 10 mg/l to 30 mg/l (API, 2010).

Algae exposed to WAFs of distillate fuels produced 72-hour EL50 values based on growth rate that ranged from 2.2 to <46 mg/l, while values based on algal biomass ranged from 1.8 to 25 mg/l (API, 2003a). Data for kerosene and distillate fuels represent the potential toxicity of substances used as cutter stocks in heavy fuel oils.

The heavy fuel oil, kerosene, and gas oil ecotoxicity data described above are listed in Tables 4-6. Together, these data encompass values that represent the potential toxicity of all members in the Heavy Fuel Oil HPV category.

Table 4. Acute Toxicity of Heavy Fuel Oil, Kerosene/Jet Fuel Oil, and Gas Oil to Fish.

Test Substance/ Species	Description	Exposure Type	Effect / conc. (mg/l)	Reference
Heavy Fuel Oil				
Rainbow trout *(Oncorhynchus mykiss)*	CAS No. 68476-33-5 (light) residual fuel oil	WAF	96-h LL50 = >1000	Shell, 1997a
Rainbow trout (*O. mykiss*)	CAS No. 68476-33-5 (heavy) residual fuel oil	WAF	96-h LL50 = >100, <1000	Shell, 1997b
Bluegill (*Lepomis macrochirus*)	No. 6 fuel oil	OWD	96-h LL50 = >10,000	Mobil, 1987a
Kerosene/Jet Fuel				
Various species	Various CAS numbers	WAF	96-h LL50 = 18 20 >10, <100 25	API, 2003a: 2010
Gas Oil				
Various species	Distillate fuels	WAF	96-h LL50 = 57 3.2 6.6 57 21 65	API, 2003b, 2012b

Table 5. Acute Toxicity of Heavy Fuel Oil, Kerosene/Jet Fuel Oil, and Gas Oil to Aquatic Invertebrates.

Test Substance/ Species	Description	Exposure Type	Effect / conc. (mg/l)	Reference
Heavy Fuel Oil				
Daphnia magna	CAS No. 68476-33-5 (light) residual fuel oil	WAF	48-h EL50 = >1000	Shell, 1997c
D. magna	CAS No. 68476-33-5 (heavy) residual fuel oil	WAF	48-h EL50 = >220, <460	Shell, 1997d
D. magna	No. 6 fuel oil	OWD	48-h EL50 = >10,000	Mobil, 1987b
Kerosene/Jet Fuel				
D. magna	Various CAS numbers	WAF	48-h EL50 = 21 1.4 >40, <89 1.9	API, 2003a; 2010
Gas Oil				
D. magna	Distillate fuels	WAF	48-h EL50 = 7.8 5.3 14 42 2.0 210 68 13 >100, <300 13 6.4 36 9.6	API, 2003b; 2012b

Table 6. Toxicity of Heavy Fuel Oil, Kerosene/Jet Fuel Oil, and Gas Oil to Freshwater Algae.

Test Substance/ Species	Description	Exposure Type	Effect / conc. (mg/l)	Reference
Heavy Fuel Oil				
Raphidocelis subcapitata	CAS No. 68476-33-5 (light) residual fuel oil	WAF	96-h ELr50 = >100, <300 96-h ELb50 = >3,<10	Shell, 1997e
R. subcapitata	CAS No. 68476-33-5 (heavy) residual fuel oil	WAF	96-h ELr50 = >30, <100 96-h ELb50 = >30, <100	Shell, 1997f
R. subcapitata	No. 6 fuel oil	OWD	96-h ELb50 = >5,000	Mobil, 1987c
Kerosene/Jet Fuel				
R. subcapitata	Various CAS numbers	WAF	96-h ELr50 = 6.2 5.0 96-h ELb50 = 11 5.9 72-h ELr50 = >10, <30 72-h ELb50 = >10, <30	API, 2003a; 2010
Gas Oil				
R. subcapitata	Distillate fuels	WAF	72-h ELr50 = 2.9 2.2 78 22 >22, <46 72-h ELb50 = 1.8 2.2 25 10 >10, <22	API, 2003b: 2012b

WAF = Water Accommodated Fraction
OWD = Oil-Water Dispersion

5.1.4 Chronic Toxicity to Aquatic Invertebrates

No standard guideline studies on the chronic ecotoxicity of heavy fuel oils were identified, but potential chronic ecotoxicity may be inferred for this category from the range of partition coefficients (e.g., 1.7 - >6) for representative constituent hydrocarbons. Many of the category

members have ranges of molecular weight hydrocarbons that exceed the water solubility cut-off for producing toxic effects. Thus, for those streams having hydrocarbons of C15 and higher, no chronic toxicity would be expected. This was shown by chronic effects test data on aromatic extracts and lubricating oil basestocks, which have constituent hydrocarbons of similar types and molecular weights to those of many of the heavy fuel oil streams. For those two categories, no chronic toxicity was found in standard 21-day *D. magna* tests for reproductive effects at the maximum loading rate of 1000 mg/L (API, 2011, 2012b). However, the practice of adding cutter stocks of middle distillate streams to heavy fuel oils may result in an increase in the water soluble fractions of the lower molecular weight hydrocarbons. The increase in the biological availability of those fractions could potentially cause chronic toxicity in exposed organisms. For this reason, chronic toxicity characteristics of the blended heavy fuel oils and those streams whose definition includes a lower range of low-end molecular weight hydrocarbons may be more reflective of middle distillate streams. Chronic effects testing of two middle distillate streams were conducted for the gas oils category. The NOELR and LOELR for the gas oil stream demonstrating the greatest chronic toxicity was 0.05 mg/L and 0.10 mg/L, respectively based on loading. These values may be used as read-across data that may reflect the chronic toxicity of blended heavy fuel oils and those streams that by definition contain hydrocarbon constituents below C15.

5.2. Assessment Summary for Environmental Effects

When the acute aquatic toxicity values for heavy fuel oil and heavy fuel oil blending streams were compared on the basis of the loading rates of water accommodated fractions, acute toxicity endpoints for fish and invertebrates were always >100 mg/L. In some instances, no adverse effects were observed at the maximum loading rate of 1000 mg/L. Based on the limited data for the category members, algae appeared to be the more sensitive aquatic species. The lowest EL50 values for algae fell within the range of 3 to 10 mg/L when evaluated on the basis of growth biomass. In recognition that members of the heavy fuel oil category are complex substances that are commonly blended with lower molecular weight petroleum substances, ecotoxicity data from the gas oil and kerosene categories were used to bridge potential adverse effects that could be attributed to constituents having carbon numbers as low as seven. Gas oil and kerosene streams typically show greater toxicity due to the higher solubility of their constituent compounds. In general, toxicity values for these substances tend to fall within the range of 1 to 100 mg/L on the basis of loading rates. Using the range of 1 to 100 mg/L for read-across to all members of the heavy fuel oil category may overestimate the aquatic toxicity of some category members, but reflects a potential toxicity based on consideration of the variable nature of these substances. For chronic aquatic toxicity, test data on gas oils may be used as read-across for the heavy fuel oil category because many of the heavy fuel oil streams are blended with middle distillates or by definition overlap with middle distillates at the low-end range of their molecular weight hydrocarbons. The lowest NOELR and LOELR were 0.05 mg/L and 0.10 mg/L, respectively, for a 21-day *D. magna* reproduction study.

6.0. HUMAN HEALTH ENDPOINTS

Reviews of this category of fuels have been published by two organizations (CONCAWE, 1998; IARC, 1989). In preparing this Category Assessment document, the approach has been to review the available toxicology studies and in the text, provide summaries of studies by CAS numbers

[CAS RN] to each SIDS Level 1 endpoint. Robust summaries contain extensive detail for each study and are provided in a separate document

The Category Assessment document addresses the health effects endpoints of the category by:

- Evaluating the toxicology database for the heavy fuel oil related refinery streams and products,
- Using read-across information whenever possible among category members, and other API HPV categories, and
- Modeling data based on PAC profile for repeat dose, developmental toxicity, and *in vitro* genetic toxicity endpoints to predict toxicity of untested streams (Appendices D and E describe Modeling Methodology). Sufficient direct data are available for acute toxicity and in vivo cytogenetic determinations.

6.1. Human Health Effects

6.1.1. Acute Toxicity

6.1.1.1. Oral

Table 7. Acute Oral Toxicity

CAS RN	LD_{50} value	Species	Observations	Reference
64741-45-3	>5000 mg/kg	Rat	Stained coats; dark red areas in lung lobes	ARCO, 1990a
64741-62-4	4320♀ 5270♂ mg/kg	Rat	Mortalities; hypoactivity; piloerection; staining around mouth, nose, urogenital; hair loss; weight loss; intestinal mucosal damage	API, 1982a
64741-81-7	>5000 mg/kg (4 samples)	Rat	Decreased activity; chromorhinorrhea, decreased fecal output; urogenital staining; decreased urine Oral, nasal discharge; lethargy; abnormal stools; pale & mottled kidneys	Mobil 1988b,c; 1992a ARCO, 1988
68553-00-4	5.13 - >25 ml/kg (4 samples)	Rat	Lethargy; grease on fur	API 1980a,b,c,d

6.1.1.2 Dermal

Table 8. Acute Dermal Toxicity

CAS RN	LD_{50} value	Species	Observations	Reference
64741-45-3	>2000 mg/kg	Rabbit	Abnormal stool; dark red areas in lung	ARCO, 1992b
64741-57-7	>2000 mg/kg	Rabbit	Decreased food consumption; soft stool; decreased fecal output	Mobil 1988a
64741-62-4	>2000 mg/kg	Rabbit	No signs of systemic toxicity; no gross findings	API, 1982a

64741-81-7	>2000 mg/kg (4 samples)	Rabbit	Erythema & edema; mottled kidneys	Mobil ,1988b; 1992a ARCO 1989a, 1992a
68553-00-4	>5 ml/kg (4 samples)	Rabbit	Erythema; slight congestion of liver	API 1980a,b,c,d

6.1.1.3 Skin Irritation

Table 9. Skin Irritation: 24-hours occluded

CAS RN	Irritation Index	Species	Observations	Reference
64741-45-3	3.5	Rabbit	Moderately irritating	ARCO, 1992d
64741-57-7	1.7	Rabbit	-	Mobil 1988a,b,c; 1992a
64741-62-4	0.2	Rabbit	-	API, 1982a
64741-81-7	2.7 - 5.6 (4 samples)	Rabbit	Moderately irritating	Mobil 1988b,c, 1992a, ARCO 1989d
68512-62-9	0.18	Rabbit	Not irritating	ARCO 1989e
68553-00-4	0.27 – 1.54 (4 samples)	Rabbit	Minimal – slight irritant	API 1980a,b,c,d

6.1.1.4 Eye Irritation

Table 10. Eye Irritation: 24-hours

CAS RN	Irritation Indices 24 & 72 hr	Species	Observations	Reference
64741-45-3	0.0 & 0.0 un-rinsed only	Rabbit	Not irritating	ARCO, 1991
64741-57-7	10.3 3.3 at 48hrs.	Rabbit	Un-rinsed only	Mobil 1988a,
64741-62-4	2.0 & 0 rinsed & un-rinsed	Rabbit	Minimal irritant	API, 1982a
64741-81-7	1.7 – 5.3 2.3 – 4.0 at 48 hrs 5.7 & 0.0 un-rinsed 5.3 & 0.0 rinsed	Rabbit	 Un-rinsed - not irritating Rinsed – not irritating	Mobil 1988b,c, 1992a ARCO, 1989f
68512-62-9	5.0 & 4.7 un-rinsed 5.7 & 4.7 rinsed	Rabbit	Un-rinsed - not irritating – Rinsed - minimal irritant	ARCO 1989g
68553-00-4 [4 samples]	2.67 – 7.67 & 0 – 1.33 rinsed 4.0 – 7.33 & 0.0 – 1.33 un-rinsed	Rabbit	Minimal – mild irritant	API 1980a,b,c,d

6.1.1.5 Sensitization

Table 11. Sensitization

CAS RN	Challenge Response	Species	Observations	Reference
CAS 68553-00-4 ARCO F74-01	-	Guinea Pig	3 samples non-sensitizer 1 sample mild sensitizer[a] Non-sensitizer	API 1980a,b,c,d [4 samples] ARCO, 1986a
64741-45-3	0/10	Guinea Pig	Non-sensitizer	ARCO 1992c
68512-62-9	0/10	Guinea Pig	Non-sensitizer	ARCO 1989c
64741-57-7	1/10	Guinea Pig	Non-sensitizer	ARCO 1990c
64741-62-4	0/10	Guinea Pig	Non-sensitizer	API 1984
64741-81-7	0/10	Guinea Pig	Non-sensitizer	ARCO 1989b

a- The mild sensitization result for one Residual Fuel Oil sample is considered an anomaly because in studies of approximately 40 petroleum samples over a range of categories performed by API, no others were found to be sensitizers.

Conclusions.
Multiple acute toxicity studies have been reported on representative samples of the heavy fuel oil category. These data and data from the other 12 API HPV Categories show the acute toxicity of a wide-array of petroleum hydrocarbon streams is consistently low, with many oral LD50's greater than 5 g/kg, and dermal LD50s greater than 2 g/kg. Acute toxicity data on two vacuum residuum samples (CAS no. 64741-56-6, API samples 81-13 and 81-14) in the API HPV Asphalt Category Assessment Document [API, 2012a] further support the position that substances in this category of materials would have low acute toxicities. In total these data demonstrate that the substances in the Heavy Fuel Oil Category demonstrate low oral and dermal toxicity, minimal eye irritation, minimal to moderate skin irritation with single exposures and that these substances are not skin sensitizers.

6.1.2 Repeat dose and Developmental Toxicity Statistical Modeling of Heavy Fuel Oils

The development of these models began with the observation that the more biologically significant effects of several types of refinery streams in both repeated-dose and developmental studies appeared to be related to the total amount of 3-7 ring polycyclic aromatic compounds (PACs) (Feuston et al, 1994). The relationship was qualitative and not predictive for individual samples.

The statistical models, developed by the Petroleum High Production Volume Testing Group (HPVTG), quantitatively predict effects by individual samples on selected sensitive endpoints based on the PAC profile in each sample (API, 2008). The models are empirically based on a number of toxicity studies on petroleum substances for which there are also analyses of PAC content profile using PAC Method-2 (Gray et al., 2012). The analyses provided the weight percent of each aromatic ring class that served as a basis for the models (the ARC in Table 12). The systemic endpoints used in the models were selected by an extensive analysis to determine the most sensitive endpoints among studies of both developmental toxicity Murray et al., 2012a) and repeated-dose toxicity (Roth et al., 2012) and will be discussed in the relevant section. Seventeen out of 37 reports evaluated were used to develop the PAC models for repeated-dose toxicity. Twenty of the 76 reports were used to develop the PAC models for developmental toxicity. Although the number of samples used to develop the PAC models differed for repeated-dose and developmental toxicity studies, the types of test material samples were the same and included

crude oils, gas oils, heavy fuel oils, a lubricating oil basestock, a heavy paraffinic distillate aromatic extract, and one waste stream. Modeling is only appropriate for petroleum streams that have a final boiling point ≥ 650^{0}F [≥343^{0}C] and for which toxicity is related to polycyclic aromatic carbon content.

Table 12. PAC Analytical Profile of Heavy Fuel Oils

CAS RN	Sample No.	DMSO wt %[1]	ARC 1[2] (%)	ARC 2 (%)	ARC 3 (%)	ARC 4 (%)	ARC 5 (%)	ARC 6 (%)	≥ARC 7 (%)
64741-45-3 Atmospheric Tower Residuals									
64741-45-3 [14:1]	070904	5.6	0.0	0.5	1.1	1.1	1.1	1.1	0.5
64741-45-3 [26:4]	070907	1.9	0.0	0.2	0.6	0.6	0.4	0.2	0.1
64741-45-3 [1:3]	060905	2.6	0.0	0.0	0.5	0.8	0.5	0.5	0.1
64741-45-3 [17:9]	060917	3.0	0.0	0.0	0.6	1.2	0.9	0.6	0.1
64741-45-3	091691		0.1	0.3	2.0	2.0	2.0	0.6	0.1
64741-45-3	[39:1]		0.0	0.3	1.3	1.0	0.8	0.4	0.1
64741-57-7 Heavy Vacuum Gas Oils									
64741-57-7	085244	6.2	0.0	0.1	2.5	1.9	1.2	0.5	0.0
64741-57-7	085289	7.1	0.0	0.0	1.4	1.4	1.4	2.1	0.7
64741-57-7	086010	6.4	0.0	0.1	1.3	1.9	1.9	1.3	0.0
64741-57-7	086269	12.6	0.0	0.6	5.0	3.8	2.5	0.9	0.0
64741-57-7	086281	11.9	0.0	0.6	6.0	3.6	1.2	0.2	0.0
64741-57-7	086289	16.6	0.0	0.7	1.0	11.6	1.7	0.8	0.0
64741-57-7	091649		0.1	0.3	3.0	2.0	2.0	0.7	0.0
64741-57-7	091650		0.0	0.4	4.0	2.0	0.6	0.2	0.0
64741-57-7	091654		0.1	0.4	4.0	3.0	0.9	0.4	0.0
64741-57-7	091689		0.0	0.4	4.0	1.0	0.4	0.1	0.0
64741-57-7	094627		9.0	9.0	0.2	0.0	0.0	0.0	0.0
64741-57-7	060906	4.3	0.0	0.0	0.4	1.3	1.3	0.9	0.3
64741-57-7 [17:7]	060916	3.7	0.0	0.0	0.4	1.1	1.1	0.7	0.3
64741-57-7	060922	5.4	0.0	0.1	1.6	1.6	1.1	0.5	0.1
64741-57-7	086176	8.5	0.0	0.6	0.9	2.6	1.7	0.9	1.7
64741-57-7	086179	10.3	0.0	0.5	1.0	3.1	2.1	1.0	2.1
64741-57-7	086189-1	6.2	0.0	0.1	0.3	0.6	1.2	2.5	1.2
64741-57-7	086189-2	9.1	0.0	0.1	0.0	0.9	1.8	3.6	2.7
64741-57-7	[41:4]		0.0	0.6	4.5	2.4	0.8	0.2	0.0
64741-57-7	[8:3]		0.1	1.6	1.6	2.4	1.6	0.8	0.1
64741-57-7	[28:10]		0.0	0.3	1.9	2.5	1.3	0.6	0.0
64741-57-7	[16:1]		0.0	0.1	1.7	1.7	1.4	0.7	0.1
64741-57-7	[25:15]		0.0	0.1	1.6	1.6	1.1	0.5	0.1
64741-57-7	[1:8]		0.0	0.0	0.4	1.3	1.3	0.9	0.3
64741-61-3 Heavy Catalytic Cracked Distillates									
64741-61-3 [41:8]	070909	28.0	0.0	0.8	11.2	8.4	5.6	2.0	0.6
64741-61-3 [26:20]	030928	38.5	0.0	3.9	15.4	11.6	3.9	1.5	0.0
64741-61-3 [13:1]	060912	35.0	0.0	3.5	21.0	10.5	1.8	0.0	0.0
64741-61-3 [31:1]	060930	47.0	0.0	0.5	28.2	14.1	1.4	0.0	0.0
64741-61-3	091028	50.5	0.0	3.0	32.8	13.6	1.5	0.0	0.0
64741-61-3	091029	51.4	0.0	3.6	33.4	13.9	0.5	0.0	0.0
64741-61-3	091030	50.8	0.0	3.0	33.0	13.2	1.5	0.0	0.0
64741-61-3	091686		0.0	4.0	40.0	4.0	0.6	0.0	0.0
64741-61-3	[16:5]		0.0	6.2	28.7	5.3	0.4	0.0	0.0
64741-62-4 Catalytic Cracked Clarified Oils									
64741-62-4	086001	64.2	0	2.6	25.7	19.3	6.4	3.2	0.6
64741-62-4	087277	19.1	0.0	0.4	3.8	5.7	5.7	3.8	0.8
64741-62-4	087278	30.3	0.0	0.9	9.1	9.1	6.1	3.0	0.9
64741-62-4	087279	20.2	0.0	0.8	6.1	6.1	4.0	2.0	0.6

CAS RN	Sample No.	DMSO wt %[1]	ARC 1[2] (%)	ARC 2 (%)	ARC 3 (%)	ARC 4 (%)	ARC 5 (%)	ARC 6 (%)	≥ARC 7 (%)
64741-62-4	091645		0.0	0.7	10.0	30.0	20.0	6.0	0.0
64741-62-4 [30.3]	010923	43.2	0.0	1.3	13.0	13.0	8.6	4.3	1.7
64741-62-4 [17:10]	010924	31.0	0.0	0.3	6.2	12.4	6.2	3.1	1.6
64741-62-4 [12:2]	010929	52.0	0.0	1.0	15.6	15.6	10.4	5.2	2.6
64741-62-4	086002	61.7	0.0	1.9	12.3	24.7	12.3	6.2	1.2
64741-62-4	086015	31.2	0.0	0.3	6.2	12.5	9.4	6.2	1.2
64741-62-4	086066	52.6	0.0	0.5	10.5	21.0	10.5	5.3	1.6
64741-62-4	086123	13.4	0.1	4.0	4.0	2.7	2.7	1.2	0.3
64741-62-4	086180	63.5	0.0	1.3	12.7	25.4	12.7	6.4	1.3
64741-62-4	086185	63.7	0.0	1.9	25.5	19.1	12.7	5.1	0.6
64741-62-4	086196	74.9	0.0	1.5	22.5	30.0	15.0	7.5	1.5
64741-62-4	086484	48.8	0.0	1.0	9.8	19.5	9.8	4.9	1.0
64741-62-4	091692		0.0	3.0	20.0	30.0	10.0	4.0	0.0
64741-67-9 Catalytic Reformer Fractionator Residuals									
64741-67-9 [47:1]	060949	49.0	3.9	44.1	2.9	0.0	0.0	0.0	0.0
64741-75-9 Hydrocracked Residuals									
64741-75-9 [46:4]	060946	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0
64741-80-6 Thermal Cracked Residuals									
64741-80-6 [14:5]	060915	4.4	0.0	0.0	1.3	2.2	0.9	0.2	0.0
64741-81-7 Heavy Thermal Cracked Distillates									
64741-81-7 [26:9]	071021	63.0	0.0	6.3	44.1	6.3	4.4	0.0	0.0
64741-81-7	086198	9.4	5.6	2.8	0.6	0.1	0.0	0.0	0.0
64741-81-7	094625		7.0	9.0	7.0	5.0	2.0	0.0	0.0
64741-81-7	083366	12.7	0.1	2.5	5.1	2.5	1.3	0.9	0.1
64741-81-7	086161	14.9	0.0	0.7	6.0	4.5	3.0	1.5	0.3
64741-81-7	086181	24.8	0.2	2.5	12.4	7.4	2.5	0.5	0.0
64741-81-7	086193	4.2	0.8	2.9	0.4	0.0	0.0	0.0	0.0
64741-81-7	086194	16.0	0.0	0.5	3.2	4.8	4.8	1.6	0.5
64741-81-7	086230	6.8	0.3	2.0	2.7	1.4	0.4	0.1	0.0
64741-81-7	086272	16.2	0.3	4.9	8.1	1.6	0.3	0.2	0.0
64741-81-7	091653		0.0	0.9	20.0	5.0	0.0	0.0	0.0
64741-81-7	[30:2]		0.0	0.6	3.7	5.5	3.7	3.7	1.8
64741-81-7	[8:1]		0.0	0.5	6.6	5.0	3.3	1.3	0.3
64741-81-7	[9:3]		0.0	0.7	2.3	3.4	2.3	1.1	0.2
64741-81-7	[2:6]		0.0	1.0	4.0	2.0	1.0	0.9	0.3
64742-59-2 Hydrotreated Vacuum Gas Oils									
64742-59-2 [32:1]	071017	2.9	0.0	0.6	0.9	0.6	0.6	0.3	0.0
64742-59-2 [21:4]	071026	5.8	0.0	0.5	1.7	1.7	1.2	0.6	0.1
64742-78-5 Hydrodesulfurized Atmospheric Residuals									
64742-78-5 [46.1]	071030	13.0	0.0	3.9	5.2	1.2	1.0	1.0	0.5
64742-86-5 Hydrodesulfurized Heavy Vacuum Gas Oils									
64742-86-5	091690		0.1	0.7	3.0	2.0	1.0	0.3	0.0
64742-86-5	[21:1]		0.0	0.4	1.1	0.7	0.5	0.3	0.1
68333-22-2 Atmospheric Residuals0.7									
68333-22-2 [19:2]	071016	6.2	0.0	0.1	1.9	1.9	1.2	0.6	0.1
68410-00-4 Crude Oil Distillates									
68410-00-4 [26:7]	030932	3.2	0.0	1.0	1.3	0.6	0.2	0.0	0.0
68410-00-4 [31:5]	030933	5.5	0.1	4.4	1.1	0.0	0.0	0.0	0.0
68410-00-4 [12:15]	030934	5.5	0.0	1.7	1.7	1.1	0.6	0.2	0.0
68410-00-4	091647		0.1	4.0	4.0	0.0	0.0	0.0	0.0
68410-00-4	091681		0.2	4.0	4.0	0.0	0.0	0.0	0.0
68410-00-4	[11:1]		0.0	1.2	1.9	1.2	0.6	0.6	0.2
68476-33-5 Residual Fuel Oils									
68476-33-5	086104	14.6	0.0	1.5	7.3	2.9	1.3	0.6	0.1
68476-33-5	086119	8.8	0.0	2.6	2.6	1.8	0.9	0.6	0.2

CAS RN	Sample No.	DMSO wt %[1]	ARC 1[2] (%)	ARC 2 (%)	ARC 3 (%)	ARC 4 (%)	ARC 5 (%)	ARC 6 (%)	≥ARC 7 (%)
68476-33-5 [11:3]	070903	6.0	0.2	1.8	1.2	1.2	1.2	0.5	0.1
68476-33-5	086108	9.0	0.3	2.7	2.7	0.9	0.9	0.7	0.3
68478-17-1 Heavy Coker Gas Oil and Vacuum Gas Oil Residuals									
68478-17-1 [12:20]	071012	18.0	0.0	0.5	5.4	5.4	3.6	1.8	0.4
68478-17-1 [46:3]	071031	20.0	0.0	0.2	4.0	6.0	4.0	4.0	0.8
68478-17-1	[12:19]		0.0	0.5	5.4	5.4	3.6	1.8	0.4
68512-62-9 Light Vacuum Residuals									
68512-62-9	092009	3.3	0.0	0.0	0.7	0.7	0.7	1.0	0.7
68512-62-9 [36:3]	081022	3.1	0.1	2.2	0.9	0.0	0.0	0.0	0.0
68553-00-4 Fuel Oil, No. 6									
68553-00-4 [26:14]	070908	21.0	0.0	2.1	8.4	6.3	2.1	1.3	0.2
68553-00-4 [20:2]	030936	36.1	0.0	1.8	14.4	10.8	3.6	2.9	0.7
68553-00-4 [26.13]	030937	32.6	0.0	2.3	13.0	9.8	6.5	3.3	1.0
68553-00-4	091034	42.4	0.0	2.5	16.1	14.0	6.8	2.5	0.0
68553-00-4	091035	42.7	0.0	3.0	17.1	13.7	6.0	2.6	0.0
68553-00-4	091036	43.3	0.0	4.3	16.5	13.9	6.1	2.6	0.0
68553-00-4	091674	13.1	0.1	2.6	5.2	1.3	1.3	1.3	0.9
68783-08-4 Heavy Atmospheric Gas Oils									
68783-08-4 [26:17]	071020	3.0	0.0	0.0	1.2	0.9	0.6	0.3	0.0
68783-08-4 [31:3]	071025	5.8	0.1	3.5	1.7	0.0	0.0	0.0	0.0
68783-08-4 [26:25]	081009	5.8	0.0	0.5	2.3	1.7	0.6	0.2	0.0
68783-08-4	081010	5.7	0.0	0.5	2.3	1.7	0.6	0.2	0.0
68783-08-4	081011	5.8	0.0	0.4	2.9	1.7	0.6	0.2	0.0
68783-08-4	081012	5.9	0.0	0.4	3.0	1.8	0.6	0.2	0.0
68783-08-4 [5:2]	081013	2.4	0.0	1.0	1.0	0.2	0.1	0.0	0.0
68783-08-4	094626		0.7	4.0	1.0	0.7	0.5	0.0	0.0
68955-27-1 Distillates, petroleum residues vacuum									
68955-27-1	[32:2]		0.0	0.0	0.5	1.9	3.0	3.1	0.9
68955-27-1	[36:1]		0.0	0.0	0.0	0.2	0.4	0.1	0.0
70592-76-6 Intermediate Vacuum Distillates									
70592-76-6 [10:7]	071011	5.8	0.0	0.1	1.7	1.7	1.2	0.6	0.2
70592-76-6 [23:13]	071018	5.0	0.0	2.0	3.0	0.1	0.0	0.0	0.0
70592-76-6 [39:2]	071029	5.8	0.0	1.2	2.9	1.2	0.5	0.2	0.0
70592-76-6 [9:5]	071032	6.1	0.0	0.6	2.4	1.8	1.2	0.4	0.0
70592-77-7 Light Vacuum Distillates									
70592-77-7 [14:4]	071015	11.0	0.0	2.2	7.7	1.1	0.0	0.0	0.0
70592-77-7 [3:1]	071022	6.3	0.0	0.3	2.5	1.9	0.6	0.6	0.0
70592-77-7 [30:5]	071023	8.2	0.0	0.8	4.1	2.5	0.8	0.5	0.0
70592-77-7 [36:2]	071027	8.3	0.0	1.7	5.0	1.7	0.5	0.2	0.0
70592-78-8 Vacuum Distillates									
70592-78-8 [14:3]	071014	9.3	0.0	0.1	0.9	3.7	2.8	1.9	0.2
70592-78-8 [25:16]	071019	5.2	0.0	0.1	1.0	1.0	1.0	1.0	1.0
70592-78-8 [30:6]	071024	7.2	0.0	0.0	1.4	2.2	2.2	1.4	0.7
70592-78-8	[43:2]		0.0	0.0	0.3	1.0	1.4	1.4	0.6
70592-78-8	[1:1]		0.0	0.0	0.0	0.1	0.6	1.4	1.4
70592-78-8	[10.6]		0.0	0.0	0.2	0.2	0.2	0.1	0.0
70913-85-8 Solvent Extracted, Vacuum Distilled Atmospheric Residuals									
70913-85-8 [23:15]	070905	1.9	0.0	0.0	0.0	0.0	0.2	0.8	0.8
70913-85-8 [1:2]	060904	2.0	0.0	0.0	0.0	0.2	0.4	0.6	0.6
No Analytical Data Available[3]									
68187-58-6									
68333-26-6									
68333-27-7									
68476-32-4									

CAS RN	Sample No.	DMSO wt %[1]	ARC 1[2] (%)	ARC 2 (%)	ARC 3 (%)	ARC 4 (%)	ARC 5 (%)	ARC 6 (%)	≥ARC 7 (%)
68478-13-7									
68607-30-7									
68783-13-1									
70592-79-9									
70955-17-8									

1 – Percent of DMSO-extractable PACs determined by PAC-2 Method as described by Gray et al, 2012. The DMSO wt % does not contain the total PACs for each sample; blank DMSO wt% spaces indicate value was not measured. DMSO does not extract highly alkylated PACs. DMSO wt % does not correlate with modeling. PDR10 is based upon the PAC Profile only. References for individual sample PAC Profiles are presented separately

2 – ARC is "aromatic ring class". ARC 1 (%) is the weight percent of PACs that have 1 aromatic ring within the total sample; "ARC 2 (%) is the percent of PACs with 2 aromatic rings, and so forth to 7 aromatic rings determined by the PAC-2 method.

3 - These CAS RN are streams for which samples could not be obtained and are likely no longer in use in the field.

6.1.3. Repeated Dose Toxicity

Exposure to heavy fuel oils is primarily through the dermal route, rather than oral or by inhalation. Inhalation of heavy fuel oil is unlikely due to the very low vapor pressure of these materials. Dermal studies of up to 13 weeks duration have been reported for representative products and streams and are described below organized by CAS number [CAS RN]. Table 13 summarizes the results of repeated dose dermal toxicity studies and indicates the Heavy Fuel Oil 13 week studies used in developing the PAC models. Lowest observable adverse effect level (LOAEL) and no-observable-adverse-effect level (NOAEL) as determined by study investigators are used to assess toxicity.

For CAS numbers for which no repeat dose data are available, statistical modeling based on PAC analytical profiles and read-across from actual studies were used to predict PDR_{10} and BMD_{10} values for representative PAC-sensitive toxicity endpoints (thymus weight, liver weight relative to body weight, platelet count, hemoglobin concentration) as described in Section 6.1.2 .(Roth et al., 2012). The PDR_{10} (Predicted Dose for a Response of 10% from Control) is a value that has been derived using the statistical models described in Appendix D. The PDR_{10} is not necessarily an indicator of an adverse effect. The BMD_{10} is a Benchmark Dose value calculated using methods developed by Crump (1984) used by EPA and is derived from data from actual studies. Table 13 shows results of modeling of endpoints based on analytical distribution of 1-7 ring PAC to provide estimates of effects for streams where animal data are not available.

CAS RN. 64741-45-3 Atmospheric Tower Residuals

Four week dermal study in rats

Dose levels of 0.01 (9.4 mg), 0.25 (235 mg) or 1.0 (940 mg) ml/kg/day of an atmospheric residuum F-132 (CAS RN. 64741-45-3, were applied undiluted to the skin of male and female rats 5 times/week for 4 weeks (ARCO, ATX 90-0066, 1992i). There were no clinical observations made that were considered to be treatment-related. The only treatment-related finding at gross necropsy was a dark staining of the treated skin site. There were no compound-related effects on either hematology or clinical chemistry values. Nor were there any treatment-related differences in body weights or organ weights or organ/body weight ratios. The only treatment-related histopathological findings consisted of trace to mild acanthosis and trace to moderate hyperkeratosis in skin of high

dose animals. The study authors concluded that there were no systemic effects at the highest dose level tested.

CAS RN 64741-57-7 Heavy Vacuum Gas Oils

13 week dermal study in rats

An undiluted heavy vacuum gas oil (CAS no. 64741-57-7) was applied to the skin of male and female rats 5 days each week for 13 weeks (Mobil, 1988d, Study # 61590). Dose levels were 0, 30, 125, 500 & 2000 mg/kg/day. The unscheduled deaths of two of ten males in the high dose group were considered to be compound-related. Growth rates of males and females in the highest dose group were reduced compared to controls. At five and thirteen weeks, the 2000 mg/kg/day dose group had reduced erythrocytes and platelets. Similar reductions were also found in the 500 mg/kg/day females. Changes in several clinical chemistry values were also seen in the 2000 mg/kg/day dose group. In addition in females dosed with 500 mg/kg/day had reduced serum glucose levels, and in the 500 mg/kg/day males, cholesterol levels were elevated.

At gross necropsy, in the 500 and 2000 mg/kg/day dose groups, relative thymus weights were reduced while relative liver weights were increased. Histological examination revealed decreased erythropoiesis and fibrosis of the bone marrow in the 2000 mg/kg/day males. There was a reduction in thymic lymphocytes in both sexes in the 2000 mg/kg/day group. Decreased hematology values in red blood cells, hemoglobin and hematocrit in both sexes seen at 125mg/g day were not considered definitive for establishing LOAEL. Examination of the testes of animals in the 2000 mg/kg/day dose group revealed no compound-related effects on sperm morphology. A LOAEL = 250mg/kg and a NOAEL = 125mg/kg were determined by the investigators.

Four week dermal studies in rats: Supplemental data

A heavy paraffinic vacuum distillate (F-128; CAS RN 64741-57-7) was applied undiluted to the shaved backs of Sprague Dawley rats (10/sex/group) at concentrations of 0, 94, 940, 2350mg/kg/day, 5 days/week for 4 weeks (ARCO, ATX 90-0034, 1992j). Treatment sites were occluded for 6 hours after administration. No significant systemic effects were seen in males at any dose level. Females showed increased absolute and relative (to body weight) liver weight at the mid and high dose levels. No adverse histopathologic changes were seen in any organs including ovaries and testes. NOAEL males ≥ 2350mg/kg/day [highest dose]. LOAEL females = 940mg/kg/day based on increased liver weights, NOAEL = 94mg/kg/day identified by authors.

A heavy vacuum gas oil stock (F-113-01; CAS RN 64741-57-7) was applied undiluted to the shaved backs of Sprague Dawley rats (10/sex/group) at concentrations of 0, 9.3, 93, 930mg/kg/day (0.01, 0.10, 1.0ml/kg/day), 5 days/week for 4 weeks (ARCO, ATX 890011, 1993f). Treatment sites were occluded for 6 hours after administration. No statistically significant terminal body weight changes were seen in either sex. Relative liver weights were increased at 930mg/kg in both sexes and female absolute weights were decreased in brain and kidney at mid and high doses. Organ weight changes were not accompanied by adverse histological effects and were not used to establish adverse effect levels. Reproductive organs were normal. Significant decreases in hemoglobin and hematocrit were seen in mid and high dose levels in both sexes. LOAEL = 930mg/kg for both sexes based on hematologic changes. NOAEL = 93mg/kg.

CAS RN 64741-61-3 Heavy Catalytic Cracked Distillates

4-week rat dermal study

Heavy cycle oil (F-134; CAS RN 64741-61-3, ARCO, ATX 90-0082, 1992j) were applied to the shaved backs of Sprague Dawley rats (10/sex/group) at concentrations of 0, 9.9, 99, 990mg kg/day. Skin irritation was slight-moderate and correlated with dose. Terminal body weights were slightly decreased in high dose males. Exposure related decreases in hematology parameters were reported at the mid and high dose levels in females and high dose in males. Liver weights, absolute and relative to body weight were increased at the highest dose and relative liver weights were increased at the mid dose for females. Male LOAEL = 990mg/kg NOAEL = 99mg/kg; female LOAEL = 99, NOAEL = 9.9mg/kg

CAS RN 64741-62-4 Catalytic Cracked Clarified Oils

13-week dermal studies in rats

Dose levels of 8, 30,125, 500 and 2000 mg/kg/day of a clarified slurry oil (CAS no. 64741-62-4) were applied undiluted to the skin of male and female rats (Cruzan et al., 1986; Mobil, 1985, Study # 20525). The test material was applied 5 days/week for 13 weeks. There was an adverse, dose-related effect on mortality, with none of the rats in the highest dose group (2000 mg/kg/day) surviving past the second week of the study. Compound-related effects were observed on body weights, and several hematology and clinical chemistry parameters. Based on these changes, and histopathology findings, the target organs of toxicity were judged by the study directors to be the liver, thymus and bone marrow. The investigators concluded that none of the dose levels used in the study represented a NOAEL. The LOAEL was 8 mg/kg/day.

Catalytic cracked clarified oil (Syntower bottoms .CAS RN 64741-62-4) was applied undiluted to the shaved backs of Sprague Dawley rats (10/sex/group) at concentrations of 0, 8, 30, 125, 500mg/kg/day, 5 days/week for 13 weeks (Mobil 1988, study #62710). Application sites were not occluded; animals wore Elizabethan collars to minimize oral ingestion through grooming. Sites were wiped off weekly. Sperm evaluations were performed at study termination. Mortality was 100% at 500mg/kg/day and 90% at 125mg/kg/day. Body weight gains were statistically significantly decreased in the remaining rats at 125mg/kg/day and slightly decreased (8%) in the 30mg/kg/day group. Due to the small number of surviving female rats in the 125mg/kg/day group, only data from the 30 and 8mg/kg/day groups are reported. Hematology parameters (red blood cells, hemoglobin and hematocrit) were decreased in 30mg/kg/day males and platelets decreased in females at 30 [40%] and 8mg/kg/day [20%]. Various changes were seen in serum chemistry parameters at 30mg/kg/day animals and glucose levels were increased 24% in 8mg/kg/day females. Absolute and relative (to body weight) liver weights were increased in 30mg/kg/day females and relative liver weights in 30mg/kg/day males. Relative and absolute thymus weights were decreased in both sexes at 30mg/kg/day. Histologically, changes were seen in bone marrow, liver and lungs at 30mg/ kg/day and above. No adverse effects were seen in reproductive organs or sperm counts or morphology. LOAEL = 8mg/kg/day due to decreased platelet count and increased glucose values in females determined to be test material related. Therefore, NOAEL is less than 8 mg/kg.

Catalytic cracked clarified oil (CAS RN 64741-62-4) was applied diluted in acetone to the shaved backs of Sprague Dawley rats (10/sex/group) at concentrations of 0, 5, 25, 50 mg/kg/day, 5 days/week for 13 weeks (Wil Laboratories, 2012a). Sham and vehicle (acetone) control groups were included. Application sites were not occluded; animals wore Elizabethan collars for 5 days of dosing to minimize oral ingestion through grooming. Sites were wiped off daily to remove unabsorbed test substance and at the end of each week residual substances were removed using a warm water and mild soap solution. Collars were removed for the 2 day non-dosing period. Eight animals (5 males, 3 females) from the 50mg/kg group and 1 female from the 25mg/kg group

died or were sacrificed moribund. All 9 had bone marrow depression and centrilobular hepatocellular atrophy and 5 had thrombosis in the heart and renal tubular necrosis. Reduced body weight and/or body weight gain were statistically significant in 50mg/kg males but not in 25mg/kg males. Terminal body weights in 25 and 50mg/kg females were statistically significantly lower by 5% than controls. The study investigators did not consider these small differences to be biologically significant. Treatment-related hematological effects included lower absolute red blood cell counts, hemoglobin, hematocrit, absolute and relative eosinophil counts and platelet counts. These differences were significant at both the 25 and 50 mg/kg/day levels and were considered to have been treatment-related (Table 4). The reductions in eosinophil counts were also significant at the 5 mg/kg/day level. Other observations included small but statistically significant reductions in white blood cell counts (males), mean corpuscular hemoglobin (females), percent monocytes (females) and basophils (males, 25 and 50mg/kg). Changes in serum chemistry parameters were primarily seen in the 50mg/kg group. Thymus weights, absolute and relative to body weight or brain weight were significantly reduced in both sexes in 25 and 50 mg/kg/day groups. Liver weights and spleen weights, absolute and relative were increased and were significantly different in the 25 and 50 mg/kg/day males and females. Spleen weights were significantly higher in 25 and 50 mg/kg/day group females but the relationship to test article administration was uncertain because there was no correlating histologic changes and no consistent change in males in either group. Significant reductions in absolute brain weights in the 50 mg/kg/day males and absolute kidney weights in the 50 mg/kg/day females was reported, but the differences in kidney weights may have been due to the significant reductions in body weight gains in these groups as the differences were not significant when compared on a "relative to body weight" basis. Test substance-related microscopic findings were noted in the bone marrow, liver, kidney, heart, spleen, lymph nodes, thymus, and Peyer's patch as lymphoid depletion, pituitary gland, adrenal cortex, exorbital lacrimal gland, testis, epididymis, ovary, and uterus of the 25 and/or 50 mg/kg/day groups. Lesions in the male reproductive system included increased incidence of seminiferous tubular degeneration in the testis and hypospermia and luminal cellular debris in the epididymis of 3/10 males in the 50 mg/kg/day group. Scattered individual to small numbers of seminiferous tubules contained degenerated spermatogonia, spermatocytes, and/or spermatids with mild disorganization of maturation. These are minimal effects and occurred in a dose group where 5 of 10 male animals died or were terminated. In females decreased corpora lutea, increased atretic follicles and atrophy of the uterus with increased prominence of stromal cells were noted in 6/10 of the 50 mg/kg/day females. LOAEL for both sexes was 25mg/kg/day, based on increased liver weights, reduced thymus weights and hematologic changes at 25 and 50 mg/kg/day and decreased eosinophil counts (absolute and percentage, males; absolute counts only, females). Decreased eosinophil values at 5mg/kg were small, generally within historical control ranges, and showed inconsistencies in response between genders, making them less likely to have been due to treatment than the effects on red blood cells and not definitive for establishing a NOAEL. The NOAEL = 5mg/kg/day for both sexes.

Clarified slurry oil (F-179, CAS RN 64741-62-4) was applied to the shaved backs of rats (20/sex/group) at concentrations of 0, 0.001, 0.01, 0.05, 0.1, 0.5ml/kg/day [0, 1.06, 10.6, 53, 106, 530mg/kg /day] 5 days/week for 13 weeks (ARCO, ATX 91-0012, 1993d). Treatment sites were occluded for 6 hours after application then wiped to remove residual material. No skin irritation was observed. Mortality occurred in 35% males and 10% females and terminal body weights were decreased in the remaining males at the 530mg/kg/day dose level. Increased absolute and relative liver weights were seen in both sexes and lung weights were increased in females at 10.6mg/kg and above. Varying changes in absolute and relative weights in other organs were reported. Thymus weights were decreased and histological examination revealed thymus atrophy in males at 10.6mg/kg/day and females at 106mg/kg/day. Reproductive organs were not adversely

affected by exposure to F-179. Hematology parameters were decreased in both sexes at 53mg/kg and above with decreased platelets in males at 10.6mg/kg/day. LOAEL = 10.6mg/kg/day based on liver wt changes in both sexes, thymic atrophy and decreased platelets in males and increased lung weight in females. NOAEL = 1.06mg/kg/day

4 -week dermal studies in rats. Supplemental data

Two 4-week dermal studies were performed with a Fluid Catalytic Cracker Unit (FCCU) Clarified oil (F-115-01; CAS RN 64741-62-4) and a Carbon Black oil (F-73-01; CAS RN 64741-62-4).

FCCU Clarified oil (F-115-01) was applied in acetone at concentrations of 0, 0.01, 0.1, 1.0, 10.0, 50.0mg/kg/day or undiluted at 1.0, 10.0, 50mg/kg/day (ARCO, ATX 89-0077, 1993e). There were no body weight changes in male rats compared to controls; a 13% decrease in terminal body weight was seen in females exposed to undiluted oil at 50mg/kg/day. Decreases in hematology parameters were seen in male rats at doses as low as 10mg/kg/day acetone diluted group but only in the 50mg/kg/day undiluted group. Serum chemistry parameters values varied in all treated groups to varying degrees with a significant increase in cholesterol level (32%) in females at 10mg/kg/day acetone-diluted group. Increases in relative liver weight were reported in male and female acetone-diluted group and female undiluted group at 10mg/kg/day. In males absolute and relative thymus weights were decreased following treatment with undiluted material at a concentration of 50mg/kg/day. LOAEL females, acetone-diluted and undiluted and LOAEL males acetone diluted = 10mg/kg/day; NOAEL = 1.0mg/kg/day. LOAEL males, undiluted = 50mg/kg/day; NOAEL males undiluted = 10.0mg/kg/day.

Carbon Black oil (F-73-01) was applied undiluted at concentrations of 542, 1084 and 2710mg/kg/day, doses well above those employed in the other 4 week dermal studies (ARCO, ATX 86-0007, 1987a). No skin irritation was observed. Terminal body weight and weight gain were significantly decreased in male rats at all dose levels and in females terminal weights were decreased only at the high dose level by 11% but weight gains were significantly decreased al all dose levels. Hematology parameters were decreased in males at all dose levels as were eosinophil counts in females. Absolute and relative liver weights were increased in both sexes in all treatment groups. Spleen weight and ovarian weights were decreased in females in the mid and high dose groups. Histological examination of control and high dose animals did not identify adverse effects in any organs including testes and ovaries. LOAEL was 542mg/kg/day and a NOAEL was not established in this study.

CAS RN 64741-75-9 Hydrocracked Residual

4 week dermal study in rats

Hydrocracker recycle oil (F-127, CAS RN 64641-75-9, (ARCO, ATX 90-0026, 1992e) was applied undiluted to the shaved backs of rats (10/sex/group) 5 days/week for 4 weeks. Treatment sites were occluded for 6 hours after application. Hydrocracker recycle oil (F127) containing 1% 3-7 ring PAC, was administered at 0, 8.4, 42, 210mg/kg/day. Light to moderate irritation was seen. No adverse effects were observed on body weight, organ weights, hematology, serum chemistry or hematology for either sex at any dose. NOAEL ≥ 210mg/ kg/day, highest dose tested

CAS RN 64741-80-6 Thermal Cracked Residuals

13 week dermal study in rats

A visbreaker residual (CAS RN 64741-80-6) containing 3% 3-7 PAC, was applied undiluted to the shaved backs of Sprague Dawley rats (10/sex/group) as a 67% concentration at 0, 60,250, and 1000mg/kg/day, 5 days/week for 13 weeks (Mobil 1992c, study #64002). Application sites were not occluded; animals wore Elizabethan collars to minimize oral ingestion through grooming. Sites

were wiped off weekly. Sperm evaluations were performed at study termination. Body weight gain and hematology parameters were decreased in males only at 1000mg/kg/day. Serum chemistry parameters were altered to varying degrees in both sexes and organ weights (liver, spleen, adrenals, kidney) increased at levels of 250 and 1000mg/ kg/day. No adverse histopathology changes were seen in either sex and sperm counts and morphology were comparable to controls. Effects seen at doses as low as 60 mg/kg included decreased ALT, increased absolute and relative liver weights and absolute adrenal weights but were judged not to be significant due to lack of histopathology. LOAEL = 250mg/kg/day; NOAEL = 60mg/kg/day based on changes in hematology, body weight and organ weights at 250 and 1000 mg/kg/day.

CAS RN. 68471-81-7 Heavy Thermal Cracked Distillates

13-week dermal studies in rats

Dose levels of 8, 30 and 125 mg/kg/day of visbreaker gas oil (CAS RN. 68471-81-7) were applied undiluted to the skin of male and female Sprague-Dawley rats (Feuston et al., 1994; Mobil, 1992b, study # 63257). The test material was applied 5x/ week for 13 weeks. There were no deaths during the study. No clinical signs of toxicity were observed, with the exception of dose-related skin irritation. There were no compound-related effects on body weights or hematology and clinical chemistry values. Urinalysis found no treatment-related effects. At necropsy, the only treatment-related findings were effects on the skin and enlarged lymph nodes (the latter predominantly in the higher dose groups). Microscopic examination of the skin revealed thickened epidermis with parakeratosis, chronic inflammation in the subcutis, ulcers and increased mitosis in the epidermal basal cells. The skin changes were more severe in females than the males. Lymph nodes were enlarged in the high dose animals and in most instances, microscopic examination revealed non-specific reactive hyperplasia. Epididymides and testes from the male rats in the control and 125 mg/kg/day groups were given an in-depth histopathology examination, including spermatid (testes) and spermatozoa (epididymides) counts. Treatment with visbreaker gas oil did not cause any changes in testicular spermatid or epididymal spermatozoa count nor in sperm morphology. The investigators concluded the NOAEL in the study was ≥ 125 mg/kg.

Three 13-week dermal studies were performed on heavy coker gas oils (CAS RN 64741-81-7) from different refineries. Test materials were applied to the shaved backs of Sprague Dawley rats (10/sex/group) and not occluded, 5 days/week for 13 weeks. Animals were fitted with Elizabethan collars to minimize oral ingestion of test material. Test materials were wiped off at the end of each week of treatment. Heavy coker gas oils (Mobil, 1994a study #64165 and Mobil, 1995, study #64184) were applied at concentrations of 0, 8, 30, 125mg/kg/day and heavy coker gas oil (Mobil, 1994d, study #50391) was applied at concentrations of 0, 30, 125, 500, 2000mg/kg/day. Sperm counts and morphology evaluations were performed in each study. Significant mortality occurred in the coker gas oil study [#50391] at concentrations of 500 and 2000mg/kg/day and all animals were terminated in these groups. Body weight gains were decreased in males at 125mg/kg/day in all three studies and at 30 kg/day in one study. Moderate irritation was seen in all studies with more severe irritation at higher concentrations in one study. Hematology parameters were decreased at 125mg/kg/day in all studies. Varying changes were seen in serum chemistry parameters were seen primarily at 125mg/kg/day although male rats treated with one of the coker gas oil samples exhibited increases in blood urea nitrogen and decreased calcium levels at 30mg/kg/day. Increases in absolute and/or relative (to body weight) liver weights occurred in both sexes in all three studies at 125mg/kg/day and relative liver weights were increased in the 30mg/ kg/day group in both sexes of one of the heavy coker gas oil studies. Decreases in absolute and relative thymus weight were seen at 125mg/kg/day accompanied by lymphatic tissue reduction in

all studies. Other histopathologic effects included increased bone marrow granulocytes and focal fibrosis in bone marrow (1 male, 2 females) and spleen (6 males) in the 125mg/kg/day...No adverse effects were seen in reproductive organs and sperm counts and morphology were unaffected in all studies. However epididymis weight was decreased in males in the 30mg/kg/day group and above in one test sample. Systemic effects were generally similar for all three heavy coker gas oils with some variation in affected organs likely related to the relative content of 3-7 ring PAC in streams from different crude sources. LOAEL values were 30mg/kg/day for two studies [#64165, 50391] and 125mg/kg/day for one study [#64184]. NOAEL was 8mg/kg/day for the study # 64165 and 30mg/kg/day for study #64184.
A NOAEL was not established for study # 50391 since 30mg kg/day was the lowest dose tested.

4- week dermal studies in rats: Supplemental data
Two coker heavy gas oils (F-97-01; F-136; CAS RN 64741-81-7) were tested in 4-week dermal studies over similar dose ranges. Coker heavy gas oil (F-136) was applied to the shaved backs of Sprague Dawley rats (10/sex/group) at concentrations of 0, 9.3, 93, 930mg/kg/day (ARCO, ATX 90-0098, 1992f). Coker heavy gas oil (F-97-01) was applied diluted 10% in acetone at a lowest dose of 0.93mg/kg/day and undiluted at 93 and 930mg/ kg/day (ARCO, ATX 88-0092, 1990c). Skin irritation was slight-moderate in both studies and correlated with dose. Terminal body weights were slightly decreased in the F-97-01 females at 930mg/kg/day. Exposure related decreases in hematology parameters were reported in the F-97-01 coker heavy gas oil at the mid and high dose levels while no significant effects were reported with coker heavy gas oil F-136. Serum chemistry parameters showed no significant differences compared to controls except for increase in cholesterol levels in coker heavy gas oil in F-136 high dose females. Liver weights, absolute and relative to body weight were increased at the highest dose in both studies and relative liver weights were increased at the mid dose for F-97-01 males.

The LOAEL for Coker heavy gas oil F-136 was 930mg/kg/day both sexes; NOAEL = 93mg/ kg/day both sexes. Coker heavy gas oil F-97-01 demonstrated slightly more toxicity with LOAEL = 93mg/ kg/day and NOAEL = 0.93mg/ kg/day. The extremely low NOAEL for F-97-01 resulted from the absence of any doses between 93 and 0.93mg/kg/day.

CAS RN 68476-33-5 Residual Fuel Oil

Four week dermal studies in rats
Heavy Fuel Oil (F-74-01; CAS RN 68476-33-5) was applied undiluted to the skin of male and female rats at concentrations of 0.5 (496 mg), 1.0 (992 mg), or 2.5 (2480 mg) ml/kg/day 5x/ week for 4 weeks (ARCO, ATX 86-0088, 1987b). The test material produced minimal reversible dermal irritation at all dose levels. Daily observations of the animals revealed no compound-related effects other than test material staining at the site of application. Similarly, there were no compound-related findings at necropsy other than the staining of the skin produced by the test article. Statistically significant values obtained from the hematology or clinical chemistry assays were within normal limits and did not exhibit any clear dose-related trends. Absolute liver weights were significantly higher for the females in all dose groups and in the high-dose males. With the exception of the liver/brain weight ratios in the low-dose males, liver/body weight and liver/brain weight ratios were significantly higher for both sexes in all dose groups and were considered compound-related. Changes in spleen weights and ratios were not considered dose related. No compound related changes in selected tissues in control and high dose animals were seen histologically. LOAEL based on changes in absolute and relative liver weights alone is 496mg/kg, the lowest dose tested and a NOAEL could not be identified

Heavy fuel oil (F-92-01; CAS RN 68476-33-5) was applied undiluted to the shaved backs of Sprague Dawley rats (10/sex/group) at concentrations of 0,480, 960, 1920mg/kg/day, 5 days/week for 4 weeks (ARCO, ATX 86-0090, 1986b). Treatment sites were occluded for 6 hours after administration. Terminal body weights were decreased 6% in males only at the highest dose. Red blood cell counts, hemoglobin and hematocrit values were decreased to varying degrees in both sexes as were serum chemistry values. Absolute and relative (to body weight) liver weights were increased in both sexes at all doses. Absolute and relative spleen weights were increased in males at all doses and females at the mid and high dose groups. Kidney weights were decreased in males at 1920mg/kg. No adverse histopathological changes were seen in any organs of high dose rats, including ovaries and testes. Based on the effects on organ weight and hematology data the LOAEL = 480mg/kg, the lowest dose tested. NOAEL could not be determined in this study.

The range of lowest observable adverse effect level (LOAEL) values for 4 week rat dermal studies for this CAS RN is 480-496; a No observable adverse effect level (NOAEL) was not experimentally defined.

CAS RN 68783-08-4 Heavy Atmospheric Gas Oil

No studies are available for this material. However the compositionally similar CAS 68915-97-9 also identified as heavy atmospheric gas oil from the Gas Oil Category is provided as supplemental data which demonstrates the compositional and toxicologically continuity among PAC-rich petroleum streams.

Supplemental data: Related material *from Gas Oil Category Assessment Document*

Dose levels of 30, 125 or 500 mg/kg/day of test material (CAS RN 68915-97-9) were applied undiluted to the skin of male and female rats, 5 days/week for 13 weeks (Mobil, 1992d). At the end of the study the epididymides and testes from the male rats in the control and 500 mg/kg/day groups were given an in-depth histopathology examination, including spermatid (testes) and spermatozoa (epididymides) counts. In general, application of the test material produced only "slight" skin irritation. One of ten high dose males was sacrificed *in extremis*, the investigators considered the death to be treatment-related. There were treatment-related changes in a number of serum chemistry and hematological parameters in the rats in the mid- and high dose groups. At necropsy, treatment-related macroscopic findings in both sexes included increased liver size, decreased thymus size, thickening of the limiting ridge between the non-glandular and glandular sections of the stomach and enlarged and reddened lymph nodes. There were some organ weight (absolute and relative) differences in the 125 and 500 mg/kg/day groups. The histopathology examination found treatment-related changes only in animals in the 500mg/kg/day groups. These changes included a severe reduction in hematopoiesis in the bone marrow; liver hypertrophy and connective tissue formation; increased areas of hematopoiesis, focal necrosis and individual cell death in the liver; and a reduction in the numbers of lymphocytes in the thymus glands. There were no treatment-related effects on any of the epididymal sperm or testicular spermatid parameters. The investigators concluded the LOAEL was 125 mg/kg/day and the NOAEL was 30mg/kg/day.

Conclusions

Repeated dose dermal studies of heavy fuel oils (Table 13) indicate that toxicity induced by these streams when present affected essentially the same organ systems (liver, spleen, thymus and bone marrow). Skin irritation tended to be slight at exposed sites with some dose-related increased irritation seen in studies with some cracked stocks. Streams with higher aromatic content and broader ARC profiles tended to be more toxic with lower LOAEL and NOAEL values. CAS RN 64741-62-4 catalytic cracked clarified oil samples contained approximately 46-67% 1-7 ring PAC and demonstrated a LOAEL = 8.0 -11.0mg/kg and NOAEL as low as 1.1mg/kg in 13 week studies. Alternatively, two oils which contained low levels of total DMSO extractable aromatics, CAS RN 64741-80-6 Thermal Cracked Residual [total aromatic 4.4%] and CAS RN 64741-75-9, Hydrocracked Residual [total aromatic 1.0%] demonstrated less systemic toxicity. For CAS RN 64741-80-6 the LOAEL was 250mg/kg and NOAEL = 60mg/kg in a 13 week study and for CAS RN 64741-75-9, the NOAEL was 210mg/kg in a 4 week study. Toxicity levels for residual fuel oils blended from HFO streams may fall anywhere in that range of activity.

In some instances, samples with same CAS RN can demonstrate different PAC profiles and different levels of toxicity. PAC profiles are determined by crude oil stocks and the severity of processing. For example CAS RN 64741-81-7, Heavy Thermal Cracked Distillate includes a visbreaker gas oil sample with a total DMSO extractable aromatic content of 4.2% [of which 3.7% was 1 and 2 ring PAC and 0.4% 3-7 ring PAC] and a NOAEL >125mg/kg, the highest dose tested while heavy gas oils with the same CAS RN contained higher levels of PAC [13-25%] and NOAELs from 30mg/kg to below lowest tested level. None of the heavy fuel oils induced adverse histological changes in reproductive organs or sperm number or morphology when these parameters were evaluated.

These results illustrate the significant role that PAC content and aromatic ring distribution profile play in determining the systemic toxicity of Heavy Fuel Oils.

Table 13. Repeat Dose Dermal Toxicity [4 week and 13 week exposures]

CAS RN	Study: Species/ Route/Duration	Dose/ Frequency	Results	References
64741-45-3 Atmospheric Tower Residuals				
Atmosphere Tower Bottoms F-132 [64741-45-3]	Rats (M/F) dermal, 4 weeks	0, 0.01, 0.25, 1.0ml/kg/d (9.4, 235, 940 mg/kg/d), 5 days/week	NOAEL = 940 mg/kg [highest dose] No systemic effects. Dark staining without irritation of treated skin. No adverse effects on testes or ovarian weight or abnormal histopathology.	ARCO, 1992i ATX-90-0066
64741-57-7 Heavy Vacuum Gas Oils				
Heavy Vacuum gas oil Sample # 85244 [64741-57-7]	Rats (M/F) dermal, 13 weeks	0, 30, 125, 500, 2000mg/kg/day, 5 days/week Elizabethan collars, weekly wipe off	LOAEL=500mg/kg Based on reduced body weight gain, decreased hematology, serum chemistry parameters, changes in organ weights (liver, thymus); effects on bone marrow and thymus lymphocytes. No adverse effects on testes/ovaries. Minimal skin irritation NOAEL = 125 mg/kg	Mobil 1988d Study 61590 Used in PAC model [a]
Vacuum distillate F-128 [64741-57-7]	Rats (M/F) dermal, 4 weeks	0, 0.1, 1.0, 2.5ml/kg/d (94, 940, 2350 mg/kg/d), 5 days/week	NOAEL males = 2350 mg/kg [highest dose] NOAEL females = 94mg/kg/d by authors I LOAEL females = 940 mg/kg Based on increased absolute/relative liver weight. which may be considered adaptive only. Slight skin irritation. No systemic histopathology, no adverse effects on testes or ovaries	ARCO, 1992j ATX-90-0034
Heavy Vacuum Gas Oil Stock F113-01 [64741-57-7]	Rats (M/F) dermal, 4 weeks	0, 0.01, 0.1, 1.0ml/kg/d (9.3, 93, 930mg/kg/d)	LOAEL = 930mg/kg based on hematology [hemoglobin, hematocrit] NOAEL = 93mg/kg No statistically significant terminal body weight changes. Organ weight changes seen in liver, [both sexes] and absolute weight decreases in female brain and kidney not accompanied by adverse histological effects and not used to establish adverse effect levels. Reproductive organs were normal.	ARCO 1993f ATX-89-0011
64741-61-3 Heavy Catalytic Cracked Distillate				
Heavy cycle oil (F-134) [64741-61-3]	Rats (M/F) dermal, 4 weeks	0.01, 0.1, 1.0ml/kg/d (9.9, 99, 990 mg/kg/d) 5days/week. occluded	LOAEL males = 990mg/kg, based on decreased terminal body wt, increased liver wt, decreased hematology parameters.	ARCO,1992j, ATX-90-0082

CAS RN	Study: Species/ Route/Duration	Dose/ Frequency	Results	References
		for 6 hours post dose	LOAEL females = 99mg/kg, based on increased liver wt, decreased hematology parameters No adverse effects in histopathology including testes/ovaries Slight skin irritation NOAEL males 99mg/kg; females 9.9mg/kg	
64741-62-4 Catalytic Cracked Clarified Oils				
Clarified Slurry Oil Sample # 86001 [64741-62-4]	Rat (M/F) dermal, 13 weeks	0, 8, 30, 125, 500, 2000mg/kg/d. 5 days/week Elizabethan collars, weekly wipe off	LOAEL = 8 mg/kg Based on decreased body weight gain, effects on hematology, serum chemistry. Histopathology of liver, thymus, bone marrow. No adverse effects on testes/ovaries. 100% mortality at 2000mg/kg. Slight skin irritation first 2 weeks. NOAEL: not established, <8mg/kg	Cruzan et al, 1986 Mobil 1985 Study # 20525 Used in PAC model [a]
Catalytically cracked clarified oil (Syn Tower bottoms) Sample # 86484 [64741-62-4]	Rats (M/F) dermal, 13 weeks	0, 8, 30, 125, 500 mg/kg/d, 5 days/week Elizabethan collars, weekly wipe off	LOAEL = 8 mg/kg Based on 100% mortality at 500mg/kg; 90% mortality at 125mg/kg. Decreased body weight gain, effects on hematology, serum chemistry. Histopathology of liver, lungs, bone marrow at ≥30mg/kg. No adverse effects on testes/ovaries. Slight dermal flaking at application site week 3 NOAEL: not established, <8mg/kg	Mobil, 1988 Study #62710 Used in PAC model [a]
Catalytically cracked clarified oil Sample # 010929 [64741-62-4]	Rats (M/F) dermal, 13 weeks	0, 5,25, 50 mg/kg/d, 5 days/week Elizabethan collars, daily and weekly wipe off	LOAEL = 25mg/kg Based on increased liver weights, reduced thymus weights and decreased eosinophil counts (absolute and percentages in males, absolute counts in females. Histologic effects seen on male and female reproductive organs at 50mg/kg NOAEL = 5mg/kg	WIL Laboratories, 2012a
Catalytic cracked slurry oil (F-179) Sample # 91645 [64741-62-4]	Rats (M/F) dermal, 13 weeks	0, 0.001, 0.01, 0.05, 0.1, 0.5ml/kg (1.06, 10.6, 53, 106, 530 mg/kg/d), 5days/week	LOAEL = 10.6 mg/kg Based on increased liver, lung wts, decreased platelets, thymic atrophy. No adverse effects on testes/ovaries NOAEL = 1.06mg/kg	ARCO , 1993d ATX-91-0012
FCCU clarified oil (F115-01) [64741-62-4]	Rats (M/F) dermal 4 weeks	0, 1, 10, 50 mg/kg/d neat 0.01, 0.1, 1.0, 10, 50 mg/kg diluted in acetone. 5days/week occluded for 6 hrs	Neat group: LOAEL males = 50 mg/kg; NOAEL males = 10mg/kg LOAEL females = 10mg/kg; NOAEL female =1.0mg/kg Acetone group LOAEL = 10 mg/kg both sexes	ARCO, 1993c ATX-89-0077

CAS RN	Study: Species/ Route/Duration	Dose/ Frequency	Results	References
		postdose.	NOAEL = 1.0mg/kg both sexes Based on increased liver wt, changes in hematology, No adverse effects histopathologically on any organs including testes/ovaries. Slight skin irritation	
Carbon Black Oil (F-73-01) [64741-62-4]	Rats (M/F) dermal 4 weeks	0, 542, 1084, 2710 mg/kg undiluted. 5days/week, occluded for 6 hrs postdose.	LOAEL = 542mg/kg both sexes. Based on decreased body weight and weight gain changes in hematology, increased liver wt and decreased spleen and ovary wts in females. No adverse effects histopathologically on any organs including testes/ovaries. No skin irritation NOAEL not established. <542mg/kg	ARCO, 1987a ATX-86-0007
64741-75-9 Hydrocracked Residuals				
Recycle Oil, Hydrocracker (F-127) [64641-75-9]	Rat (M/F) dermal 4 weeks	0, 0.01, 0.05, 0.25ml/kg (8.4, 42, 210mg/kg/d) 5 days/week, occluded for 6 hours postdose	NOAEL = 210 mg/kg [Highest dose tested] No systemic effects.	ARCO, 1992e, ATX-90-0026
64741-80-6 Thermal Cracked Residuals				
Visbreaker residual Sample #86192 [64741-80-6]	Rat (M,F) dermal 13 weeks	0, 60, 250, 1000 mg/kg/d, 5days/week Elizabethan collars, weekly wipe off	LOAEL = 250 mg/kg Based on decreased body wt gain, changes in hematology, serum chemistry, organ wts. No adverse histopathology including ovaries testes/sperm. No adverse effects on sperm counts or morphology. No skin irritation related to test compound. NOAEL = 60mg/kg	Mobil, 1992c Study #64002
64741-81-7 Heavy Thermal Cracked Distillates				
Visbreaker gas oil Sample #86193 [64741-81-7]	Rat (M,F) dermal 13 weeks	0, 8, 30, 125 mg/kg/d, 5days/week Elizabethan collars, weekly wipe off	NOAEL systemic = 125 mg/kg [highest dose tested] Excludes skin changes grossly and microscopically resulting from physical treatment. Some non-specific hyperplasia. No significant adverse effects on body weight, hematology or serum chemistry or histopathology of organ systems. No adverse effects on sperm counts or morphology.	Mobil, 1992b Study # 63237 Feuston, 1994 Used in PAC model [a]
Heavy coker gas oil (J)	Rat (M,F) dermal 13	0, 8, 30, 125 mg/kg/d,	LOAEL = 30 mg/kg	Mobil 1994a

CAS RN	Study: Species/ Route/Duration	Dose/ Frequency	Results	References
Sample #86181 [64741-81-7]	weeks	5days/week Elizabethan collars, weekly wipe off	Based on changes in hematology, increased BUN, decreased Calcium and histopathologic changes in thymus. Decreased epididymides wt., increased relative liver wt in females. Moderate skin irritation in all groups NOAEL = 8mg/kg	Study #64165
Heavy coker gas oil (T) Sample # 86272 [64741-81-7]	Rat (M,F) dermal 13 weeks	0, 8, 30, 125 mg/kg/d, 5days/week Elizabethan collars, weekly wipe off	LOAEL = 125mg/kg Based on decreased body wt gain (males only), changes in hematology and serum chemistry, increased liver wt., decreased thymus wt. and thymocytes, increased bone marrow granulocytes. Moderate to severe skin irritation. No adverse effects on sperm number or morphology or testes/ovary histopathology NOAEL = 30 mg/kg	Mobil 1995 Study #64184 Used in PAC model [a]
Heavy coker gas oil (P) Sample # 83366 [64741-81-7]	Rat (M,F) dermal 13 weeks	0, 30, 125, 500, 2000 mg/kg/d, 5 days/week Elizabethan collars, weekly wipe off	LOAEL = 30 mg/kg Based on decreased body wt gain, changes in hematology, organ wts. Histopathologically, adverse effects in thymus (lymphoid reduction), spleen (fibrous foci), bone marrow (Focal fibrosis). 2000, 500mg/kg groups 100% terminated No adverse effects on sperm number or morphology or testes/ovaries. NOAEL not determined, <30mg/kg	Mobil, 1994d Study #50391 Used in PAC model [a]
Coker, heavy gas oil (F-97-01) [64741-81-7]	Rats (M/F) dermal, 4 weeks	0, 0.001 (in acetone), 0.1, 1.0ml/kg/d (neat) (0.93, 93, 930 mg/kg/d) 5 days/week. Occluded for 6 hours post dose	LOAEL = 93 mg/kg Based on increased liver wt (males only), hematologic changes both sexes. No adverse effects in histopathology including testes/ovaries. Slight – moderate skin irritation NOAEL = 0.93 mg/kg	ARCO, 1990c ATX-88-0092
Coker heavy gas oil (F-136) [64741-81-7]	Rats (M/F) dermal, 4 weeks	0.01, 0.1, 1.0ml/kg/d (9.3, 93, 930 mg/kg/d) 5 days/week. occluded for 6 hours post dose	LOAEL = 930 mg/kg Based on increased liver wt., changes in hematology, increased cholesterol (females only) No adverse effects in histopathology including testes/ovaries. Very slight skin irritation NOAEL = 93mg/kg	ARCO, 1992f, ATX 90-0098
68476-33-5 Residual Fuel Oils				

CAS RN	Study: Species/ Route/Duration	Dose/ Frequency	Results	References
Residual Fuel Oil [68476-33-5] (74-01)	Rats (M/F) dermal, 4 weeks	0, 0.5, 1.0, 2.5 ml/kg/d (496, 992, 2480mg/kg/d); 5 days/week	LOAEL = 496 mg/kg Based on increased liver wt absolute, relative. No adverse liver histopathology to correlate with weight changes. Minimal reversible skin irritation at all doses. No adverse effects on testes or ovaries weight or abnormal histopathology. NOAEL: not determined, <496mg/kg	ARCO, 1987b ATX-86-0008
Resid. Fuel Oil (F92-01) [68476-33-5]	Rats (M/F) dermal, 4 weeks	0, 0.5, 1.0, 2.5 ml/kg/d (480, 960, 1920 mg/kg/d), 5 days/week	LOAEL = 480 mg/kg Based on liver and spleen wt, hematocrit, hemoglobin changes in both sexes, RBC in females. Mild skin irritation at highest dose. No adverse effects on testes or ovarian weight or abnormal histopathology. NOAEL: not determined; <480mg/kg	ARCO, 1986b ATX-86-0090
Supplemental Data from Gas Oil Closure Assessment Document				
Heavy atmospheric gas oil Sample #86271 [68915-97--9]	Rats (M/F) dermal, 13 weeks	0, 30, 125, 500 mg/kg/d, 5 days/week Elizabethan collars, weekly wipe off	LOAEL = 125 mg/kg Based on serum chemistry, hematology & organ wt changes; Histopathology effects at 500mg/kg in bone marrow, liver, thymus. No adverse effects on epididymal or testicular sperm or reproductive organs at any dose level. Slight skin irritation NOAEL = 30mg/kg	Mobil, 1992d Study #63456 Used in PAC Model[a]

a –Heavy Fuel Oil 13 weeks studies were used in developing the PAC Modeling program. NOAEL and LOAEL were provided by study investigators and also appear in robust summaries. BMD10 and PDR 10 are presented in Tables 13 and 14

6.1.3.1 Modeled results

Repeated dose toxicity is also characterized using predictive models based on PAC profiles (Appendix D) as well as read-across from similar materials. Values in Table 14 are the PDR_{10}s and where appropriate BMD_{10}s based on the method of Crump, 1984 employing data from actual studies. The PDR_{10} identifies a change of 10% from control value for a given sensitive endpoint but is not necessarily an indicator of adverse effect. The most sensitive endpoints are liver weight, thymus weight, platelet counts and hemoglobin concentration. The lowest value of all the endpoints [highlighted in yellow] for each sample constitutes the overall sample PDR_{10}. The study BMD_{10} is also the lowest of the original BMD_{10} endpoint values. The BMD_{10} calculations from 13 week dermal rat studies that meet the criteria for the modeling domain give similar values to the PDR_{10}s. Samples [highlighted in blue] which have both PDR10 and BMD10 were used to develop the repeated dose model.

Table 15 shows the doses at which effects are projected to occur based on analytical distribution of 1-7 ring PAC [see Table 12]. Given the complex composition of heavy fuels even when identified by the same CAS RN, individual streams will vary in aromatic ring distribution which may alter the values expressed as PDR_{10}s. Knowledge of the PAC profiles allows estimation of potential toxicity within or between CAS RNs for read-across when animal data are not available. PDR_{10}s and BMD_{10}s are also useful when animal studies are available but the dose ranges are widely spaced. In addition toxic potency for individual samples can be ranked based on PAC content and aromatic distribution ring profile

Table 14. Repeated-dose PDR_{10} and BMD_{10} for Heavy Fuel Oils by Endpoint

CAS RN/ Sample No.	PDR_{10} or BMD_{10} mg/kg/day								Sample PDR_{10} mg/kg/day [Endpoint]	Sample BMD_{10} mg/kg/day [Endpoint]
	Relative Liver Wt.		Thymus Weight		Platelet Count		Hemoglobin Count			
	Male	Female	Male	Female	Male	Female	Male	Female		
64741-45-3 Atmospheric Tower Residuals										
070904	170	168	179	158	328	333	945	943	158 Thymus wt, F	na
070907	414	409	278	245	435	442	2000	2000	245 Thymus wt, F	na
060905	347	344	340	300	453	461	932	930	300 Thymus wt, F	na
060917	214	212	157	138	251	256	1026	1024	138 Thymus wt, F	na
64741-57-7 Heavy Vacuum Gas Oil										
085244	121	119	98	86	358	364	926	925	86 Thymus wt, F	na
085244 BMD	>125, < 500	>125, <500	-	-	>500, <2000	>125, <500	>500, <2000	>500, <2000	na	>125, <500 Liver M,F; platelet, F
085289	135	134	2000	2000	-	-	270	270	134, Rel liver wt, F	na
086010	104	102	89	79	249	254	872	870	79 Thymus wt, F	na
086269	58	57	36	32	107	109	-	-	32 Thymus wt, F	na
086281	75	75	55	49	146	148	530	529	49 Thymus wt, F	na
086289	39	39	14	13	11	11	47	47	11 Platelets, M,F	na
091649	-	-	-	-	-	-	-	-	-	na
091650	125	124	114	100	594	604	670	669	100	na

CAS RN/ Sample No.	PDR_{10} or BMD_{10} mg/kg/day								Sample PDR_{10} mg/kg/day [Endpoint]	Sample BMD_{10} mg/kg/day [Endpoint]
	Relative Liver Wt.		Thymus Weight		Platelet Count		Hemoglobin Count			
	Male	Female	Male	Female	Male	Female	Male	Female		
									Thymus wt, F	
091654	113	111	113	100	149	151	216	216	100 Thymus wt, F	na
091689	147	145	243	214	-	-	1467	1464	145 Rel. Liver F	na
094627	-	-	-	-	-	-	-	-	-	na
060906	170	168	130	115	235	239	1143	1141	115 Thymus wt, F	na
060916	200	198	145	129	277	282	1684	1680	129 Thymus wt, F	na
060922	148	147	106	93	249	254	1319	1316	93 Thymus wt, F	na
41:4	2000	104	82	72	261	265	806	804	72 Thymus wt, F	na
8:3	-	-	-	-	-	-	2000	2000	2000 Hemoglobin	na
28:10	118	116	68	60	98	100	799	798	60 Thymus wt, F	na
16.1	125	124	97	85	289	294	1406	1403	85 Thymus wt, F	na
25:15	149	147	107	94	250	254	1319	1317	94 Thymus wt, F	na
1.8	171	169	130	115	236	240	1144	1142	115 Thymus wt, F	na
64741-61-3 Heavy Catalytic Cracked Distillates										
070909	46	45	40	36	255	259	-	-	36 Thymus wt, F	na
030928	10	10	3	3	7	7	-	-	3 Thymus wt	na
060912	20	20	8	13	21	22	-	-	8 Thymus wt, M	na
060930	59	58	-	-	-	-	18	18	18 Hemoglobin	na
16:5	25	25	32	28	-	-	-	-	28 Thymus wt, F	na
64741-62-4 Catalytic Cracked Clarified Oils										
086484	13	13	11	9	9	9	18	18	9 Thymus wt, F, platelets	na
086484BMD	>0, <8	>0, <8	>0, <8	>0, <8	>8, <30	>0, <8	>8, <30	>8, <30	na	>0, <8 Liver, thymus, platelets F
086001	19	19	21	19	-	-	47	46	19 Liver, Thymus F	na
086001BMD	0>,<8	10	7	15	-	-	>0, <8	>8, <30	na	7 Thymus, M
091645	202	200	290	249	162	165	253	252	162 Platelets, M	na
091645 BMD	>11, <106	>11, <106	>0, <11	38	29	32	67	99	na	>0, <11 Thymus, M
087277	39	38	19	17	65	66	-	-	17 Thymus wt, F	na
087278	32	32	14	13	36	37	-	-	13 Thymus wt, F	na
087279	38	38	19	16	43	44	-	-	16 Thymus wt, F	na
010923	29	29	8	7	22	23	-	-	7 Thymus wt, F	na
010924	40	40	-	-	29	30	25	25	25	na

CAS RN/ Sample No.	PDR_{10} or BMD_{10} mg/kg/day								Sample PDR_{10} mg/kg/day [Endpoint]	Sample BMD_{10} mg/kg/day [Endpoint]
	Relative Liver Wt.		Thymus Weight		Platelet Count		Hemoglobin Count			
	Male	Female	Male	Female	Male	Female	Male	Female		
									Hemoglobin	
64741-67-9 Catalytic Reformer Fractionator Residuals										
060949	-	-	54	48	6	6	2000	2000	6 PLatelets	na
64741-75-9 Hydrocracked Residuals										
060946	2000	2000	2000	2000	2000	2000	2000	2000	2000 Non-toxic	na
64741-80-6 Thermal Cracked Residuals										
060915	169	168	83	73	103	105	761	760	73 Thymus wt, F	na
64741-81-7 Heavy Thermal Cracked Distillates										
071021	13	13	5	4	-	-	-	-	4 Thymus wt, F	na
086181	34	34	26	23	37	38	82	82	23 Thymus wt, F	
086181 BMD	18	33	>8, <30	23	91	43	78	83	na	>8, <30 thymus wt. M
083366	71	71	42	37	77	78	2000	2000	37 Thymus wt, F	na
083366 BMD	49	39	26	>0 <30	>30 <125	100	-	-	na	>0 <30 thymus wt. F
086193	-	-	512	452	93	95	2000	2000	93 Platelets, M	na
086193 BMD	-	-	>125	-		>125	>125	>125	na	>125
086272	97	96	123	109	159	162	745	744	96 Rel. Liver wt F	na
086272 BMD	52	57	35	35	38	72	122	>125	na	35 thymus wt.M,F
086161	49	49	32	28	99	101	-	-	28 Thymus wt, F	na
086194	41	41	16	14	47	48	-	-	14 Thymus wt, F	na
086230	-	-	-	-	-	-	-	-	-	na
091653	36	36	96	84	-	-	164	163	36 Rel. Liver M,F	na
30-2	45	45	27	24	46	46	2000	2000	24 Thymus wt, F	na
8:1	51	51	39	34	137	139	2000	2000	34 Thymus wt, F	na
9:3	68	67	32	28	56	56	-	-	28 Thymus wt, F	na
2:6	102	102	95	84	298	303	857	855	84 Thymus wt, F	na
64742-59-2 Hydrotreated Vacuum Gas Oils										
071017	286	283	216	190	381	387	2000	2000	170 Thymus, F	na
071026	132	131	82	73	154	156	2000	2000	73 Thymus, F	na
64742-78-5 Hydrodesulfurized Atmospheric Residuals										
071030	91	90	66	59	112	114	-	-	59 Thymus wt, F	na
64742-86-5 Hydrodesulfurized Heavy Vacuum Gas Oils										
091690	125	124	96	85	185	188	567	566	85 Thymus, F	na
21:1	293	290	250	220	520	529	2000	2000	220 Thymus wt, F	

CAS RN/ Sample No.	PDR_{10} or BMD_{10} mg/kg/day								Sample PDR_{10} mg/kg/day [Endpoint]	Sample BMD_{10} mg/kg/day [Endpoint]
	Relative Liver Wt.		Thymus Weight		Platelet Count		Hemoglobin Count			
	Male	Female	Male	Female	Male	Female	Male	Female		
68333-22-2 Atmospheric Residuals										
071016	132	131	98	86	213	217	844	842	86 Thymus, F	na
68410-00-4 Crude Oil Distillates										
030932	455	450	272	240	237	241	2000	2000	237 Platelets, M	na
030933	2000	2000	1015	895	65	66	2000	2000	65 Platelets, M	na
030934	216	214	104	92	106	108	2000	2000	92 Thymus, F	na
091647	333	330	2000	2000	242	246	2000	2000	242 Platelets, M	na
091681	332	329	2000	2000	246	250	2000	2000	246 Platelets, M	na
11:1	202	200	158	139	165	167	1128	1125	139 Thymus wt, F	na
68476-33-5 Residual Fuel Oils										
086104	62	61	46	41	--	-	2000	2000	41 Thymus, F	na
086119	120	119	51	45	-	-	-	-	45 Thymus, F	na
070903	269	265	149	132	92	94	715	714	92 Platelets. M	na
086108	-	-	-	-	-	-	-	-	-	na
68478-17-1 Heavy Coker Gas Oil and Vacuum Gas Oil Residuals										
071012	48	47	31	27	70	71	2000	2000	27 Thymus, F	na
071031	52	51	81	71	85	86	115	114	51 Rel. Liver, F	na
12:19	48	48	31	28	70	71	2000	2000	28 Thymus wt, F	na
68512-62-9 Light Vacuum Residuals										
092009	282	279	1625	1433	2000	2000	635	634	279 Rel Liver, F	na
081022	2000	2000	2000	2000	154	156	2000	2000	154 Platelets, M	na
68553-00-4 Fuel Oil, No 6										
070908	33	33	13	12	-	-	-	-	12 Thymus, F	na
030937	15	14	4	3	11	11	-	-	3 Thymus wt, F	na
68783-08-4 Heavy Atmospheric Gas Oils										
071020	240	237	208	183	1062	1080	1658	1655	183 Thymus, F	na
071025	2000	2000	2000	2000	105	107	2000	2000	105 Platelets, M	na
081009	172	170	109	96	173	175	1105	1103	96 Thymus, F	na
081010	171	169	108	96	172	175	1105	1102	96 Thymus, F	na
081011	153	151	118	104	307	313	943	941	104 Thymus, F	na
081012	149	147	114	100	275	280	854	853	100 Thymus, F	na
081013	819	812	758	669	421	428	2000	2000	421 Platelets, M	na

CAS RN/ Sample No.	PDR_{10} or BMD_{10} mg/kg/day								Sample PDR_{10} mg/kg/day [Endpoint]	Sample BMD_{10} mg/kg/day [Endpoint]
	Relative Liver Wt.		Thymus Weight		Platelet Count		Hemoglobin Count			
	Male	Female	Male	Female	Male	Female	Male	Female		
68955-27-1 Distillates, petroleum residues vacuum										
32:2	82	81	125	110	1605	1633	483	482	81 Rel Lliver, F	na
36:1	624	618	363	320	1400	1424	2000	2000	320 Thymus wt, F	na
70592-76-6 Intermediate Vacuum Distillates										
071011	139	138	102	91	246	251	1150	1148	91 Thymus, F	na
071018	356	352	2000	2000	2000	2000	2000	2000	352 Rel Liver, F	na
071029	172	171	138	121	272	276	2000	2000	121 Thymus, F	na
071032	118	116	72	64	168	171	2000	2000	64 Thymus, F	na
70592-77-7 Light Vacuum Distillates										
071015	109	108	788	695	-	-	650	648	108 Rel Liver, F	na
071022	160	159	151	133	227	230	434	433	133 Thymus, F	na
071023	106	105	81	71	156	159	592	591	71 Thymus, F	na
071027	115	114	103	91	334	340	1832	1828	91 Thymus, F	na
70592-78-8 Vacuum Distillates										
071014 [	74	73	45	40	62	63	462	461	40 Thymus, F	na
071019	202	200	257	226	799	812	915	913	200 Rel Liver, F	na
071024	98	96	80	70	208	212	1006	1004	70 Thymus, F	na
43:2	170	168	245	216	814	828	694	693	168 Rel Liver, F	na
1:1	589	583	-	-	-	-	552	551	551 Hemoglobin, F	na
10:6	903	894	740	653	2000	2000	2000	2000	653 Thymus wt, F	na
70913-85-8 Solvent extracted, Vacuum Distilled Atmospheric Residuals										
070905	2000	2000	-	-	-	-	803	802	802 Hemoglobin, F	na
060904	751	743	2000	2000	2000	2000	1513	1510	743 Rel Liver, F	na

Dash indicates data for this endpoint is outside model domain. No reliable predictions can be made for this endpoint.
Highlighted entries indicate definitive value selected for sample PDR10 or BMD10 as the lowest value causing 10% change in activity for the most sensitive endpoint.
"BMD" after the sample number indicates a BMD10 calculation based on repeat dose toxicity study values.
na = not applicable; no BMD10 was calculated because no repeat dose toxicology study was conducted on this sample.

Table 15 illustrates how modeled data can be used to rank and compare severity of biological activity for streams with a PAC aromatic ring distribution profile whether or not animal data are available.

Table 15. Modeled Repeat dose PDR10 Values for Heavy Fuel Oils from Most to Least severe within each CAS RN

CAS RN/Sample No.	Repeat Dose PDR10 mg/kg	Total 1-7 ring wt %[1]	ARC 1[2] (%)	ARC 2 (%)	ARC 3 (%)	ARC 4 (%)	ARC 5 (%)	ARC 6 (%)	≥ARC 7 (%)
64741-45-3 Atmospheric Tower Residuals									
060917	138 Thymus wt, F	3.4	0.0	0.0	0.6	1.2	0.9	0.6	0.1
070904	158 Thymus wt, F	5.4	0.0	0.5	1.1	1.1	1.1	1.1	0.5
070907	245 Thymus wt, F	2.1	0.0	0.2	0.6	0.6	0.4	0.2	0.1
060905	300 Thymus wt, F	2.4	0.0	0.0	0.5	0.8	0.5	0.5	0.1
64741-57-7 Heavy Vacuum Gas Oil									
086289	11 Platelets, M,F	15.8	0.0	0.7	1.0	11.6	1.7	0.8	0.0
086269	32 Thymus wt, F	12.8	0.0	0.6	5.0	3.8	2.5	0.9	0.0
086281	49 Thymus wt, F	11.6	0.0	0.6	6.0	3.6	1.2	0.2	0.0
28:10	60 Thymus wt, F	6.6	0.0	0.3	1.9	2.5	1.3	0.6	0.0
41:4	72 Thymus wt, F	8.5	0.0	0.6	4.5	2.4	0.8	0.2	0.0
086010	79 Thymus wt, F	6.5	0.0	0.1	1.3	1.9	1.9	1.3	0.0
16.1	85 Thymus wt, F	5.7	0.0	0.1	1.7	1.7	1.4	0.7	0.1
085244	86 Thymus wt, F	6.2	0.0	0.1	2.5	1.9	1.2	0.5	0.0
060922	93 Thymus wt, F	5.0	0.0	0.1	1.6	1.6	1.1	0.5	0.1
25:15	94 Thymus wt, F	5.0	0.0	0.1	1.6	1.6	1.1	0.5	0.1
091650	100 Thymus wt, F	7.2	0.0	0.4	4.0	2.0	0.6	0.2	0.0
091654	100 Thymus wt, F	8.8	0.1	0.4	4.0	3.0	0.9	0.4	0.0
060906	115 Thymus wt, F	4.2	0.0	0.0	0.4	1.3	1.3	0.9	0.3
1.8	115 Thymus wt, F	4.2	0.0	0.0	0.4	1.3	1.3	0.9	0.3
060916	128 Thymus wt, F	3.6	0.0	0.0	0.4	1.1	1.1	0.7	0.3
085289	134, Rel liver wt, F	7.0	0.0	0.0	1.4	1.4	1.4	2.1	0.7
091689	145 Rel. Liver wt F	5.9	0.0	0.4	4.0	1.0	0.4	0.1	0.0
8:3	2000 Hemoglobin	6.5	0.1	1.6	1.6	2.4	1.6	0.8	0.1
64741-61-3 Heavy Catalytic Cracked Distillates									
030928	3 Thymus wt	36.3	0.0	3.9	15.4	11.6	3.9	1.5	0.0
060912	8 Thymus wt, M	36.8	0.0	3.5	21.0	10.5	1.8	0.0	0.0
060930	18 Hemoglobin	44.2	0.0	0.5	28.2	14.1	1.4	0.0	0.0
16:5	28 Thymus wt, F	40.6	0.0	6.2	28.7	5.3	0.4	0.0	0.0
070909	36 Thymus wt, F	28.6	0.0	0.8	11.2	8.4	5.6	2.0	0.6
64741-62-4 Catalytic Cracked Clarified Oils									

CAS RN/Sample No.	Repeat Dose PDR10 mg/kg	Total 1-7 ring wt %[1]	ARC 1[2] (%)	ARC 2 (%)	ARC 3 (%)	ARC 4 (%)	ARC 5 (%)	ARC 6 (%)	≥ARC 7 (%)
010923	7 Thymus wt, F	41.9	0.0	1.3	13.0	13.0	8.6	4.3	1.7
086484	9 Thymus wt, F, platelets	46.0	0.0	1.0	9.8	19.5	9.8	4.9	1.0
087278	13 Thymus wt, F	29.1	0.0	0.9	9.1	9.1	6.1	3.0	0.9
087279	16 Thymus wt, F	19.6	0.0	0.8	6.1	6.1	4.0	2.0	0.6
087277	17 Thymus wt, F	20.2	0.0	0.4	3.8	5.7	5.7	3.8	0.8
086001	19 Liver, Thymus F	57.8	0	2.6	25.7	19.3	6.4	3.2	0.6
010924	25 Hemoglobin Count	36.0	0.0	0.3	6.2	12.4	6.2	3.1	1.6
091645	162 Platelets, M	66.7	0.0	0.7	10.0	30.0	20.0	6.0	0.0
64741-67-9 Catalytic Reformed Fractionator Residuals									
060949	6 Platelets	50.9	3.9	44.1	2.9	0.0	0.0	0.0	0.0
64741-75-9 Hydrocracked Residuals									
060946	2000 Non-toxic	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
64741-80-6 Thermal cracked Residuals									
060915	73 Thymus wt, F	4.6	0.0	0.0	1.3	2.2	0.9	0.2	0.0
64741-81-7 Heavy Thermal Cracked Distillates									
071021	4 Thymus, F	61.1	0.0	6.3	44.1	6.3	4.4	0.0	0.0
086194	14 Thymus wt, F	15.4	0.0	0.5	3.2	4.8	4.8	1.6	0.5
086181	23 Thymus wt, F	25.5	0.2	2.5	12.4	7.4	2.5	0.5	0.0
30-2	24 Thymus wt, F	19.0	0.0	0.6	3.7	5.5	3.7	3.7	1.8
9:3	28 Thymus wt, F	10.0	0.0	0.7	2.3	3.4	2.3	1.1	0.2
086161	28 Thymus wt, F	16.0	0.0	0.7	6.0	4.5	3.0	1.5	0.3
8:1	34 Thymus wt, F	17.0	0.0	0.5	6.6	5.0	3.3	1.3	0.3
091653	36 Rel liver wt, M,F	25.9	0.0	0.9	20.0	5.0	0.0	0.0	0.0
083366	37 Thymus wt, F	12.5	0.1	2.5	5.1	2.5	1.3	0.9	0.1
2:6	84 Thymus wt, F	9.2	0.0	1.0	4.0	2.0	1.0	0.9	0.3
086193	93 Platelets, M	4.1	0.8	2.9	0.4	0.0	0.0	0.0	0.0
086272	96 Rel. liver wt, F	15.4	0.3	4.9	8.1	1.6	0.3	0.2	0.0
64742-59-2 Hydrotreated Vacuum Gas Oils									
071026	73 Thymus wt, F	5.8	0.0	0.5	1.7	1.7	1.2	0.6	0.1
071017	170 Thymus wt, F	3.0	0.0	0.6	0.9	0.6	0.6	0.3	0.0
64742-78-5 Hydrodesulfurized Atmospheric Residuals									
071030	59 Thymus wt, F	12.8	0.0	3.9	5.2	1.2	1.0	1.0	0.5
64742-86-5 Hydrodesulfurized Heavy Vacuum Gas Oils									
091690	85 Thymus wt, F	7.1	0.1	0.7	3.0	2.0	1.0	0.3	0.0
21:1	220 Thymus wt, F	3.1	0.0	0.4	1.1	0.7	0.5	0.3	0.1

CAS RN/Sample No.	Repeat Dose PDR10 mg/kg	Total 1-7 ring wt %[1]	ARC 1[2] (%)	ARC 2 (%)	ARC 3 (%)	ARC 4 (%)	ARC 5 (%)	ARC 6 (%)	≥ARC 7 (%)
68333-22-2 Atmospheric Residuals									
071016	86 Thymus wt, F	5.8	0.0	0.1	1.9	1.9	1.2	0.6	0.1
68410-00-4 Crude Oil Distillates									
030933	65 Platelets, M	5.6	0.1	4.4	1.1	0.0	0.0	0.0	0.0
030934	92 Thymus wt, F	5.3	0.0	1.7	1.7	1.1	0.6	0.2	0.0
11:1	139 Thymus wt, F	5.7	0.0	1.2	1.9	1.2	0.6	0.6	0.2
030932	237 Platelets, M	3.1	0.0	1.0	1.3	0.6	0.2	0.0	0.0
091647	242 Platelets, M	8.1	0.1	4.0	4.0	0.0	0.0	0.0	0.0
091681	246 Platelets, M	8.2	0.2	4.0	4.0	0.0	0.0	0.0	0.0
68476-33-5 Residual Fuel Oils									
086104	41 Thymus wt, F	13.7	0.0	1.5	7.3	2.9	1.3	0.6	0.1
086119	45 Thymus wt, F	8.7	0.0	2.6	2.6	1.8	0.9	0.6	0.2
070903	92 Platelets. M	6.2	0.2	1.8	1.2	1.2	1.2	0.5	0.1
68478-17-1 Heavy Coker Gas Oil and Vacuum Gas Oils Residuals									
071012	27 Thymus wt, F	17.1	0.0	0.5	5.4	5.4	3.6	1.8	0.4
12:19	28 Thymus wt, F	17.1	0.0	0.5	5.4	5.4	3.6	1.8	0.4
071031	51 Rel. Liver, F	19.0	0.0	0.2	4.0	6.0	4.0	4.0	0.8
68512-62-9 Light Vacuum Residuals									
081022	154 Platelets, M	3.2	0.1	2.2	0.9	0.0	0.0	0.0	0.0
092009	279 Rel Liver wt, F	3.8	0.0	0.0	0.7	0.7	0.7	1.0	0.7
68553-00-4 Fuel Oil No. 6									
030937	3 Thymus wt, F	35.9	0.0	2.3	13.0	9.8	6.5	3.3	1.0
070908	12 Thymus wt, F	20.4	0.0	2.1	8.4	6.3	2.1	1.3	0.2
68783-08-4 Heavy Atmospheric Gas Oils									
081009	96 Thymus wt, F	5.3	0.0	0.5	2.3	1.7	0.6	0.2	0.0
081010	96 Thymus wt, F	5.3	0.0	0.5	2.3	1.7	0.6	0.2	0.0
081012	100 Thymus wt, F	6.0	0.0	0.4	3.0	1.8	0.6	0.2	0.0
081011	104 Thymus wt, F	5.8	0.0	0.4	2.9	1.7	0.6	0.2	0.0
071025	105 Platelets, M	5.3	0.1	3.5	1.7	0.0	0.0	0.0	0.0
071020	183 Thymus wt, F	3.0	0.0	0.0	1.2	0.9	0.6	0.3	0.0
081013	421 Platelets, M	2.4	0.0	1.0	1.0	0.2	0.1	0.1	0.0
68955-27-1 Distillates, petroleum residues vacuum									
32:2	81 Rel Lliver, F	9.4	0.0	0.0	0.5	1.9	3.0	3.1	0.9
36:1	320 Thymus wt, F	0.7	0.0	0.0	0.0	0.2	0.4	0.1	0.0
70592-76-6 Intermediate Vacuum Distillates									
071032	64 Thymus wt, F	6.4	0.0	0.6	2.4	1.8	1.2	0.4	0.0

CAS RN/Sample No.	Repeat Dose PDR10 mg/kg	Total 1-7 ring wt %[1]	ARC 1[2] (%)	ARC 2 (%)	ARC 3 (%)	ARC 4 (%)	ARC 5 (%)	ARC 6 (%)	≥ARC 7 (%)
071011	91 Thymus wt, F	5.5	0.0	0.1	1.7	1.7	1.2	0.6	0.2
071029	121 Thymus wt, F	6.0	0.0	1.2	2.9	1.2	0.5	0.2	0.0
071018	352 Rel Liver, F	5.1	0.0	2.0	3.0	0.1	0.0	0.0	0.0
70592-77-7 Light Vacuum Distillates									
071023	71 Thymus wt, F	8.7	0.0	0.8	4.1	2.5	0.8	0.5	0.0
071027	91 Thymus, F	9.1	0.0	1.7	5.0	1.7	0.5	0.2	0.0
071015	108 Rel Liver wt, F	11.0	0.0	2.2	7.7	1.1	0.0	0.0	0.0
071022	133 Thymus wt, F	5.9	0.0	0.3	2.5	1.9	0.6	0.6	0.0
70592-78-8 Vacuum Distillates									
071014	40 Thymus wt, F	9.6	0.0	0.1	0.9	3.7	2.8	1.9	0.2
071024	70 Thymus wt, F	7.9	0.0	0.0	1.4	2.2	2.2	1.4	0.7
43:2	168 Rel Liver, F	4.7	0.0	0.0	0.3	1.0	1.4	1.4	0.6
071019	200 Rel Liver, F	5.1	0.0	0.1	1.0	1.0	1.0	1.0	1.0
1:1	551 Hemoglobin, F	3.5	0.0	0.0	0.0	0.1	0.6	1.4	1.4
10:6	653 Thymus wt, F	0.7	0.0	0.0	0.2	0.2	0.2	0.1	0.0
70913-85-8 Solvent Extracted, Vacuum Distilled Atmospheric Residuals									
060904	743 Rel Liver wt, F	1.8	0.0	0.0	0.0	0.2	0.4	0.6	0.6
070905	802 Hemoglobin, F	1.8	0.0	0.0	0.0	0.0	0.2	0.8	0.8

1 - Percent of DMSO-extractable PACs as determined by PAC-2 Method.
2 - ARC is "aromatic ring class". ARC 1 (%) is the weight percent of PACs that have 1 aromatic ring.

In general, samples with the highest 1-7 ring PAC content have the lowest PDR_{10} values. Substances predicted to have the lowest PDR_{10} values were catalytically cracked clarified oils(CAS RN 64741-62-4, heavy thermal cracked distillates (CAS RN 68478-17-1) and vacuum gas oils (CAS RN 64741-57-7) which tend to have higher content of 3-7 ring PACs in the aromatic profiles. Catalytic reformed fractionator residual (CAS RN 64741-67-9) had a PDR_{10} of 5 mg/kg with a high 1-2 ring PAC content of 48% and only 2.9% 3-7 ring PAC. Residual petroleum hydrocracked contain no measurable 1-7 ring PAC and was predicted to be virtually non-toxic (PDR_{10} = 2000mg/kg)

Table 16 presents the relationship between NOAELs/LOAELS from animal studies, PDR_{10} and BMD_{10} determinations and PAC content

Ranking by PDR_{10} indicates that in general, cracked substances had the greatest toxic potential compare to other substances in the category. Dose levels identified by modeled data which identify a 10% change from controls correlate reasonably well with LOAEL and NOAEL values established by animal testing.

Table 16. Comparison of Repeated Dose LOAEL/NOAEL with range of Modeled values and PAC Content

CAS No/ Name.	LOAEL mg/kg	NOAEL mg/kg	PDR_{10} mg/kg	BMD_{10} mg/kg	DMSO wt%[1]	Wt % 3-7 ring PAC[2]	Comments
13 week studies							
64741-62-4 Cat Cracked Clarified Oils [3 studies]	8-11	1.06 - <8	7-19	>0, <11	19 - 67	19 - 66	#091645 had PDR10 = 162mg/kg and 66% PAC
64741-62-4 CCCO (010929) New study	5 Lowest dose	<5	-	Not calculated	52	49	#019029 Extrapolated no PDR10 determined
64741-81-7 Heavy Thermal cracked Distillates [4 studies]	30-125	8 - 125	14-96	Range >8, <30 >125 (1 study)	4 - 25	0.4 - 25	#086193 had lowest values of 4.2% Total DMSO and 0.4% 3-7 ring
64741-57-7 Heavy Vacuum Gas Oil #085244	500	125	11-2000	>125, <500	4 - 18	4 - 16	
64741-80-6 Thermal cracked Residual (1 sample).	250	60	73	Not calculated	4	4	
4 week studies							
64741-75-9 Hydrocracked Residual	>210	210 highest dose	2000 non toxic	Not calculated for 4 week studies	0.2	0.0	
64741-45-3 Atmospheric Tower Residual	>928	928 highest dose	138-300		2 - 7	2 - 5	
64741-61-3 Heavy Cat Cracked Distillate	990 M 99 F	99.0 M 9.9 F	3 – 36		28 - 47	28 - 44	
68476-33-5 Residual Fuel Oil [2 studies]	480-496 lowest doses	<480	41-92		9 - 15	4 - 12	

1 - Wt % Total DMSO extract of tested and modeled samples
2 - Wt % 3-7 ring PAC of tested and modeled samples

For EU global hazard communication purposes under the 2008 Classification, Labelling and Packaging (CLP) regulation (EC 1272/2008, 2008), implemented in accordance with CONCAWE (2012), all CAS RNs in the Heavy Fuel Oil Components category carry the same hazard classifications. These classifications do not indicate toxic potency. However some CAS RN streams or some samples within a group identified by a given CAS RN may be less toxic than others. Toxic potency for individual samples can be ranked based on the aromatic ring profile. However potency ranking may have no practical significance as the blending and co-mingling of residual fuels after leaving the refinery obscure any provenance.

6.1.4. Genetic Toxicity *In Vitro*

Table 17. *In vitro* Genetic Toxicity

CAS RN	Assay	Results
64741-57-7	Optimized Ames[a] [6 samples]	Positive with activation
	Cytogenetic assay with Chinese Hamster Ovary cells [Heavy vacuum gas oil] Mobil 1987e	Negative with/without activation
64741-62-4	Ames Bacterial Assay [CSO] API 1986b	Positive with/without activation
	Optimized Ames[a] [8 samples]	Positive with activation
	Mouse lymphoma [CSO] API 1985e	Positive with/without activation
	Sister chromatid exchange [CSO] API, 1985f	Positive with activation
	Cell transformation [CSO] API, 1986a	Negative without activation Positive with activation
	Unscheduled DNA synthesis [CSO] API 1985b	Positive
	Mammalian cell (Chinese hamster ovary) forward mutation [CSO] API 1985a	Negative with/without activation
64741-81-7 [7 samples]	Optimized Ames[a]	Positive with activation-
68476-33-5 [3 samples]	Optimized Ames[a]	Positive with activation-
68553-00-4 [2 samples]	Optimized Ames[a]	Positive with activation-

CSO = Clarified slurry oil
a- Optimized Ames test (previously Modified Ames test) was developed to increase the sensitivity of the Ames assay for PAC-rich petroleum streams. (Study references available in Robust Summary)

In vitro genetic toxicity studies (Table 17) demonstrate that representative streams in the heavy fuels category induce gene mutation in bacterial and some mammalian cells. In addition to the standard Ames Test (Ames et al, 1975), the Optimized Ames test (previously the Modified Ames test) was developed to enhance exposure of PAC-rich petroleum derived materials to PAC-sensitive *Salmonella* strain TA98. Modifications involved a single step extraction into DMSO, use of hamster liver homogenate and increased cofactor to maximize metabolic activation. Positive results require a dose responsive increase in mutant colonies compared to negative controls and calculation of a Mutagenicity Index (MI) derived from the dose response curves [see Appendix E] Table 18 summarizes the results of Optimized Ames tests on 32 heavy fuel samples. Samples selected for testing were those that, based on knowledge of product chemistry and experience with dermal carcinogenesis were considered likely to give a range of gene mutation activity based on PAC content and ring distribution profiles. These data along with data from 210 samples of other high PAC petroleum streams with final boiling point > 650 ºF [>343^{0}C] were used to develop a modeling procedure that employs the PAC analytical profile to predict statistically whether a sample is likely to induce gene mutation in *Salmonella* strain TA98 with metabolic activation. Using this model, the chemical characterization of untested streams compared to the known MI allows prediction of whether a sample will have a mutagenicity index equal to or greater than 1.0 (GE 1) or be non-mutagenic (LT 1) (Nicolich et al, 2010 abst., Appendix E, McKee et al., 2012).

Table 18. Heavy Fuel Oils: Optimized Ames Test Results and Modeled Mutagenicity Indices

CAS RN	CRU Number	1-Ring Weight %	2-Ring Weight %	3-Ring Weight %	4-Ring Weight %	5-Ring Weight %	6-Ring Weight %	7-Ring Weight %	Measured Optimized Ames MI	Modeled MI
64741-57-7 Heavy Vacuum Gas Oils										

64741-57-7	86281	0.0	0.6	3.6	2.7	1.8	0.7	0.1	11.2	GE 1
64741-57-7	86010	0.0	0.1	1.3	1.9	1.9	1.3	0.0	7.8	GE 1
64741-57-7	86179	0.0	0.5	1.0	3.1	2.1	1.0	2.1	7.0	GE 1
64741-57-7	85244	0.0	0.1	2.5	1.9	1.2	0.5	0.0	5.6	GE 1
64741-57-7	86176	0.0	0.6	0.9	2.6	1.7	0.9	1.7	5.3	GE 1
64741-57-7	86189	0.0	0.1	0.2	0.6	1.2	2.5	1.2	3.2	GE 1
64741-62-4 Catalytic Cracked Clarified Oils										
64741-62-4	86196	0.0	1.5	22.5	30.0	15.0	7.5	1.5	860.9	GE 1
64741-62-4	86185	0.0	1.9	25.5	19.1	12.7	5.1	0.6	774.8	GE 1
64741-62-4	86001	0.0	2.6	25.7	19.3	6.4	3.2	0.6	739.0	GE 1
64741-62-4	86002	0.0	1.9	12.3	24.7	12.3	6.2	1.2	726.2	GE 1
64741-62-4	86180	0.0	1.3	12.7	25.4	12.7	6.4	1.3	688.1	GE 1
64741-62-4	86066	0.0	0.5	10.5	21.0	10.5	5.3	1.6	555.4	GE 1
64741-62-4	86015	0.0	0.3	6.2	12.5	9.4	6.2	1.2	466.4	GE 1
64741-62-4	86484	0.0	1.0	9.8	19.5	9.8	4.9	1.0	437.8	GE 1
64741-62-4	87279	0.0	0.8	6.1	6.1	4.0	2.0	0.6	168.7	GE 1
64741-62-4	87278	0.0	0.9	9.1	9.1	6.1	3.0	0.9	167.7	GE 1
64741-62-4	87277	0.0	0.4	3.8	5.7	5.7	3.8	0.8	141.8	GE 1
64741-62-4	86123	0.1	4.0	4.0	2.7	2.7	1.2	0.3	33.7	GE 1
64741-81-7 Heavy Thermal Cracked Distillates										
64741-81-7	86181	0.2	2.5	12.4	7.4	2.5	0.5	0.0	142.7	GE 1
64741-81-7	86161	0.0	0.7	6.0	4.5	3.0	1.5	0.3	122.6	GE 1
64741-81-7	86272	0.3	4.9	8.1	1.6	0.3	0.2	0.0	111.7	GE 1
64741-81-7	83366	0.1	2.5	5.1	2.5	1.3	0.9	0.1	89.1	GE 1
64741-81-7	86194	0.0	0.5	3.2	4.8	4.8	1.6	0.5	76.2	GE 1
64741-81-7	87213	0.1	4.2	6.3	0.3	0.0	0.0	0.0	13.3	GE 1
64741-81-7	86230	0.3	2.0	2.7	1.4	0.4	0.1	0.0	3.5	GE 1
68476-33-5 Residual Fuel Oils										
68476-33-5	086104	0.0	1.5	7.3	2.9	1.3	0.6	0.1	84.8	GE 1
68476-33-5	086108	0.3	2.7	2.7	0.9	0.9	0.7	0.3	21.9	GE 1
68476-33-5	086119	0.0	2.6	2.6	1.8	0.9	0.6	0.2	8.0	GE 1
68553-00-4 Fuel Oil, No. 6										
68553-00-4	091674	0.1	2.6	5.2	1.3	1.3	1.3	0.9	23.1	GE 1
68553-00-4	091675	0.3	6.1	4.6	1.5	0.8	1.5	0.9	17.5	GE 1

Positive results in these *in vitro* assays tend to correlate with profile of biologically active PACs. Results of Optimized Ames tests performed with representative streams (Table 18) demonstrate that streams derived from catalytically cracked stock have higher MI and generally higher profile of

biologically active PAC than the fuel oil product or streams derived from vacuum distillation, and are thus more likely to induce mutagenicity.

Table 19: Representative Optimized Ames Mutagenic Indices

Category groups	CAS RN [Number of samples]	MI range
Fuel Oil No. 6	68553-00-4 [2]	17.5-23.1
Residual Fuel Oils	68476-33-5 [3]	8.0 - 84.8
Cat. Cracked Clarified Oils	64741-63-4 [12]	33.7 – 860.9
Heavy Thermal Cracked Distillates	64741-81-7 [7]	3.5 –142.7
Heavy Vacuum Gas Oils	64741-57-7 [6]	3.2 – 11.2

Conclusions: In vitro genotoxicity

In vitro studies demonstrate that streams in the heavy fuel oil category are generally mutagenic. However the level of activity is related to PAC content over a continuum from low activity in distillate streams containing less biologically active PAC to high activity in streams derived from cracked stocks with higher aromaticity. Variations in mutagenic response within a CAS RN results from differences in starting crude oil and processing steps which can alter the PAC ARC profile and content.

6.1.5 Genetic Toxicity *In Vivo*

Table 20. In vivo Genetic Toxicity

CAS RN	Assay	Species	Results
64741-57-7	Micronucleus [Heavy vacuum gas oil] [CAS RN 64741-57-7]	Rat (M,F)	Negative at up to 2000 mg/kg/day; 5x/week for 13 weeks via dermal route Mobil 1987f, study 61591
64741-62-4	Cytogenetic (chromosome Aberrations) Assay [clarified slurry oil] [CAS RN 64741-62-4]	Rat (M,F)	Negative at up to 1 g/kg/day by gavage for 5 days API 1985e pub 32-30534
	Micronucleus [CSO identified as Catalytic cracked clarified oil] [CAS RN 64741-62-4]	Mice (M, F)	Negative Oral gavage 0.04 to 3.0 g/ kg Intraperitoneal 0.188 to 3.0g/ kg 1 dose on each of 2 consecutive days, similar non-clastogenic results by both routes. Przygoda et al 1999
	Micronucleus [CSO identified as Syntower bottoms] [CAS RN 64741-62-4]	Rat (M,F)	Positive at lowest dose (8mg/kg); compared to controls. At higher doses with no cell toxicity up to 500mg/kg/day, 5 days/week for 13 weeks via dermal route. Mobil 1989b, study 62711

CAS RN	Assay	Species	Results
	Sister Chromatid Exchange [CSO] [CAS RN 64741-62-4]	Mice (M,F)	Single IP dose - positive at 4.0 (♀, ♂) & 2.0 (♂) g/kg; negative at 0.4 g/kg API 1985d, pub 32-32254
	Unscheduled DNA Synthesis [CSO] [CAS RN 64741-62-4]	Rat (M)	Positive at 100 & 1000 mg/kg by gavage; negative at 50 mg/kg API 1985c, pub 33-32406
64741-81-7	Micronucleus [Heavy coker gas oil - J] [CAS RN 64741-81-7]	Rat (M,F)-	Negative up to 125 mg/kg/day; 5x/week for 13 weeks via dermal route –Mobil, 1993, study 64166
	Micronucleus [Heavy coker gas oil - J] [CAS RN 64741-81-7]	Rat (F pregnant)	Negative at 250mg/kg Part of dermal developmental toxicity GD0-19 Mobil, 1994e study 64169
	Micronucleus [heavy coker gas oil T] [CAS RN 64741-81-7]	Rat (M,F)	Positive at 125mg/kg/day [highest dose], 5x/week for 13 weeks via dermal route. Weak clastogen. Mobil, 1991a, study 64185
	Micronucleus [Heavy Thermocracked distillate - Heavy coker gas oil -B] [CAS RN 64741-81-7]	Rat (M,F)-	Negative up to 2000 mg/kg/day; 5x/week for 13 weeks via dermal route Mobil 1986, study 50392
	Visbreaker Gas oil [CAS RN 64741-81-7]	Rat (M,F)-	Negative up to 125mg/kg/day; 5x/week for 13 weeks via dermal route –Mobil 1990c, study 63238

In vivo studies evaluating cytogenetic damage in a selection of streams in the Heavy Fuel Oils category indicate most of these materials, often those with substantial PAC and regardless of processing, do not induce significant increases in chromosome damage or increased micronuclei in bone marrow cells regardless of exposure route. Although samples of clarified slurry oil [CAS RN 64741-42-6] were negative in two separate studies by the oral or intraperitoneal [IP] routes up to very high doses (negative for chromosome damage up to 1.0g/kg by gavage for 5 days; negative for micronucleus formation up to 3.0g/kg by gavage or IP for 2 days), clarified slurry oil was weakly active in the micronucleus assay with dermal exposure. This effect of dermal exposure seems spurious since the increase occurred only at the lowest dose (8mg/kg) while higher doses up to 500mg/kg had micronucleus values comparable to controls. Positive results for sister chromatid exchanges and unscheduled DNA synthesis reported for clarified slurry oil, the potentially most toxic stream evaluated for all endpoints, indicated that perturbation of DNA can occur but that this damage is likely repaired prior to expression as mutation *in vivo*. For CAS RN 64741-81-7 four of 5 streams did not cause increases in micronucleus formation.

Conclusions: *In vivo* genotoxicity

Overall, the weight of evidence from studies for chromosome damage or micronucleus formation indicate that heavy fuel oils are generally not clastogenic in animals regardless of crude source or processing. This conclusion is further supported by extensive testing of other PAC category petroleum-derived streams (aromatic extracts, asphalt, crude oils and gas oils) in bone marrow chromosome and micronucleus assays that demonstrated that these substances did not induce significant cytogenetic damage in these test systems regardless of route of exposure (McKee et al, 2010 abst.; McKee et al., 2012.)

6.1.6. Developmental/Reproductive Toxicity

6.1.6.1. Developmental Toxicity

CAS RN 64741-45-3 Atmospheric Tower Residuals

In a developmental screening study, dose levels of 50, 333, & 1000 mg/kg/day of an atmospheric residuum (CAS RN. 64741-45-3, ATX 91-0267, ARCO, 1994g) were applied to the skin of presumed-pregnant female rats on days 0-20 of gestation. There were no deaths or treatment-related clinical effects amongst the dams. The study directors considered decreased body weight changes and the increase in gestation length at a dose of 1000 mg/kg to be signs of compound-related maternal toxicity. Signs of developmental toxicity considered by the study investigators to be compound-related included decreased pup body weights on Lactation Days 0 and 4 at a dose of 1000 mg/kg. The study investigators concluded that for maternal toxicity and signs of developmental toxicity, the LOAEL = 1000mg/kg and the NOAEL for maternal and developmental effects was 333.0 mg/kg/day.

CAS RN 64741-57-7 Heavy Vacuum Gas Oils

In a developmental screening study, dose levels of 0, 30, 125, 500 and 1000 mg/kg/day of a heavy vacuum gas oil (HVGO, CAS RN. 64741-57-7) were applied to the skin of presumed-pregnant rats (Mobil, 1987i). The test material was administered on days 0 to 19 of gestation and all animals were sacrificed on day 20. Clinical signs of maternal toxicity considered by the study authors to be compound-related were seen primarily in the 1000 mg/kg/day dose group. In the dams, the only treatment-related findings seen at necropsy were lungs that had a pale appearance (500 and 1000 mg/kg/day) and a reduction in thymus size. Organ weight data confirmed that the thymus weights in the highest dose group were reduced and relative liver weights were increased in the 500 and 1000 mg/kg/day animals. A number of developmental parameters were affected by treatment with HVGO. Fetuses of dams in both the 500 and 1000 mg/kg/day dose groups had treatment-related decreases in body weights. Upon external examination, one fetus in the 1000 mg/kg/day group was found to be edematous, pale in color, with both hind paws malformed. Malformations of the vertebral columns were observed in several fetuses, but only in the 500 mg/kg/day group. While a variety of skeletal malformations were observed in both treated and control groups, the degrees of malformation were more severe in the HVGO-exposed groups. Visceral malformations were restricted to two fetuses in the 500 mg/kg/day group. Of the two fetuses, one had microphthalmia and the other had a diaphragmatic hernia that displaced the heart from the left- to right-hand side. The study investigators concluded that 500mg/kg/day was the LOAEL for maternal and developmental toxicity and the NOAEL for maternal and developmental effects was 125 mg/kg/day.

In a developmental range finding toxicity study, test article F-196 (CAS RN 64741-57-7) was applied to the shaved backs of presumed pregnant rats at concentrations of 0 (acetone), 75, 150 and 300mg/kg/day from GD 0 to 19, sacrificed on GD20 (ARCO ATX 92-0012, 1993b). All doses caused reduction in maternal body weight gains and food consumption. All doses also reduced fetal body weights and delayed ossification. Maternal and fetal LOAEL = 75mg/kg and NOAEL maternal and fetal was less than 75mg/kg and not determined in this study.

Test article F-197 (CAS RN 64741-57-7) was applied to the shaved backs of presumed pregnant rats at concentrations of 0, 50, 100 and 250mg/kg/day from GD 0 to 19, sacrificed on GD20 (ARCO ATX 92-0154, 1993c). All doses caused skin reactions and reduced food consumption. Treatment at 250mg/kg caused reduced maternal body weight gain. Developmental effects

occurred at the highest maternally toxic dose, the 250mg/kg group and included reduced fetal body weight, increased variations in ossification. Maternal LOAEL = 50mg/kg; NOAEL maternal < 50mg/kg and developmental LOAEL = 250mg/kg; NOAEL developmental = 100mg/kg.

Test article F-225 (CAS RN 64741-57-7, ATX 91-0264, ARCO, 1994k) was applied to the shaved backs of presumed pregnant rats at concentrations of 0, 50, 150 and 500mg/kg/day from GD 0 to 20. All litters were maintained from LD 0 to 4. Decreased maternal body weight and weight gain, and decreased food consumption were seen in the 150 and 500mg/kg groups. Increased vaginal discharge occurred at 500mg/kg. Reduced number of total and live pups per litter were observed in the 500mg/kg group at LD 0 and 3 females did not deliver litters. Lower pup body weights occurred at LD0 and 4 in the 150 and 500mg/kg/day groups. Maternal and developmental LOAEL = 150mg/kg; NOAEL maternal and developmental = 50 mg/kg.

CAS RN 64741-61-3 Heavy Catalytic Cracked Distillates

Test article F-222, (CAS RN 64741-61-3) was applied to the shaved backs of presumed pregnant rats at concentrations of 0, 50, 150 and 500mg/kg/day from GD 0 to 20 (ARCO, ATX 91-0270, 1994o). All litters were maintained from LD 0 to 4. Maternal toxicity included decreased body weight and weight gain, decreased food consumption and increased vaginal discharge at 150 and 500mg/kg/day. Implantations were decreased and no litters were delivered from 10 pregnant rats at 500mg/kg. Only one female delivered a litter out of 12 pregnant rats at 150mg/kg and 7 of 10 rats delivered litters at 50mg/kg. Gestation duration was increased to 22.7 days at 50mg/kg compared to 22 days in controls. Decreased numbers of total and live pups/litter at LD0 was seen in 50 and 150mg/kg groups and pup weights were decreased in the 50mg/kg groups at LD0 but were not statistically different from controls at LD4. Maternal and developmental LOAEL = 150mg/kg; NOAEL maternal and developmental was less than 50mg/kg and could not be determined in this study.

CAS RN 64741-62-4 Catalytic Cracked Clarified Oils

A developmental toxicity screening study has been reported on a clarified slurry oil (CSO, CAS RN 64741-62-4; F-179) (Hoberman et al., 1995b, ARCO, 1992h). Undiluted test material was applied daily on days 0 to 19 of gestation to the clipped backs of presumed-pregnant female rats. Dose levels included 0.05, 1.0, 10, 50 or 250 mg/kg/day. Additional groups of animals were treated with 50 or 250mg/kg/day CSO on GD 0-2, GD 3-5, GD 6-8. GD 9-11, GD 12-14, GD 15-17 or GD 18-19 to identify critical periods of embryolethality. No deaths occurred among the dams and no dam aborted or prematurely delivered a litter. Neither maternal toxicity nor fetal developmental effects were seen at the 0.05 mg/kg/day dose level. Nor were any fetal malformations or variations observed in the 0.05 mg/kg/day group. Dose-related signs of maternal toxicity were seen at dose levels greater than 0.05 mg/kg/day. The effects included decreased food consumption and decreased body and gravid uterine weights, and the occurrence of red vaginal exudates. Fetal developmental effects, as measured by number of live fetuses, total resorptions, early resorptions, % dead or resorbed conceptuses/litter and fetal body weights were seen at doses that were maternally toxic. There were no treatment-related incidences of fetal malformations. However, increased incidences of fetal variations that are generally interpreted as reversible delays in development associated with significant decreases in body weight were produced in fetuses in the 1.0, 10 and 50 mg/kg/day dose groups. These variations included moderate dilation of the renal pelvis, slight dilation of the lateral ventricles of the brain, bifid thoracic vertebral centrum and decreased average numbers of ossified caudal vertebrae, metacarpals and hindpaw phalanges. The reproductive and fetal effects occurred at dose levels that produced systemic maternal toxicity in females treated from GD 0-19. Critical periods of embryo deaths for short duration exposures

were GD6-8 and GD9-11. The study authors concluded the maternal and fetal LOAEL = 1.0mg/kg and NOAEL maternal and fetal = 0.05 mg/kg/day.

An earlier developmental toxicity study on a similar clarified slurry oil (CAS RN 64741-62-4, F115-01) was performed at concentrations of 0, 1.0, 10, 50 and 250mg/kg/day (ARCO ATX 89005, 1989h) . Doses of 1.0mg/kg and above, significantly inhibited maternal body weight, weight gain and food consumption. Significant increases in resorptions and decreases in live litter sizes were seen at all doses. There were no live fetuses in the 250mg/kg group. Decreased fetal body weights were interrelated with significant increases in litter and/or fetal incidences of retarded development of soft tissue and skeletons. NOAEL maternal/developmental <1.0mg/kg. The subsequent study described above showed similar effects and identified a NOAEL = 0.05mg/kg/day.

Clarified slurry oil (CSO - CAS RN 64741-62-4) was applied to the shaved backs of presumed pregnant rats at concentrations of 0, 4, 8, 30, 125, and 250mg/kg/day from GD 0 to 19 and sacrificed on GD20 (Mobil 50541, 1987h). Maternal toxicity at dose levels as 8mg/kg/day and above included decreased body weight and weight gain, food consumption, increased relative liver weight, thymic atrophy, vaginal bleeding and abnormal serum chemistry values. All embryo/fetuses died in the 250mg/kg group. Increased number of resorptions/litter and decreased number of viable fetuses/litter were seen at concentrations of 30mg/kg/day or greater; the 125mg/kg group contained only 2 viable fetuses. Fetuses were smaller in dose groups above 8mg/kg. External abnormal development seen in viable and dead fetuses at 8, 30 and 125mg/kg groups included cleft palate, micrognathia, kinked tail and edema. Abnormal development was also seen in soft tissue and skeletal evaluations. Maternal and developmental LOAEL = 8mg/kg; NOAEL maternal and developmental = 4mg/kg.

In a subsequent study to identify sensitive gestation days and monitor bioavailability of CSO components (Mobil 62492, 1988f), clarified slurry oil was applied to the shaved backs of presumed pregnant rats on GD9 to 12 at concentrations of 0, 10, 100 and 1000mg/kg/day. Animals were sacrificed on GD20. Maternal toxicity was expressed as decreased body weight and food consumption in 100 and 1000mg/kg groups, decreased absolute and relative thymus weights, increased absolute and relative liver weights and variations in serum chemistry at 1000mg/kg. Developmentally litter size was decreased, the number of dams with resorptions increased and in utero death of embryo/fetuses increased at 1000mg/kg. Fetal body weight was decreased and variations in development were seen externally in 100 and 1000mg/kg groups and viscerally in 1000mg/kg in utero exposed fetuses. Developmental effects occurred only at maternally toxic doses. Methods employed in the bioavailability study are described in the paragraph below employing STB (Mobil, 1989, study #62934). The placenta acted as an effective barrier against transport of carbazole and benzo(a)pyrene as only very low doses of these radiolabeled materials were seen in the fetus compared to maternal tissues. Either these materials are not responsible for CSO teratogenic effects or only very small quantities are needed to elicit adverse effects. NOAEL maternal and developmental = 10mg/kg.

In another developmental toxicity study, a clarified slurry oil identified as Ferndale Syn Tower bottoms (STB) was applied to the shaved backs of presumed pregnant rats at dose levels of 0, 4, 8, 30, 125mg/kg/day from GD0 – 19 and at a dose of 500mg/kg/day from GD 10-12 to identify any effects obscured by fetal mortality from longer term exposure (Mobil 1989 study 62934). Maternal effects included vaginal bleeding, mean body weight reduction and decreased food consumption at 8mg/kg and above. Body weight gain was decreased at all dose levels. Thymus weight was reduced in 125 and 500mg/kg/day animals and aberrant serum chemistry values were seen at

125mg/kg. At 125mg/kg, absolute liver weight was reduced and all fetuses were resorbed. The number and percent resorptions were statistically significantly increased at 30mg/kg and above with a three-fold increase at 8mg/kg. Decreased litter size and decreased male fetus body weight was seen at the dose of 8mg/kg and above. Similar effects were observed 4mg/kg and while not statistically significant were considered biologically significant by the authors and informed the developmental LOAEL and NOAEL values. Soft tissue and skeletal effects were seen in fetuses exposed to the highest dose of 500mg/kg/day from GD10-12. LOAEL maternal and fetal = 4mg/kg and NOAEL maternal and fetal < 4mg/kg. In the accompanying bioavailability study four of the rats in the 500mg/kg group were treated with STB radiolabeled with ^{14}C-carbazole and ^{3}H-benzo(a)pyrene, applied within a protective chamber. On GD13, 24 hours after the last dose, females were sacrificed and maternal blood, fetuses and placental fluid removed. Maternal organs were also examined for distribution of labeled material. Over 72 hours of exposure, 2.5% of ^{14}C-carbazole was measured in maternal tissue and less than 0.01% in fetal tissue. Only 0.8% ^{3}H-benzo(a)pyrene accumulated in maternal tissue and less than 0.01% in fetal tissue. These low levels of radiolabeled material in fetal tissue demonstrated that the placenta is an effective barrier to transport of carbazole and benzo(a)pyrene. No selective accumulation of either material was seen in fetal tissue. These bioavailability results confirm those reported in Mobil study 62492 (1988f) above.

Catalytic cracked clarified oil (Clarified Slurry Oil, CSO CAS RN 64741-62-4; Sample # 010929) (WIL Laboratories, 2012b) diluted in acetone (99%) was applied to the shaved backs of presumed pregnant rats (25/group) at concentrations of 0 [sham and vehicle controls], 5, 25, and 50mg/kg/day from GD 0 to 19 and sacrificed on GD20. Two females in the 50mg/kg group died, one on GD 18 and the other on GD19. All other females survived to termination on GD20. Lower maternal mean body weight and weight gains were seen throughout the gestation period at 25 and 50mg/kg/day groups. Gravid uterine weights in the 25 and 50 mg/kg/day groups were significantly lower than the vehicle control group and were attributed to the decreased number of viable fetuses and lower mean fetal weights noted at these exposure The decreased number of viable fetuses and lower fetal weights in the 25 and 50 mg/kg/day groups also contributed to the lower body weights and reduced body weight gains in these groups, especially during the latter part of gestation Lower mean thymus weights (absolute and relative to brain) were seen in dams of the 25 and 50mg/kg day groups Mean liver and brain weights were similar to controls Parameters measured for pregnant females in the 5mg/kg/day group were comparable to controls.

The number of gravid females was similar across groups and no statistically significant differences were seen in numbers of corpora lutea or implantation sites. However, the number of early resorptions was significantly increased, and the number of viable fetuses was significantly decreased in the 25 and 50 mg/kg/day groups. The mean litter proportions of postimplantation loss in the 25 and 50 mg/kg/day groups were significantly higher than the vehicle control group resulting from increased mean litter proportion of early resorptions at 25 mg/kg/day and increased mean litter proportions of early and late resorptions at 50 mg/kg/day. One and 8 females in the 25 and 50 mg/kg/day groups, respectively, had 100% post-implantation loss. Corresponding significantly lower mean litter proportions of viable fetuses and mean number of viable fetuses were noted in the 25 and 50 mg/kg/day groups. In the 25 and 50 mg/kg/day groups, significantly lower mean male, female and combined fetal weights were noted compared to the vehicle control group values. Intrauterine growth and survival were unaffected at 5mg/kg/day. No significant soft tissue or skeletal malformations was observed at any dose group. Skeletal variations and delayed ossification were observed in the 25 and 50mg/kg/day groups considered secondary to reduced fetal weights in these groups. Maternal and fetal LOAEL = 25mg/kg; NOAEL maternal and fetal = 5mg/kg.

Test article F-229, FCCU Clarified Oil, carbon black oil (CAS RN 64741-62-4, ATX 91-0268, ARCO, 1994m) was applied to the shaved backs of presumed pregnant rats at concentrations of 0, 5.0, 10, and 50mg/kg/day from GD 0 to 20. All litters were maintained from LD 0 to 4. Maternal toxicity at 50mg/kg included decreased maternal body weight on GD16 and 20, decreased body weight gain between GD 0–4, 4–8, 16–20 and LD 0–4 with increased incidence of vaginal discharge. Gestation length was increased at 50mg/kg (22.8 days compared to 22.1 days in control rats and lower dose groups). Developmental toxicity was expressed as decreased total and live pups/litter and increased proportion of dead pups at LD0, decreased proportion of male pups on LD0 and 4 and decreased pup weights at LD0 in the 50mg/kg group. Maternal and developmental LOAEL = 50mg/kg; NOAEL maternal and developmental = 10mg/kg.

In order to further explore the suspected teratogenic potential of refinery streams, Feuston and Mackerer (1996) conducted a developmental toxicity study in which the test materials were given by gavage on a single day of gestation. This study design was chosen in order to limit the embryolethal effects of these compounds and to maximize the chances of detecting any teratogenic potential. While the oral route of exposure is not considered a relevant route of exposure for human hazard assessment of petroleum streams, the results of this study are included here for the sake of completeness.

Feuston and Mackerer (1996) administered a single oral dose (2000 mg/kg/day) of heavy paraffinic distillate aromatic extract (DAE, CAS RN 64742-04-7) [see Aromatic Extract Category Closure Document,(API 2011)], clarified slurry oil (CSO), or syntower bottoms (STB) on gestation day (GD) 11, 12, 13, 14, or 15 (DAE and STB only on GD 15). Additional rats were given oral doses of 125, 500, or 2000 mg/kg/day of DAE, CSO, or STB on GD 12. The controls were administered tap water by gavage on GD 11-15 (DAE and STB) or GD 11-14 (CSO). Dams were sacrificed and necropsied on GD 20 and fetuses were examined. For each refinery stream tested, evidence of maternal toxicity (i.e., decreased body weight; decreased thymus weight) was observed at doses of 500 mg/kg/day and greater. Statistically significant increases in resorptions were observed at 2000 mg/kg/day of CSO or STB, but not DAE. According to the study authors, a common pattern of fetal malformations (including cleft palate, diaphragmatic hernia, and paw and tail defects) was observed in the studies of these three high boiling, aromatic-rich substances. The increases in fetal malformations were statistically significant at doses of 500 mg/kg/day or greater for CSO and STB and 2000 mg/kg for DAE. The investigators noted that the ability to produce adverse effects on development was greatest for CSO and least for DAE. Developmental toxicity was not observed in the absence of maternal toxicity with any of these petroleum streams. Although the oral route of administration has little relevance to human occupational exposure, DAE, CSO, and STB were shown to have teratogenic potential when a large dose was given by gavage to pregnant rats on a single day during the critical period of gestation in conjunction with maternal toxicity. The laboratory studies using heavy fuel oils from which this publication was derived were Clarified slurry oil Mobil, 1990b, Study 63122 and Syn tower bottoms Mobil 1990a, Study 63123, described in their entirety in Robust Summaries.

CAS RN. 64741-81-7 Heavy Thermal Cracked Distillates

Doses of 8, 30, 125 and 250 mg/kg/day of a heavy coker gas oil (CAS RN. 64741-81-7) were applied daily to the skin of presumed-pregnant female rats in a developmental screening study (Mobil, 50431 1987g). There were groups of control rats, one group had shaved backs and was

handled in the same way as the exposed animals (Sham-treated) and one group were housed separately and were not shaved or handled. Animals were treated on days 0-19 of gestation. A separate group was administered 125mg/kg/day from GD10-12 to evaluate possible abnormal development in the absence of fetal mortality. A bioavailability study using radiolabeled carbazole and benzo(a)pyrene was also performed with rats in this groups as described above for clarified slurry oil identified as Ferndale Syn Tower bottoms (STB). All animals were sacrificed on day 20. Treatment-related clinical observations in the dams consisted of erythema, flaking, scabbing, edema, eschar and fissuring and the occurrence of a red vaginal discharge. Eschar and fissuring occurred in the highest two dose groups only. Vaginal bleeding was seen in the groups receiving doses of 30 mg/kg/day and higher. There was a dose-related decrease in mean body weight gains over the course of the experiment. At necropsy, the only treatment-related observation in the dams was an apparent reduction in thymus size, which was noted at all treatment levels. Absolute thymus weights were decreased, while absolute liver weights were increased. A number of clinical chemistry values were affected, but only at the highest dose of 250 mg/kg/day. Select reproductive parameters were adversely affected, but only in the 125 and 250 mg/kg/day groups. Viable and non-viable fetuses from these two dose levels were observed to have signs of abnormal external development, including reduced (shortened) lower jaws and edema. Visceral anomalies seen in these same two dose groups included displacement of esophagus from a left-sided to a right-sided position and distension of the ureters. Malformations of the vertebral column were restricted to fetuses of dams exposed to the test material. Among animals exposed to 125mg/kg/day from GD10-12, there was a decrease in litter size but only compared to controls that were housed separately and were not shaved or sham-treated. Although signs of aberrant development were observed in sham treated control animals, the degree of the observed effects was not as severe in the control groups as the groups exposed to test material. Bioavailability results were similar to previous studies with CSO that demonstrated the placenta acted as an efficient barrier to transport of radiolabeled carbazole or benzo(a)pyrene to the fetus. The authors concluded that the NOAEL for maternal toxicity was 8mg/kg; LOAEL maternal = 30mg/kg based on vaginal bleeding. Developmental LOAEL = 125mg/kg; NOAEL developmental = 30 mg/kg/day.

A heavy coker gas oil (CAS RN 64741-81-7) was tested for developmental toxicity. Test material was applied to the shaved backs of presumed pregnant rats at concentrations of 0, 8, 30, 125, 250mg/kg/day from GD0 to 19 and animals sacrificed on GD20 (Mobil 64168, 1994c). Maternal toxicity was observed to varying degrees at all dose levels. Skin irritation varied from slight (8mg/kg) to severe (250mg/kg). Decreased absolute and relative thymus weight and increased relative liver weight, red vaginal discharge, paleness, emaciation were seen at 30mg/kg with morbundity at 250mg/kg. Serum chemistry values were affected at 125 and 250mg/kg. Resorptions were significantly increased and fetal weights decreased at 125 and 250mg/kg/day. Resorptions were also increased at 30mg/kg. Maternal LOAEL = 8; NOAEL maternal <8.0mg/kg. Developmental LOAEL = 30mg/kg; NOAEL developmental = 8mg/kg.

Test article F-274, (CAS RN 64741-81-7) was applied to the shaved backs of presumed pregnant rats at concentrations of 0, 1.0, 50 and 250mg/kg/day from GD 0 to 20 (ARCO ATX 93-0069, 1994n). All litters were maintained from LD 0 to 4. Dermal irritation was seen at all dose levels. Decreased maternal body weight, weight gain, food consumption and relative food consumption were seen in 50 and 250mg/kg groups. Implantation sites were decreased, resorptions were increased and no litters were delivered at the 250mg/kg dose level. Gestation length was slightly increased in the 50mg/kg group (22.5 days compared to 22.0 days in Controls). Decreased numbers of total and live pups delivered per litter at LD0 were seen at 50mg/kg/day. No adverse effects were seen on pup weights at LD0 and 4 and pup survival was no statistically significantly

lower than controls at LD4. NOAEL maternal <1.0mg/kg based on skin irritation. Developmental LOAEL = 50mg/kg; NOAEL developmental = 1.0mg/kg.

In contrast to the previous studies identified as CAS RN 64741-81-7, another material, Visbreaker gas oil, V.B. Mittelol (Mobil 64643, 1994b) showed minimal developmental toxicity at similar doses. Test material was applied to the shaved backs of presumed pregnant rats at concentrations of 0, 30, 125, 250mg/kg/day from GD0 to 19 and animals sacrificed on GD20. Maternal toxicity was only expressed as decreased mean body weight gain at 250mg/kg with no other systemic toxicity except varying degrees of skin irritation at all doses. No developmental toxicity was observed although a non-statistically significant dose-dependent trend in increasing resorptions was observed. NOAEL maternal = 125mg/kg and NOAEL developmental = 250mg/kg. This material [sample #086193] contains lower total DMSO extractables [4.5%] and a lower PAC profile distribution than other study materials described above with this CAS RN which have a range of total DMSO extractables ranging from 13 – 30 in sample #083366, 086181, 094625 (see analytical Table 2).

CAS RN 64742-86-5 Hydrodesulfurized Heavy Vacuum Gas Oils

Test article F-227, hydrodesulfuized heavy vacuum gas oil (CAS RN 64742-86-5), was applied to the shaved backs of presumed pregnant rats at concentrations of 0, 50, 333 and 1000mg/kg/day from GD 0 to 20 (ARCO ATX 91-0266,1994l). All litters were maintained from LD 0 to 4. Decreased maternal body weight and weight gain, and decreased food consumption were seen in the 333 and 1000mg/kg groups. Although all females were pregnant at 1000mg/kg and numbers of implantation sites were comparable to controls, no females in this group delivered a litter. In the 333 mg/kg groups one female did not deliver a litter. Reduced numbers of total and live pups per litter were observed in the 333mg/kg group at LD 0 and lower pup body weights occurred at LD0 and 4. Maternal and developmental LOAEL = 333mg/kg; NOAEL maternal and developmental = 50 mg/kg.

CAS RN 68410-00-4 Crude Oil Distillates

Test article F-194, VDF Diesel (CAS RN 68410-00-4) was applied to the shaved backs of presumed pregnant rats at concentrations of 0, 125 and 250mg/kg/day from GD 0 to 20, and to another groups at 1000mg/kg/day from GD5 to 9 (ARCO ATX 91-0128,1994i). All litters were maintained for LD0 to 4. Skin irritation was seen at all dose levels. Decreased maternal body weight, weight gain and decreased food consumption occurred in 250 and 1000mg/kg/day groups. Developmental toxicity included decreased pup weight on LD0 in all dose groups and on LD4 at 250 and 1000mg/kg. Administration of F-194 at 1000mg/kg/day for GD 5-9 resulted in developmental and maternal toxicity similar to longer exposures at lower doses. NOAEL maternal and developmental were less than 125mg/kg. A NOAEL was not established.

Test article F-215 (CAS RN 68410-00-4) was applied to the shaved backs of presumed pregnant rats at concentrations of 0, 50, 250 and 500mg/kg/day from GD 0 to 19, sacrificed on GD20 (ARCO ATX 92-0155, 1993a). Doses of 250 and 500mg/kg caused skin reactions and reduced body weight and weight gains in dams. Decreased food consumption was seen at 500mg/kg. No adverse effects were seen on embryo fetal viability or fetal body weights or morphology up to the highest dose. Maternal NOAEL = 50mg/kg and developmental NOAEL = 500mg/kg

In a separate study performed a year later, test article F-215 (CAS RN 68410-00-4) identified as a gas oil intermediate, C11 to C25 hydrocarbons was applied to the shaved backs of presumed pregnant rats at concentrations of 0, 50, 150 and 500mg/kg/day from GD 0 to 20 (ARCO ATX 91-

0263, 1994j). Litters were maintained from LD0 to 4. Decreased maternal body weight and weight gain was seen at 500mg/kg/day and decreased food consumption at 150 and 500mg/kg/day. Lower pup weights were reported at LD0 and 4 in the 150 and 500mg/kg groups and the proportion of pups surviving to LD 4 was decreased to 70% in the 500mg/kg/day group. The NOAEL for maternal and developmental was 50mg/kg. Combined effects for dams and pups expressed from lactation days 0-4 when there was no exposure to test material compared to the previous study suggest failure to thrive after delivery. This response could have resulted from residual effects or test material. Possible compositional changes in F-215 from storage over 1 year cannot be discounted.

CAS RN 68783-08-4 Heavy Atmospheric Gas Oil

In a developmental toxicity study test article F-275, a full range gas oil (CAS RN 687383-08-4) was applied to the shaved backs of presumed pregnant rats at concentrations of 0, 50, 250 and 500mg/kg/day from Gestation day (GD) 0 to 20 (ARCO ATX 93-0071, 1994h). Litters were maintained from Lactation day (LD) 0 to 4. Dermal irritation was observed in all treated groups. Decreased maternal body weight, weight gain and food consumption was seen in 250 and 500mg/mg groups and increased duration of gestation (22.6 days compared to 22.0 days in controls) occurred at 500mg/kg. Decreased total and live pups delivered per litter observed at 250 and 500mg/kg/day. At 500mg/kg, decreased number of litters and increased proportion of dead pups were seen at LD0 with an increase proportion of male pups. NOAEL maternal = 50mg/kg excluding skin irritation and developmental NOAEL = 50mg/kg/day.

Supplemental data: Related material *from Gas Oil Category Assessment Document*

A developmental toxicity study (Mobil, 1991b) with a similar material CAS 68915-97-9 also identified as a heavy atmospheric gas oil from the Gas Oil Category is provided as supplemental data which demonstrates the compositional and toxicologically continuity among PAC-rich petroleum streams.

Undiluted test material was applied daily on days 0 to 19 of gestation to the clipped skin of presumed-pregnant rats at concentrations of 0, 8, 30, 125 and 500 mg/kg/day. Signs of maternal toxicity considered by the study director to be related to administration of the test material included effects on body weights, body weight gain, food consumption, thymus weights (absolute & relative), liver weights (relative), and a number of clinical chemistry and hematological parameters. A red vaginal discharge (normally indicative of litter resorption) was observed in 7/11 animals in the 500 mg/kg/day group and two females dosed with 125 mg/kg/day. The investigators could not decide if the vaginal discharge was treatment-related since a similar observation had been noted in control animals. Evaluation of reproductive parameters in the 8 and 30 mg/kg found no compound-related effects. Statistically insignificant differences in preimplantation losses were seen in both the 125 and 500 mg/kg/day groups. There was a significant increase in the mean number/percent resorptions in the 500 mg/kg/day group. Mean fetal body weights were significantly decreased for all viable fetuses in the 500 mg/kg/day group and in the male fetuses of the 125 mg/kg group. There was a significant increase in incomplete ossification of a number of skeletal structures (nasal bones, thoracic centra, caudal centra, sternebrae, metatarsal and pubis) in the 125 and 500 mg/kg/day groups. There were no treatment-related abnormalities found in the soft tissues. Exposure to gas oil in the 8 and 30mg/kg/day groups did not adversely affect pup survival or development. The investigators concluded the no-observable-adverse -effect levels (NOAELs) for maternal and fetal toxicity were 30 mg/kg/day.

Conclusions

Developmental toxicity studies of Heavy Fuel Oil are summarized in Table 21 and studies used in designing the fetal development model are identified. The most severe adverse fetal effects were observed in a developmental toxicity study with clarified slurry oil [CAS RN 64741-62-4] (Hoberman et al, 1995b) in the presence of significant maternal toxicity. The range of values for the five samples tested for the entire duration of gestation and identified by CAS RN 64741-62-4 was NOAEL = 0.05 to 10mg/kg and LOAEL = 1.0 to 25mg/kg. Less severe fetal toxicity expressed primarily as decreased litter sizes and liveborns, fetal weights or pup weights at lactation day 0 and 4, occasional instances of malformations or increased resorptions (i.e. heavy vacuum gas oil at 500 and 1000mg/kg) resulted in developmental LOAELs ranging from 30mg/kg for a heavy coker gas oil [CAS RN 64741-81-7] to 1000mg/kg for an atmospheric tower residual [CAS RN 64741-45-3] and developmental NOAELs of 8mg/kg to 333mg/kg respectively for these materials. All developmental toxic effects were associated with maternal toxicity. One sample of crude oil distillate CAS RN 68410-00-4 (F-215) caused no fetal toxicity at doses as high as 500mg/kg with maternal toxicity at 250mg/kg. One sample of thermal cracked distillate CAS RN 64741-81-7 (F-274) caused decreased live pups at birth at 50mg/kg, resulting in a NOAEL of 1.0mg/kg, the next lowest dose. Overall these data indicate that streams derived from cracked stocks tend to induce greater developmental and maternal toxicity. However fairly wide dose ranges make it difficult to fully define non-toxic levels.

Table 21. Developmental Toxicity Studies of Heavy Fuel Oil in Sprague Dawley Rats by the Dermal Route of Exposure

CAS RN	Sex /Duration	Dose mg/kg/day	Results	References
64741-45-3 Atmospheric Tower Residuals				
F 228 64741-45-3 Sample # 091691	Presumed pregnant, Treated GD0-20, litters maintained to LD4	0, 50, 333, 1000	Decreased maternal body weight, increased gestation length at 1000mg/kg. decreased pup weight at LD0 and 4 NOAEL maternal/developmental = 333mg/kg	ARCO, 1994g ATX 91-0227
64741-57-7 Heavy Vacuum Gas Oils				
Heavy Vacuum gas oil [64741-57-7] Sample # 085244	Presumed pregnant, Treated GD0-19 sacrificed GD20	0, 30, 125, 500, 1000	Maternal decreased body wt at 500, 1000mg/kg reflects decreased litter sizes. Increased resorptions, decreased fetal body weights and skeletal and visceral malformations at higher doses NOAEL maternal/developmental = 125mg/kg	Mobil 1987i Study 61801 Used in PAC Model[a]
F-196 [64741-57-7] Sample # 091649	Presumed pregnant, (Range finder) Treated GD0-19, sacrificed at GD20	0, 75, 150, 300	At all doses: Maternal decreased body wt, weight gain, food consumption. Reduced fetal body weight and delayed ossification. NOAEL not established <75mg/kg	ARCO, 1993b ATX 92-0012 Used in PAC Model[a]
F-197 [64741-57-7] Sample # 091650	Presumed pregnant, Treated GD0-19, sacrificed at GD20	0, 50, 100, 250	Maternal dermal irritation, decreased food consumption at all doses. Decreased body weight gain at 250mg/kg. Reduced fetal body weight, increased ossification variations at 250mg/kg NOAEL maternal < 50mg/kg NOAEL developmental = 100mg/kg	ARCO, 1993c ATX 92-0154 Used in PAC Model[a]
F-225 [[64741-57-7] Sample # 091689	Presumed pregnant, Treated GD0-20, litters maintained to LD4	0, 50, 150, 500	Maternal decreased body weight gain, decreased relative food consumption at 150, 500mg/kg. Increased vaginal discharge at 500mg/kg. Decreased pup weights at LD0 and 4 at 150, 500mg/kg. At 500mg/kg 3 females did not deliver litters, reduced number of total/live pups. NOAEL maternal/developmental = 50mg/kg	ARCO, 1994k ATX 91-0264
64741-61-3 Heavy Catalytic Cracked Distillates				
F-222 [64741-61-3] Sample # 091686	Presumed pregnant, Treated GD0-20, litters maintained to LD4	0, 50, 150, 500	Maternal decreased body wt, weight gain, food consumption and increased vaginal discharge at 150, 500mg/kg. No litters at 500mg/kg, 1 litter at 150mg/kg and 7 of 10 females delivered at 50mg/kg Increased gestation length at 50mg/kg. Decreased	ARCO 1994o ATX 91-0270

CAS RN	Sex /Duration	Dose mg/kg/day	Results	References
			total/live pups per litter at LD0 at 50, 150mg/kg. Decreased pup weights at LD0 but not LD4 at 50mg/kg. NOAEL not established, <50mg/kg	
64741-62-4 Catalytic Cracked Clarified Oils				
Clarified Slurry Oil F-179 [64741-62-4] Sample # 091645	Presumed pregnant, Treated GD0-19, sacrificed at GD20	0, 0.05, 1.0 , 10, 50, 250	Maternal decreased body and gravid uterus weights, vaginal discharge, decreased food consumption at 1.0 – 250mg/kg. Developmental toxicity at 1.0 – 250mg/kg at doses with maternal toxicity. NOAEL maternal/ developmental = 0.05mg/kg	Hoberman et al, 1995b ARCO, 1992h, ATX 91-0042] Used in PAC Model[a]
Clarified Slurry Oil [64741-62-4] Sample # 086001	Presumed pregnant, Treated GD0-19, sacrificed at GD20	0, 4, 8, 30, 125, 250	Maternal decreased body wt, food consumption, thymus atrophy, increased relative liver wt, vaginal bleeding at 8mg/kg & above, serum chemistry changes at 250mg/kg No viable fetuses at 250, 2 viable fetuses at 125mg/kg. Increased resorptions, decreased viable fetuses at 30mg/kg. Small fetuses in groups above 8mg/kg. Abnormal development at 8mg/kg and above. NOAEL maternal/ developmental = 4mg/kg	Mobil, 1987h Study # 50541 Used in PAC Model[a]
Clarified Slurry Oil [64741-62-4] Sample # 086484 Ferndale Syn Tower bottoms	Presumed pregnant, Treated GD0-19, sacrificed at GD20	0, 4, 8, 30, 125 (GD0-19), 500mg/kg (GD10-12)	Maternal decreased body wt, food consumption, and vaginal bleeding at 8mg/kg and above. Body weight gain significantly decreased at all dose levels. Decreased thymus decreased liver wt, and aberrant serum chemistry at 125 and 500mg/kg. All fetuses resorbed at 125mg/kg. Resorptions increased, litter size and male fetal body wt decreased at 8mg/kg and above. Similar effects at 4mg/kg were considered biologically significant by the authors. Tissue and skeletal effects seen in 500mg/kg fetuses. NOAEL maternal/developmental < 4mg/kg	Mobil, 1989 Study # 62934 Feuston et al, 1997 Used in PAC Model[a]
Clarified Slurry Oil [64741-62-4] Sample # 010929	Presumed pregnant, Treated GD0-19, sacrificed at GD20	0, 5, 25, 50	LOAEL maternal/fetal = 25mg/kg based on decreased maternal weight and weight gain, organ weight changes and significant reductions in fetal survival and fetal weight and an increased incidence in early resorptions. Developmental delays secondary to reduced fetal weights, frequency of malformations not increased. No significant soft tissue or skeletal malformations observed. NOAEL maternal/fetal = 5mg/kg	WIL Laboratories, 2012 Study # 402016
Carbon Black Oil F-229 [64741-62-4] Sample # 091692	Presumed pregnant, Treated GD0-20, litters maintained to LD4	0, 5, 10, 50	Maternal decreased body wt and weight gain, increased vaginal discharge, increased gestation length at 50mg/kg. At 50mg/kg decreased total/ live pups per litter and increased proportion of dead pups at LD0; decreased pup weight at LD0 and decreased proportion of male pups at	ARCO, 1994m ATX 91-0267

CAS RN	Sex /Duration	Dose mg/kg/day	Results	References
			LD0 and 4. NOAEL maternal/developmental = 10mg/kg	
64741-81-7 Heavy Thermal Cracked Distillates				
Heavy Coker Gas oil [64741-81-7] Sample # 083366	Presumed pregnant, Treated GD0-19, sacrificed at GD20	0, 8, 30, 125, 250	Dose dependent increased maternal skin irritation. Vaginal bleeding at 30mg/kg and above, decreased body weight gain, decreased thymus wt., increased liver wt at 125, 500mg/kg. Reproductive endpoints affected at 125, 250mg/kg included abnormal external development and visceral abnormalities. NOAEL maternal = 8mg/kg NOAEL developmental = 30mg/kg	Mobil, 1987g Study 50431 Used in PAC Model[a]
Heavy Coker Gas Oil [64741-81-7] Sample # 086181	Presumed pregnant, Treated GD0-19, sacrificed at GD20	0, 8, 30, 125, 250	Dose dependent increased maternal skin irritation, Decreased thymus wt and increased liver weight, vaginal discharge at 30mg/kg and above. Serum chemistry affected at 125, 250mg/kg. Resorptions increased at 30mg/kg and above. Fetal wts decreased at 125, 250mg/kg. NOAEL maternal < 8mg/kg NOAEL developmental = 8mg/kg	Mobil, 1994c Study 64168 Used in PAC Model[a]
V.B. Mittelol [64741-81-7] Sample # 086193	Presumed pregnant, Treated GD0-19, sacrificed at GD20	0, 30, 125, 250	Maternal decreased body weight gain at 250mg/kg. Varying degrees of skin irritation. No other systemic toxicity. No developmental toxicity. NOAEL maternal = 125mg/kg NOAEL developmental = 250mg/kg [highest dose]	Mobil 1994b Study 64643 Used in PAC Model[a]
F-274 [64741-81-7] Sample # 094625	Presumed pregnant, Treated GD0-20, litters maintained to LD4	0, 1, 50, 250	Maternal dermal irritation at all doses. Decreased body wt, weight gain and food consumption at 50, 250mg/kg. No litters at 250mg/kg. Decreased total/live pups per litter at 50mg/kg. NOAEL maternal =1.0mg/kg [excludes skin irritation]; NOAEL developmental = 1.0mg/kg	ARCO, 1994n ATX 93-0069
64742-86-5 Hydrodesulfurized Heavy Vacuum gas oil				
F-227 [64742-86-5] Sample # 091690	Presumed pregnant, Treated GD0-20, litters maintained to LD4	0, 50, 333, 1000	Maternal decreased body wt, weight gain and food consumption at 333, 1000mg/kg. No litters at 1000mg/kg. At 333mg/kg one female had no litter, decreased total/live pups per litter at LD0. decreased pup weight at LD0 and 4. NOAEL maternal/developmental = 50mg/kg	ARCO, 1994l ATX 91-0266
68410-00-4 Crude Oil Distillates				

CAS RN	Sex /Duration	Dose mg/kg/day	Results	References
F-215 [68410-00-4] Sample # 091681	Presumed pregnant, Treated GD0-19 sacrificed GD20	0, 50, 250, 500	Maternal dermal irritation, decreased body wt and weight gain, food consumption at 250, 500mg/kg. No adverse effects on embryo/fetal endpoints. NOAEL maternal = 50mg/kg; NOAEL developmental = 500mg/kg [highest dose]	ARCO, 1993a ATX 92-0155
Gas Oil intermediate C11-C25 F-215 [68410-00-4] Sample # 091681	Presumed pregnant, Treated GD0-20, litters maintained to LD4	0, 50, 150, 500	Maternal decreased body wt and weight gain at 500mg/kg, decreased food consumption at 150, 500mg/kg. Decreased pup weight at 150 and 500mg/kg at LD0 and 4. Decreased pup survival at 500mg/kg. NOAEL maternal/developmental = 50mg/kg	ARCO, 1994j ATX 91-0263
VDF Diesel F-194 [68410-00-4] Sample # 091647	Presumed pregnant, Treated GD0-20, or GD5-7, litters maintained to LD4	0, 125 ,250, 1000 for GD 0-20 1000 for GD5-7	Maternal dermal irritation at all doses, decreased body wt and weight gain, food consumption at 250, 1000mg/kg. Decreased pup weight at all doses at LD0 and at LD4 for 250 and 1000mg/kg. Effects with doses at GD5-7 similar. Developmental NOAEL not established, <125mg/kg.	ARCO, 1994i ATX 91-1028
68783-08-4 Heavy Atmospheric Gas Oils				
Full range gas oil [68783-08-4] F-275 Sample # 094626	Presumed pregnant, Treated GD0-20, litters maintained to LD4	0, 50, 250, 500	Maternal dermal irritation at all doses, decreased body wt, food consumption at 250, 500mg/kg. Increased gestation length at 500mg/kg. Decreased number of total/live pups per litter at LD0 at 250, 500mg/kg; decreased number of litters and increased number of dead pups at 500mg/kg. NOAEL maternal = 50mg/kg [excludes skin irritation]; NOAEL developmental = 50mg/kg	ARCO, 1994h ATX 93-0071
Supplemental data from Gas Oils Assessment Document **Heavy atmospheric gas oil** [68915-97-9] Sample # 086271	Presumed pregnant, Treated GD0-19 sacrificed GD20	0, 8, 30, 125, 500	Decreased maternal body wt, food consumption at 125, 500mg/kg. Decreased thymus wt, increased liver wt, changes in serum chemistry/hematology at 500mg/kg. Non-significant increased preimplantation loss, decreased mean fetal body wt, incomplete ossification at 125, 500mg/kg. NOAEL maternal/fetal = 30mg/kg	Mobil, 1991 Study 64146 Used in PAC Model[a]

a Only developmental studies with treatment for GD0-19 and sacrifice at GD20 were used for PAC modeling activities [Murray et al, 2012: in press; see Appendix D].

6.1.6.1.1. Modeling results

Statistical models have been used to predict developmental effects for CAS numbers for which animal data are unavailable and for clarifying results of animal studies in which dose ranges are wide. The model was developed using only animal studies with treatment for GD0-19 days and sacrifice at GD20 (Murray et al., 2012a). Twenty of 76 reports for streams over a range of PAC categories were used to develop the models. Sensitive endpoints for developmental toxicity were fetal body weight, number of live fetuses per litter and resorptions per implantations. The lowest value of all the endpoints [highlighted in yellow] for each sample constitutes the overall sample $PDR_{10.}$ For most heavy fuel oil samples the most sensitive endpoint indicative of a 10% change in response from controls was live fetuses per litter. The study BMD_{10} is also the lowest of the original BMD_{10} endpoint values. The BMD_{10} calculations from developmental toxicity studies that meet the criteria for the modeling domain give similar values to the PDR_{10}s. Results of modeling are presented in Table 22. Samples [highlighted in blue] which have both PDR10 and BMD10 were used to develop the repeated dose model.

Table 22. Developmental Toxicity PDR_{10} and BMD_{10} for Heavy Fuels Oils by Endpoint

CAS RN/Sample No.	PDR10 or BMD10 mg/kg/day			Sample PDR10 mg/kg/day [Endpoint]	Sample BMD10 mg/kg/day [Endpoint}
	Fetal body weight	Live Fetuses per litter	Resorption per implants		
64741-45-3 Atmospheric Tower Residuals					
070904	219	38	76	38 [Live fetuses]	na
070907	1703	587	949	587 [Live fetuses]	na
060905	396	77	150	77 [Live fetuses]	na
060917	422	90	170	90 [Live fetuses]	na
64741-57-7 Heavy Vacuum Gas Oils					
091649	518	125	238	125 [Live fetuses]	na
091649 BMD	295	>75, <150	222	Na	>75<150 [Live fetuses]
085244	517	146	257	146 [Live fetuses]	na
85244 BMD	622	>125, <500	170	Na	>125<500 [Live fetuses]
091650	477	161	282	161 [Live fetuses]	na
091650 BMD	>250	>100, <250	>250	Na	>100<250 [Live fetuses]
085289	96	16	32	16 [Live fetuses]	na
086010	190	34	65	34 [Live fetuses]	na
086281	393	527	479	393 [fetal body wt]	na
086289	198	-	-	198 [fetal body wt]	na
086269	190	45	78	45 [Live fetuses]	na
091654	249	91	159	91 [Live fetuses]	na
091689	1146	224	494	224 [Live fetuses]	na
060906	338	65	124	65 [Live fetuses]	na
060916	501	102	192	102 [Live fetuses]	na
060922	600	174	298	174 [Live fetuses]	na
41:4	476	219	339	219 [Live fetuses]	na
28:10	327	107	174	107 [Live fetuses]	na
16.1	444	99	182	99 [Live fetuses]	na
25:15	600	175	298	175 [Live fetuses]	Na
1.8	339	66	125	66 [Live fetuses]	na
64741-61-3 Heavy Catalytic Cracked Distillates					

CAS RN/Sample No.	PDR10 or BMD10 mg/kg/day			Sample PDR10 mg/kg/day [Endpoint]	Sample BMD10 mg/kg/day [Endpoint}
	Fetal body weight	Live Fetuses per litter	Resorption per implants		
070909	40	8	14	8 [Live fetuses]	na
030928	15	3	5	3 [Live fetuses]	na
060912	43	13	21	13 [Live fetuses]	na
16:5	93	17	35	17 [Live fetuses]	na
64741-62-4 Catalytic Cracked Clarified Oils					
086001	14	5	8	5 [Live fetuses]	na
086001 BMD	13	>8,<30	4	Na	4 [Resorptions]
091645	5	5	5	5 [all endpoints]	na
091645 BMD			>0.05	Na	>0.05 [Resorptions]
086484	16	5	7	5 [Live fetuses]	na
086484 BMD	19	>0, <8	>0, <8	Na	>0, <8 [Live fetuses]
087277	34	5	10	5 [Live fetuses]	na
087278	27	5	8	5 [Live fetuses]	na
087279	60	12	21	12 [Live fetuses]	na
010923	11	2	3	2 [Live fetuses]	na
010924	87	81	118	81 [Live fetuses]	na
010929	9	1	3	1 [Live fetuses]	na
64741-67-9 Catalytic Reformer Fractionator Residuals					
060949	599	-	-	599 [fetal body wt]	na
64741-75-9 Hydrocracked Residuals					
060946	2000	2000	-	2000 [nontoxic]	na
64741-80-6 Thermal Cracked Residuals					
060915	1047	-	-	1047 [fetal body wt]	na
64741-81-7 Heavy Thermal Cracked Distillates					
083366	125	25	47	25 [Live fetuses]	na
083366 BMD	127	>8, <30	26	Na	>8, <30 [Live fetuses]
086181	51	15	27	15 [Live fetuses]	na
086181 BMD	66	31	35	Na	31 [Live fetuses]
086193	429	101	175	101 [Live fetuses]	na
086193BMD		250	>250	Na	250 [Live fetuses]
071021	14	2	4	2 [Live fetuses]	na
086161	100	20	37	20 [Live fetuses]	na
086194	88	15	26	15 [Live fetuses]	na
091653	128	26	56	26 [Live fetuses]	na
30-2	43	8	15	8 [Live fetuses]	na
8:1	125	28	49	28 [Live fetuses]	na
9:3	164	39	65	39 [Live fetuses]	na
2:6	182	35	68	35 [Live fetuses]	na
64742-59-2 Hydrotreated Vacuum Gas Oils					
071017	1400	296	549	296 [Live fetuses]	na
071026	421	104	182	104 [Live fetuses]	na
64742-78-5 Hydrodesulfurized Atmospheric Residuals					
071030	186	32	62	32 [Live fetuses]	na
64742-86-5 Hydrodesulfurized Heavy Vacuum Gas Oils					
091690	487	207	328	207 [Live fetuses]	na

CAS RN/Sample No.	PDR10 or BMD10 mg/kg/day			Sample PDR10 mg/kg/day [Endpoint]	Sample BMD10 mg/kg/day [Endpoint}
	Fetal body weight	Live Fetuses per litter	Resorption per implants		
21:1	935	205	390	205 [Live fetuses]	na
68333-22-2 Atmospheric Residuals					
071016	418	111	195	111 [Live fetuses]	na
68410-00-4 Crude Oil Distillates					
030932	2000	-	-	2000 [nontoxic]	na
030933	2000	-	-	2000 [nontoxic]	na
030934	1362	2000	1435	1362 [Fetal body wt]	na
091647	2000	-	-	2000 [nontoxic]	na
11:1	303	62	119	62 [Live fetuses]	na
091681	2000	1413		1413 [Live fetuses]	na
091681 BMD	>500	>500		Na	>500 [Live fetuses, fetal weight]
68476-33-5 Residual Fuel Oils					
086104	184	39	73	39 [Live fetuses]	na
086119	247	58	102	58 [Live fetuses]	na
070903	287	68	124	68 [Live fetuses]	na
68478-17-1 Heavy Coker Gas Oil and Vacuum Gas Oil Residuals					
071012	86	17	32	17 [Live fetuses]	na
071031	43	8	15	8 [Live fetuses]	na
12:19	87	18	32	18 [Live fetuses]	na
68512-62-9 Light Vacuum Residuals					
092009	234	39	80	39 [Live fetuses]	na
081022	2000	-	-	2000 [nontoxic]	na
68553-00-4 Fuel Oil No. 6					
070908	56	13	22	13 [Live fetuses]	na
030936	-	-	-	-	na
030937	13	2	4	2 [Live fetuses]	na
68783-08-4 Heavy Atmospheric Gas Oils					
071020	836	193	362	193 [Live fetuses]	na
071025	2000	-	-	2000 [nontoxic]	na
081009	632	327	461	327 [Live fetuses]	na
081010	632	372	461	372 [Live fetuses]	na
081011	612	242	391	242 [Live fetuses]	na
081012	568	230	370	230 [Live fetuses]	na
081013	2000	552	1176	552 [Live fetuses]	na
68955-27-1 Distillates, petroleum residues vacuum					
32:2	75	12	24	12 [Live fetuses]	na
36:1	2000	-	-	2000 [nontoxic]	na
70592-76-6 Intermediate Vacuum Distillates					
071011	496	129	229	129 [Live fetuses]	na
071018	2000	2000	-	2000 [nontoxic]	na
071029	773	229	405	229 [Live fetuses]	na
071032	691	263	382	263 [Live fetuses]	na
70592-77-7 Light Vacuum Distillates					

CAS RN/Sample No.	PDR10 or BMD10 mg/kg/day			Sample PDR10 mg/kg/day [Endpoint]	Sample BMD10 mg/kg/day [Endpoint}
	Fetal body weight	Live Fetuses per litter	Resorption per implants		
071015	704	114	275	114 [Live fetuses]	na
071022	223	49	94	49 [Live fetuses]	na
071023	233	59	108	59 [Live fetuses]	na
071027	452	116	216	116 [Live fetuses]	na
70592-78-8 Vacuum Distillates					
071014	112	22	41	22 [Live fetuses]	na
071019	305	55	109	55 [Live fetuses]	na
071024	227	43	81	43 [Live fetuses]	na
43:2	192	32	64	32 [Live fetuses]	na
1:1	183	29	59	29 [Live fetuses]	na
10:6	2000	786	1491	786 [Live fetuses]	na
70913-85-8 Solvent extracted, Vacuum Distilled Atmospheric Residuals					
070905	282	44	91	44 [Live fetuses]	na
060904	486	79	160	79 [Live fetuses]	na

Dash indicates data for this endpoint is outside model domain. No reliable predictions can be made for this endpoint.
Highlighted entries indicate definitive value selected for sample PDR10 or BMD10 as the lowest value causing 10% change in activity for the most sensitive endpoint.
"BMD" after the sample number indicates a BMD10 calculation based on developmental toxicity study values.
na = not applicable; no BMD10 was calculated because no developmental toxicology study was conducted on this sample.

PDR_{10} values show a range of responses generally correlated with PAC profiles that sometimes overlap between CAS RNs. Individual samples with the same CAS RN can present different values reflecting differences in crude oil and severity of processing. Table 23 presents CAS RN samples in order of average developmental PDR_{10} values organized by severity of effects from lowest PDR_{10} to highest correlated with each PAC profile.

Table 23. Modeled Developmental PDR10 Values for Heavy Fuel Oils from Most to Least severe within each CAS RN

CAS RN/ Sample No.	Developmental PDR10 mg/kg	Total 1-7 ring wt%[1]	ARC 1[2] (%)	ARC 2 (%)	ARC 3 (%)	ARC 4 (%)	ARC 5 (%)	ARC 6 (%)	≥ARC 7 (%)
64741-45-3 Atmospheric Tower Residuals									
070904	38 [Live fetuses]	5.4	0.0	0.5	1.1	1.1	1.1	1.1	0.5
060905	77 [Live fetuses]	2.4	0.0	0.0	0.5	0.8	0.5	0.5	0.1
060917	90[Live fetuses]	3.4	0.0	0.0	0.6	1.2	0.9	0.6	0.1
070907	587 [Live fetuses]	2.1	0.0	0.2	0.6	0.6	0.4	0.2	0.1
64741-57-7 Heavy Vacuum Gas Oil									
085289	16 [Live fetuses]	7.0	0.0	0.0	1.4	1.4	1.4	2.1	0.7
086010	34 [Fetal wt]	6.5	0.0	0.1	1.3	1.9	1.9	1.3	0.0
086269	45 [Live fetuses]	12.8	0.0	0.6	5.0	3.8	2.5	0.9	0.0
060906	65 [Live fetuses]	4.2	0.0	0.0	0.4	1.3	1.3	0.9	0.3
1:8	66 [Live fetuses]	4.2	0.0	0.0	0.4	1.3	1.3	0.9	0.3
091654	91 [Live fetuses]	8.8	0.1	0.4	4.0	3.0	0.9	0.4	0.0
16:1	99 [Live fetuses]	5.7	0.0	0.1	1.7	1.7	1.4	0.7	0.1
060916	102 [Live fetuses]	3.6	0.0	0.0	0.4	1.1	1.1	0.7	0.3

CAS RN/ Sample No.	Developmental PDR10 mg/kg	Total 1-7 ring wt%[1]	ARC 1[2] (%)	ARC 2 (%)	ARC 3 (%)	ARC 4 (%)	ARC 5 (%)	ARC 6 (%)	≥ARC 7 (%)
28:10	107 [Live fetuses]	6.6	0.0	0.3	1.9	2.5	1.3	0.6	0.0
091649	125 [Live fetuses]	8.1	0.1	0.3	3.0	2.0	2.0	0.7	0.0
085244	146 [Fetal wt]	6.2	0.0	0.1	2.5	1.9	1.2	0.5	0.0
091650	161[Live fetuses]	7.2	0.0	0.4	4.0	2.0	0.6	0.2	0.0
060922	174 [Live fetuses]	5.0	0.0	0.1	1.6	1.6	1.1	0.5	0.1
25:15	175 [Live fetuses]	5.0	0.0	0.1	1.6	1.6	1.1	0.5	0.1
086289	198 [Live fetuses]	15.8	0.0	0.7	1.0	11.6	1.7	0.8	0.0
41:4	219 [Live fetuses]	8.5	0.0	0.6	4.5	2.4	0.8	0.2	0.0
091689	224 [Live fetuses]	5.9	0.0	0.4	4.0	1.0	0.4	0.1	0.0
086281	393 [Live fetuses]	11.6	0.0	0.6	6.0	3.6	1.2	0.2	0.0
64741-61-3 Heavy Catalytic Cracked Distillates									
030928	3 [Live fetuses]	36.3	0.0	3.9	15.4	11.6	3.9	1.5	0.0
070909	8 [Live fetuses]	28.6	0.0	0.8	11.2	8.4	5.6	2.0	0.6
060912	13 [Live fetuses]	36.8	0.0	3.5	21.0	10.5	1.8	0.0	0.0
16:5	17 [Live fetuses]	40.6	0.0	6.2	28.7	5.3	0.4	0.0	0.0
64741-62-4 Catalytic Cracked Clarified Oils									
010929	1 [Live fetuses]	50.4	0.0	1.0	15.6	15.6	10.4	5.2	2.6
010923	2 [Live fetuses]	41.9	0.0	1.3	13.0	13.0	8.6	4.3	1.7
086484	5 [Live fetuses]	46.0	0.0	1.0	9.8	19.5	9.8	4.9	1.0
087278	5 [Live fetuses]	29.1	0.0	0.9	9.1	9.1	6.1	3.0	0.9
087277	5 [Live fetuses]	20.2	0.0	0.4	3.8	5.7	5.7	3.8	0.8
086001	5 [Live fetuses]	57.8	0	2.6	25.7	19.3	6.4	3.2	0.6
091645	5 [all]	66.7	0.0	0.7	10.0	30.0	20.0	6.0	0.0
087279	12 [Live fetuses]	19.6	0.0	0.8	6.1	6.1	4.0	2.0	0.6
010924	81[Live fetuses]	36.0	0.0	0.3	6.2	12.4	6.2	3.1	1.6
64741-67-9 Catalytic Reformed Fractionator Residuals									
060949	599 [Fetal wt]	50.9	3.9	44.1	2.9	0.0	0.0	0.0	0.0
64741-75-9 Hydrocracked Residuals									
060946	2000 [Non-toxic]	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
64741-80-6 Thermal cracked Residuals									
060915	1047 [Fetal wt]	4.6	0.0	0.0	1.3	2.2	0.9	0.2	0.0
64741-81-7 Heavy Thermal Cracked Distillates									
071021	2 [Live fetuses	61.1	0.0	6.3	44.1	6.3	4.4	0.0	0.0
30-2	8 [Live fetuses]	19.0	0.0	0.6	3.7	5.5	3.7	3.7	1.8
086194	15 [Live fetuses]	15.4	0.0	0.5	3.2	4.8	4.8	1.6	0.5
086181	15 [Live fetuses]	25.5	0.2	2.5	12.4	7.4	2.5	0.5	0.0
086161	20 [Live fetuses]	16.0	0.0	0.7	6.0	4.5	3.0	1.5	0.3
083366	25 [Live fetuses]	12.5	0.1	2.5	5.1	2.5	1.3	0.9	0.1
091653	26 [Live fetuses]	25.9	0.0	0.9	20.0	5.0	0.0	0.0	0.0
8:1	28 [Live fetuses]	17.0	0.0	0.5	6.6	5.0	3.3	1.3	0.3
2:6	35 {live fetuses]	9.2	0.0	1.0	4.0	2.0	1.0	0.9	0.3
9:3	39 [Live fetuses]	10.0	0.0	0.7	2.3	3.4	2.3	1.1	0.2
086193	101 [Live fetuses]	4.1	0.8	2.9	0.4	0.0	0.0	0.0	0.0
64742-59-2 Hydrotreated Vacuum Gas Oils									
071026	104 [Live fetuses]	5.8	0.0	0.5	1.7	1.7	1.2	0.6	0.1
071017	296 [Live fetuses]	3.0	0.0	0.6	0.9	0.6	0.6	0.3	0.0
64742-78-5 Hydrodesulfurized Atmospheric Residuals									
071030	32 [Live fetuses]	12.8	0.0	3.9	5.2	1.2	1.0	1.0	0.5
64742-86-5 Hydrodesulfurized Heavy Vacuum Gas Oils									
21:1	205 [Live fetuses]	3.1	0.0	0.4	1.1	0.7	0.5	0.3	0.1
091690	207 [Live fetuses]	7.1	0.1	0.7	3.0	2.0	1.0	0.3	0.0
68333-22-2 Atmospheric Residuals									
071016	111 [Live fetuses]	5.8	0.0	0.1	1.9	1.9	1.2	0.6	0.1
68410-00-4 Crude Oil Distillates									
11:1	62 {Live fetuses]	5.7	0.0	1.2	1.9	1.2	0.6	0.6	0.2
030934	1362 [Fetal wt]	5.3	0.0	1.7	1.7	1.1	0.6	0.2	0.0
091681	1413 [Live fetuses]	8.2	0.2	4.0	4.0	0.0	0.0	0.0	0.0

CAS RN/ Sample No.	Developmental PDR10 mg/kg	Total 1-7 ring wt%[1]	ARC 1[2] (%)	ARC 2 (%)	ARC 3 (%)	ARC 4 (%)	ARC 5 (%)	ARC 6 (%)	≥ARC 7 (%)
030933	2000 [nontoxic]	5.6	0.1	4.4	1.1	0.0	0.0	0.0	0.0
030932	2000 [nontoxic]	3.1	0.0	1.0	1.3	0.6	0.2	0.0	0.0
091647	2000 [nontoxic]	8.1	0.1	4.0	4.0	0.0	0.0	0.0	0.0
68476-33-5 Residual Fuel Oils									
086104	39 [Live fetuses]	13.7	0.0	1.5	7.3	2.9	1.3	0.6	0.1
086119	58 [Live fetuses]	8.7	0.0	2.6	2.6	1.8	0.9	0.6	0.2
070903	68 {live fetuses]	6.2	0.2	1.8	1.2	1.2	1.2	0.5	0.1
68478-17-1 Heavy Coker Gas Oil and Vacuum Gas Oils Residuals									
071031	7 [Live fetuses]	19.0	0.0	0.2	4.0	6.0	4.0	4.0	0.8
071012	17 [Live fetuses]	17.1	0.0	0.5	5.4	5.4	3.6	1.8	0.4
12:19	18 [Live fetuses]	17.1	0.0	0.5	5.4	5.4	3.6	1.8	0.4
68512-62-9 Light Vacuum Residuals									
092009	39 [Live fetuses]	3.8	0.0	0.0	0.7	0.7	0.7	1.0	0.7
081022	2000 [nontoxic]	3.2	0.1	2.2	0.9	0.0	0.0	0.0	0.0
68553-00-4 Fuel Oil No. 6									
030937	2 [Live fetuses]	35.9	0.0	2.3	13.0	9.8	6.5	3.3	1.0
070908	13 [Live fetuses]	20.4	0.0	2.1	8.4	6.3	2.1	1.3	0.2
68783-08-4 Heavy Atmospheric Gas Oils									
071020	193 [Live fetuses]	3.0	0.0	0.0	1.2	0.9	0.6	0.3	0.0
081012	230 [Live fetuses]	6.0	0.0	0.4	3.0	1.8	0.6	0.2	0.0
081011	242 [Live fetuses]	5.8	0.0	0.4	2.9	1.7	0.6	0.2	0.0
081009	327 [Live fetuses]	5.3	0.0	0.5	2.3	1.7	0.6	0.2	0.0
081010	372[Live fetuses]	5.3	0.0	0.5	2.3	1.7	0.6	0.2	0.0
081013	552 [Live fetuses]	2.4	0.0	1.0	1.0	0.2	0.1	0.1	0.0
071025	2000 [nontoxic]	5.3	0.1	3.5	1.7	0.0	0.0	0.0	0.0
68955-27-1 Distillates, petroleum residues vacuum									
32:2	12 [Live fetuses]	9.4	0.0	0.0	0.5	1.9	3.0	3.1	0.9
36:1	2000 [nontoxic]	0.7	0.0	0.0	0.0	0.2	0.4	0.1	0.0
70592-76-6 Intermediate Vacuum Distillates									
071011	129 [Live fetuses]	5.5	0.0	0.1	1.7	1.7	1.2	0.6	0.2
071029	229 [Live fetuses]	6.0	0.0	1.2	2.9	1.2	0.5	0.2	0.0
071032	263 [Live fetuses]	6.4	0.0	0.6	2.4	1.8	1.2	0.4	0.0
071018	2000 [nontoxic]	5.1	0.0	2.0	3.0	0.1	0.0	0.0	0.0
70592-77-7 Light Vacuum Distillates									
071022	49 [Live fetuses]	5.9	0.0	0.3	2.5	1.9	0.6	0.6	0.0
071023	59 [Live fetuses]	8.7	0.0	0.8	4.1	2.5	0.8	0.5	0.0
071015	114 [Live fetuses]	11.0	0.0	2.2	7.7	1.1	0.0	0.0	0.0
071027	116 [Live fetuses]	9.1	0.0	1.7	5.0	1.7	0.5	0.2	0.0
70592-78-8 Vacuum Distillates									
071014	22 [Live fetuses]	9.6	0.0	0.1	0.9	3.7	2.8	1.9	0.2
1:1	29 [Live fetuses]	3.5	0.0	0.0	0.0	0.1	0.6	1.4	1.4
43:2	32 [Live fetuses]	4.7	0.0	0.0	0.3	1.0	1.4	1.4	0.6
071024	43 [Live fetuses]	7.9	0.0	0.0	1.4	2.2	2.2	1.4	0.7
071019	55 [Live fetuses]	5.1	0.0	0.1	1.0	1.0	1.0	1.0	1.0
10:6	786 [Live fetuses]	0.7	0.0	0.0	0.2	0.2	0.2	0.1	0.0
70913-85-8 Solvent Extracted, Vacuum Distilled Atmospheric Residuals									
070905	44 [Live fetuses]	1.8	0.0	0.0	0.0	0.0	0.2	0.8	0.8
060904	78 [Live fetuses]	1.8	0.0	0.0	0.0	0.2	0.4	0.6	0.6

1 - Percent of DMSO-extractable PACs as determined by PAC-2 Method.

2 - ARC is "aromatic ring class". ARC 1 (%) is the weight percent of PACs that have 1 aromatic ring

Table 23 illustrates how modeled data can be used to estimate potential and comparative biological activity for streams with a PAC aromatic ring distribution profile whether or not animal data are available. For EU global hazard communication purposes under the 2008 Classification, Labelling and Packaging (CLP) regulation (EC 1272/2008, 2008), implemented in accordance with CONCAWE (2012), all CAS RNs in the Heavy Fuel Oil Components category carry the same hazard classifications. These classifications do not indicate toxic potency. However some CAS

RN streams or some samples within a group identified by a given CAS RN may be less toxic than others. Although toxic potency for individual samples can be ranked based on the modeled PAC profile, such ranking for these materials may have no practical significance as the blending and co-mingling of residual fuels after leaving the refinery obscure any provenance.

Table 24 presents the relationship between NOAELs/LOAELS from animal studies, PDR_{10} and BMD_{10} determinations and PAC content

Table 24. Comparison of Developmental Toxicity LOAEL/NOAEL with Range of Modeled Values and PAC Content

CAS No/Name.	LOAEL mg/kg	NOAEL mg/kg	PDR_{10} mg/kg	BMD_{10} mg/kg	DMSO Wt%[1]	Wt % 3-7 ring PAC[2]
64741-62-4 Cat Cracked Clarified Oils [4 studies]	1.0 - 50.0	0.05 - 10	1-81	>0.05, <8	19 – 67	19 – 66
64741-62-4 CCCO (010929) New study	25	5	1	Not calculated	52	49
64741-61-3 Heavy Cat Cracked Distillates	50	<50	3-17	Not calculated	28-41	28 – 41
64741-57-7 Heavy Vacuum Gas Oil [4 studies]	75-500	<75 - 125	16-393	>75, <250	4-17	4 - 16
64741-81-7 Heavy Thermal cracked Distillates [4 studies]	125 - >250	1.0 - 250	2 - 101	>8, 250	4 -55	0.4 – 55
68783-08-4 Heavy Atmospheric gas oil	250	50	193-2000	Not calculated	2 - 6	1-6
68410-00-4 Crude Distillate Oils [3 samples]	125 - >500	<125 - 500	62 -2000	>500 [1 sample]	3 - 8	1 - 4
64742-86-5 Hydrodesulfurized Heavy Vac Gas Oil	333	50	207	Not calculated	7.1	6.3
64741-45-3 Atm Tower Resid	1000	333	38-587	Not calculated	2 -7	2 - 7

1 - Wt % Total DMSO extract of tested and modeled samples
2 - Wt % 3-7 ring PAC of tested and modeled samples

Ranking by PDR_{10} indicates that in general, cracked substances had the greatest toxic potential compare to other substances in the category. These include catalytic cracked clarified oils (CAS RN 64741-62-4, heavy catalytic cracked distillates (CAS RN 64741-61-3), and heavy vacuum gas oils (CAS RN 64741-57-7) which tend to have higher content of 3-7 ring PACs in the aromatic profiles.

6.1.6.2. Reproductive Toxicity

Reproductive toxicity potential of heavy fuel oils can also be evaluated by combining relevant parameters from developmental toxicity studies with histopathological evaluations of reproductive

organs in 13 week repeat dose studies (Table 13) as recommended in the EPA HPV guidance document. The EPA guidance indicates that a reproductive toxicity study may not be required for certain petroleum substances if there is (1) a 90-day repeat-dose study in which the potential for effects on reproductive organs was assessed, and (2) a developmental toxicity study. Details of the developmental toxicity studies cited below are located in Section 6.1.6.1 and in Table 21.

No multigeneration reproductive toxicity studies are available for members of this category. However studies in which female rats were treated dermally, premating through mating and gestation to gestation day 20 [GD20] have been conducted on several samples of CAS RN 64741-57-7 Heavy Vacuum Gas Oils and on a coker heavy gas oil (CAS RN 64741-81-7). In addition two studies of catalytically cracked clarified oil (CAS RN 64741-62-4, aka clarified slurry oil, CSO) the potentially most toxic of all the heavy fuel oil category members, have been conducted with premating exposure of male and female Sprague Dawley rats separately to examine potential effects on gonadal function, mating behavior, fertility and conception rates in both sexes and estrus cycle in females (see Table 25, Hoberman et al., 1995a).

CAS RN 64741-45-3 Atmospheric Tower Residuals

Results of a dermal developmental toxicity study employing pregnant rats treated with 0, 50, 333 or 1000 mg/kg/day atmospheric residuum (CAS RN. 64741-45-3) from gestation day (GD) 0-20 showed decreased maternal body weight gain and increased gestational length [22.8 days versus 22.1 days control] at the maximum dose of 1000mg/kg (ARCO, ATX91-0227 1994g). Compound related decreased pup weights on Lactation days 0 and 4 were observed at 1000mg/kg. A NOAEL = 333mg/kg for female reproductive parameters can be assigned based on increased gestational length.

In a 4-week repeat dose dermal toxicity study of F-132 (ARCO, ATX 90-0066, 1992i) at treatment levels of 9.4, 235, and 940mg/kg/day, no adverse effects on weights of ovaries or testes or abnormal histological changes in reproductive organs were observed [see Section 6.1.3 Repeated Dose Toxicity].

CAS RN 64741-57-7 Heavy Vacuum Gas Oils

Test article F-197 (CAS RN 64741-57-7) was applied to the shaved backs of female rats from one week prior to mating through mating and gestation to GD20 at concentrations of 1.0, 241.0 and 965.0mg/kg/day (ARCO ATX 91-0131, 1994c). Females were mated to untreated males. Litters were maintained to lactation day (LD) 4. Increased vaginal discharge, decreased maternal body weight and weight gain, decreased food consumption and dermal irritation were observed in 241 and 965mg/kg dose groups. Implantation sites were reduced and no litters were delivered by females in the high dose group. At 241mg/kg the total number and number of live pups were decreased at LD0 and pup body weights were decreased at LD0 and LD4. The maternal and developmental NOAEL = 1.0mg/kg

Test article F-201, a hydrocracker feed (CAS RN 64741-57-7), was applied to the shaved backs of female rats from one week prior to mating through mating and gestation to GD20 at concentrations of 1.0, 250 and 1000mg/kg/day (ARCO ATX 91-0135, 1994a). Females were mated to untreated males. Litters were maintained to lactation day (LD) 4. One female in the 1000mg/kg group was sacrificed moribund. Increased vaginal discharge decreased maternal body weight and weight gain and decreased thymus weight was reported at 250 and 1000mg/kg groups. Food consumption was decreased at all dose levels. The number of implantation sites was decreased and no litters were delivered in the 1000mg/kg group. At 250mg/kg, there was decreased number

of implantation sites and the total number and number of live pups were decreased at LD0 and pup body weights were decreased at LD0 and LD4. The maternal and developmental NOAEL = 1.0mg/kg.

A similar study with comparable findings was performed in which test article F-196, a heavy vacuum gas oil, (CAS RN 64741-57-7) was applied to the shaved backs of female rats from one week prior to mating through mating and gestation to GD20 at concentrations of 1.0, 250 and 1000mg/kg/day (ARCO ATX 91-0130, 1994d). Females were mated to untreated males. Litters were maintained to lactation day (LD) 4. In treated females, red vaginal discharge was seen at 250 and 1000mg/kg and body weights, body weight gain and food consumption were decreased in these groups. Thymus size was significantly decreased at 250 and 1000mg/kg. No females given 1000mg/kg/day delivered litters although the number of implantation sites was comparable to controls. At 250mg/kg the number of total and live pups was decreased at LD0 and pup body weights were decreased at LD0 and 4. No significance differences in gestation length, number of implantation sites, external malformations, percentage of pups surviving to LD4 were seen at doses of 1.0 or 250mg/kg/day. The maternal and developmental NOAEL = 1.0mg/kg.

Test article F-276, also identified as hydrocracker feed (CAS RN 64741-57-7) was applied to the shaved backs of female rats from one week prior to mating through mating and gestation to GD20 at concentrations of 1.0, 250 and 500mg/kg/day (ARCO ATX 93-0073, 1994b). Females were mated to untreated males. Litters were maintained to lactation day (LD) 4. Dermal irritation was seen in all treated groups. Decreased maternal body weight and weight gain were seen at 250 and 500mg/kg and decreased food consumption seen between premating days -7 to -1 followed by increased relative food consumption. Developmental toxicity was expressed as decreased in number of total pups and live pups delivered per litter at 250 and 500mg/kg and decreased number of pups surviving to LD 4 in the 500mg/kg group. Average pup body weights decreased on LD0 at 250mg/kg and on LD0 and 4 at 500mg/kg. The maternal and developmental NOAEL = 1.0mg/kg.

Because there was such a wide range between the lowest adverse effect level of approximately 250mg/kg and the no effect level of 1.0mg/kg in the studies described above, the developmental toxicity study of Heavy Vacuum Gas Oil (HVGO) is included here to identify an intermediate NOAEL level for perspective. Pregnant females were treated with 0, 30, 125, 500 and 1000mg/kg/day HVGO (Mobil 1987i) from GD0 to GD19. Doses greater than 125mg/kg caused a decrease in mean maternal body weight which reflected decreased litter size for 500 and 1000mg/kg groups. Number of dams with viable fetuses was decreased in the 1000mg/kg group. Resorptions increased with dose. NOAEL for maternal and developmental effects = 125mg/kg.

In a 13-week dermal toxicity study of HVGO at treatment levels of 30, 125, 500 and 2000mg/kg/day no adverse effects were seen on testes or ovary weight at any dose level or histopathology of reproductive organs. Supplemental dermal studies of two vacuum distillates [F-128, F-129] that were administered for 4 weeks also did not report adverse effects on ovaries or testes [see Section 6.1.3 Repeated Dose Toxicity].

CAS RN. 64741-62-4 Catalytic Cracked Clarified Oils

To determine potential effects on gonadal function, reproductive organs and mating behavior, 0.1, 1, 10, 50 & 250 mg/kg/day of a clarified slurry oil (CAS RN. 64741-62-4) were applied dermally to male and female rats (Hoberman 1995a). Male rats were treated for 70 days before a seven-day cohabitation period with untreated virgin female rats. Separate groups of females were treated at the same dosages for 14 days prior to a 7 day mating period continuing until gestation day 0 (GD 0

identified as the day sperm was present in a vaginal smear or copulatory plug was observed in situ). Treated females were evaluated for estrous cycling during the 14 days prior to mating. Treatment of females ended at GD 0. All treated females and untreated females mated to treated males were examined daily for viability and clinical observations, and body weights were recorded on days 0, 6 and 14 of presumed gestation. On day 14 of presumed gestation, all female rats were sacrificed by carbon dioxide asphyxiation, and a gross necropsy of the thoracic and abdominal viscera was performed. Treated female rats were examined were examined for weight of uterus, ovaries, pituitary and brain. Pregnancy status was verified and uterine contents recorded. The uterus of each untreated rat was also examined for pregnancy, number and distribution of implantations, early resorptions and live and dead embryos. Male rats were killed following completion of cohabitation. Left testes were used to determine sperm concentrations and sperm motility, morphology and concentration was evaluated in sperm from the left cauda epididymis. No deaths and no skin reactions were caused by the test material. All absolute and relative organ weights were statistically comparable among the six dosage groups. There were compound-related effects on male body weights, body weight gains, and food consumption at doses of 10-250 mg/kg/day. Mating and fertility parameters were unaffected at any of the dose levels. There were no compound-related effects on any testicular parameter. Litter averages for corpora lutea, implantations, and live embryos and resorptions did not significantly differ among females mated with male animals from the six dosage groups. There were no dead embryos, and no dam resorbed all conceptuses. There were no adverse effects on reproductive parameters of treated females. Gonadal function, estrous cycle, mating behavior, conception rates and reproductive organ weights were comparable to controls resulting in a maternal reproductive NOAEL>250mg/kg and a systemic NOAEL = 10mg/kg/day due to decreased body weight gains at higher doses. The study directors concluded that the paternal systemic toxicity NOAEL = 1.0mg/kg and the reproductive NOAEL for the male rats was >250 mg/kg/day (no mating, fertility or testicular parameters in the male rats were affected by the highest dosage tested).

In a reproductive/developmental toxicity screen, female Sprague-Dawley rats were dermally exposed to catalytically cracked clarified oil, also identified as clarified slurry oil [CSO] (CAS RN. 64741-62-4, F-179) at dose levels of 0.05, 10, 250 mg/kg/day (ARCO, ATX 91-0155, 1994e). The test material was administered one week prior to the initiation of mating, throughout mating, and through Day 20 of gestation. Male rats to which the females were mated were not administered test compound. Food consumption and body weights were recorded throughout the premating, mating and gestation periods. On Day 4 of lactation, each female was sacrificed and the ovaries and uterine horns examined to determine the number of corpora lutea and implantation sites, respectively. Litters were observed during Days 0 –4 of lactation for signs of toxicity and mortality. Pups were examined daily for external abnormalities. On Days 0 and 4 of lactation, each pup was weighed and its sex was determined. On day 4 of lactation, all surviving pups were examined externally, sacrificed and discarded. No deaths occurred during the study. The study directors considered the following signs of maternal toxicity to be related to administration of the test material: a higher incidence of vaginal discharge at a dose of 250 mg/kg; decreased body weights, body weight changes, and food consumption at doses of 10 and 250 mg/kg; and decreased thymus size at a dose of 250 mg/ kg. Fertility and establishment of pregnancy and number of implantation sites was comparable in control and treated females. Signs of developmental toxicity considered to be compound-related were limited to the 250 mg/kg dose group; none of the females in this dose level delivered a litter. No adverse effects were seen between treated females that delivered a litter and controls for gestation duration, total and live pups, external appearance of pups, pup body weight, proportion of pups dead on lactation day 0 or surviving to lactation day 4 and sex ratio. The study directors concluded the no-observable-adverse-effect levels (NOAEL) maternal toxicity = 0.05 mg/kg and NOAEL developmental toxicity = 10 mg/kg.

Results of 13- week dermal toxicity studies of clarified slurry oil and supplemental studies with Syn Tower bottoms, another clarified slurry oil, and visbreaker residual did not demonstrate adverse effects on weights of ovaries or testes or abnormal histological findings for these organs.

CAS RN 64741-81-7 Heavy Thermal Cracked Distillates

Test article F-200, heavy coker gas oil (CAS RN 68471-81-7) was applied to the shaved backs of female rats from one week prior to mating through mating and gestation to GD20 at concentrations of 0, 0.10, 50 and 250mg/kg/day (ARCO ATX 91-0134 1994f). Females were mated to untreated males. Litters were maintained to lactation day (LD) 4. One death occurred and a higher incidence of vaginal discharge was observed in the 250mg/kg group. Decreased maternal body weight and weight gain was reported at 50 and 250mg/kg groups. Food consumption and thymus weight were decreased at 250mg/kg. Fewer implantations site were present and only one litter was delivered in the 250mg/kg group and pups did not survive to LD4. At 50 mg/kg there was decreased number of total and live pups at LD0 and pup body weights were decreased at LD0 and LD4. The maternal and developmental NOAEL = 0.10mg/kg.

Results of a dermal developmental toxicity study employing pregnant females treated with 0, 8, 30, 125, and 250 mg/kg/day heavy coker gas oil (HCGO, CAS RN 68471-81-7) (Mobil 1987g) from gestation day (GD) 0-19, termination on GD 20, demonstrated dose related decreases in mean maternal body weight gain, skin damage, changes in liver and thymus weights and clinical chemistry parameters at 125 and 250 mg/kg/day. Number of dams with total resorptions was 50% at 250 mg/kg. Litter size decreased and the number of resorptions increased at 125 and 250 mg/kg. NOAEL for maternal and developmental toxicity = 30 mg/kg.

Results of 13-week dermal toxicity studies on visbreaker gas oil and supplemental studies with two heavy coker gas oils did not demonstrate adverse effects on weights of ovaries or testes or abnormal histopathological findings for these organs. No adverse effects were reported on sperm counts or sperm morphology. Exposure to one heavy coker gas oil was associated with decreased epididymal weights which correlated with decreased body weight in males.

CAS RN 68410-00-4 Crude Oil Distillates

Different samples of crude oil distillates (CAS RN 68410-00-4 F-194 ARCO, 1994i; F-215 [ATX 92-0115, ARCO1993a] F-215 [ATX 91-0263] ARCO1994j]), were applied to the shaved backs of presumed pregnant rats from gestation day (GD) 0-19 or 0-20 at concentrations ranging from 50 to 500mg/kg/day and 1000mg/kg/day F-194 from GD 5-7. Developmental NOAEL for F-194 was less than the lowest dose of 125mg/kg due to decreased pup weight at all doses. F-215 [ATX 92-0155] had a developmental NOAEL = 500mg/kg the highest dose tested and another sample of F-215 [ATX 91-0263] had a NOAEL = 50mg/kg due to lower pup weights at 150 and 500mg/kg dose levels.

CAS RN 68476-33-5 Residual Fuel Oils

No developmental studies available. Repeat dose dermal toxicity studies (4 week and 13 week duration) at treatment levels ranging from 480 to 2480mg/kg/day did not demonstrate adverse effects on weights of ovaries or testes or any abnormal histopathological changes in reproductive organs at the maximum doses tested [see Section 6.1.3 Repeated Dose Toxicity].

CAS RN 68783-08-4 Heavy Atmospheric Gas Oils

Results of a dermal developmental toxicity study employing pregnant rats treated with 0, 50, 250 or 500 mg/kg/day atmospheric residuum (CAS RN. 68783-08-4, F-275) from gestation day (GD) 0-20 showed decreased maternal body weight gain and increased gestational length at the maximum dose of 500mg/kg (ARCO ATX93-0071 1994h). Decreased number of total and live pups/litter was seen at 250 and 500mg/kg and decreased number of litters and increased dead pups at 500mg/kg. NOAEL maternal and developmental = 50mg/kg.

Supplemental data: Related material *from Gas Oil Category Assessment Document*

Results of a dermal developmental toxicity study employing a compositionally similar heavy atmospheric gas oil (CAS RN 68915-97-9) from the Gas Oil Category in which pregnant females were treated with 0, 8, 30, 125 or 500 mg/kg/day from gestation day (GD) 0-19 showed decreased maternal body weight and body weight gain and other systemic parameters at 125 mg/kg and above (Mobil, 1991b). Evaluation of reproductive parameters in the 8 and 30mg/kg groups found no compound related effects. Some preimplantation losses in the 125 and 500 mg/kg groups and increase in mean number/percent resorptions were seen in the 500 mg/kg group. Other adverse effects on fetuses and pups correlate with direct maternal toxicity. NOAEL for both maternal systemic effects and developmental toxicity = 30 mg/kg.

In a 13-week dermal toxicity study of this HAGO [CAS RN 68915-97-9] at treatment levels of 30, 125 and 500mg/kg/day (Mobil, 1992d) no adverse effects were seen on epididymal or testicular sperm or reproductive organs [see Section 6.1.3 Repeated Dose Toxicity].

Conclusions

Review of results from a reproductive function assay and reproductive parameters in developmental toxicity studies addressing fertility, successful insemination and implantation demonstrate that these endpoints are not adversely affected by treatment with heavy fuel oil streams. Evaluation of reproductive organs and sperm morphology and motility from 13-week repeated dose studies consistently demonstrated no adverse effects on ovary or testes weights or abnormal histopathology or sperm.

The Hoberman et al., 1995a study indicated that reproductive endpoints (e.g., fertility and sperm production) were unaffected at 250 mg/kg/day, a dose at which foetal survival was severely compromised in a developmental toxicity study that extended to Lactation Day 4 (Hoberman et al, 1995b). Assuming that clarified slurry oil (CAS RN 64741-62-4), which has a high PAC content, is representative of other PAC-containing petroleum streams, it can be reasonably assumed that reproductive effects, such as fertility and sperm production, would not be sensitive endpoints of PAC-containing materials compared to developmental toxicity effects. The studies in which females were treated for a week prior to mating through mating and gestation to GD20 demonstrated that exposure to high concentrations of various samples of heavy vacuum gas oils (CAS RN 64741-57-7) did not adversely affect mating and establishment of pregnancy but did adversely affect successful completion of pregnancy and pup viability in a dose related manner at doses in the range of 250mg/kg – 1000mg/kg, doses at which maternal toxicity was also present However a developmental study with a heavy vacuum gas (treatment GD0-19) resulted in a NOAEL = 125mg/kg/day. The NOAEL for reproductive toxicity is not expected to be lower than the NOAEL for developmental toxicity because the most sensitive endpoints in either developmental or reproductive toxicity studies are likely to be effects on fetal survival and growth resulting from *in utero* exposure (Murray et al., 2012b). Indeed, for Heavy Fuel Oils the systemic toxicity levels in

the repeated dose studies [Section 6.1.3] are also below the no adverse effects levels for fertility and reproductive toxicity.

Table 25. Reproductive Toxicity Studies of Heavy Fuel Oil by the Dermal Route of Exposure to Sprague Dawley Rats

Category/Subgroup [CAS RN]	Sex/Duration	Dose/ mg/kg/day	Results	References
64741-45-3 Atmospheric Tower Residuals				
Atmospheric tower bottoms [64741-45-3] F228	Refer to Table 21		NOAEL maternal/developmental = 333mg/kg	ARCO, 1994g ATX 91-0227
64741-57-7 Heavy Vacuum Gas Oils				
Hydrocracker Feed F-201 [64741-57-7] Sample # 091654	Female rats only treated from 7 days premating + mating and GD0-20, litters maintained to LD4	0, 1.0, 250, 1000	Maternal decreased body wt, weight gain, increased vaginal discharge and decreased thymus weight at 250, 1000mg/kg. No litters at 1000mg/kg. At 250mg/kg, decreased implantation sites, decreased total/live pups per litter at LD0. Decreased pup weights at LD0 and 4 NOAEL maternal/developmental = 1.0mg/kg	ARCO, 1994c ATX 91-0135
Hydrocracker Feed F-276 [64741-57-7] Sample # 094627	Female rats only treated from 7 days premating + mating and GD0-20, litters maintained to LD4	0, 1.0, 250, 500	Maternal decreased body wt, weight gain at 250, 500mg/kg. No litters at 1000mg/kg. Decreased total/live pups per litter at LD0 at 250 and 500mg/kg. Decreased pup weights at LD0 and 4 at 500mg/kg, and at LD0 only for 250mg/kg NOAEL maternal/developmental = 1.0mg/kg	ARCO, 1994b ATX 93-0073
F-197 [64741-57-7] Sample # 091650	Female rats only treated from 7 days premating + mating and GD0-20, litters maintained to LD4	0, 1.0, 241, 965	Maternal decreased body wt, weight gain, increased vaginal discharge at 241, 965mg/kg. No litters at 965mg/kg. At 241mg/kg, decreased implantation sites, decreased total/live pups per litter at LD0. Decreased pup weights at LD0 and 4 NOAEL maternal/developmental = 1.0mg/kg	ARCO, 1994c ATX 91-0131
F-196 [64741-57-7] Sample # 091649	Female rats only treated from 7 days premating + mating and GD0-20, litters maintained to LD4	0, 1.0, 250, 1000	Maternal decreased body wt, weight gain and food consumption and decreased thymus size at 250, 1000mg/kg. No litters at 1000mg/kg. Decreased total/live pups per litter at LD0 and decreased pup weights at LD0 and 4 at 250mg/kg, NOAEL maternal/developmental = 1.0mg/kg	ARCO, 1994d ATX 91-0130
Heavy Vacuum Gas Oil [64741-57-7] Sample # 085244	Refer to Table 21		NOAEL maternal/developmental = 125mg/kg	Mobil 1987i Study 61801

Category/Subgroup [CAS RN]	Sex/Duration	Dose/ mg/kg/day	Results	References
64741-62-4 Catalytic Cracked Clarified Oils				
Clarified Slurry Oil [64741-62-4]	Males 70 days premating + 7 days mating Females 14 days premating + up to 7 days mating to GD0	0, o.1, 1.0, 10, 50, 250	Males: decreased body wt, weight gain and food consumption at 10-250mg/kg. No adverse effects on mating/fertility. NOAEL reproductive > 250mg/kg Females: decreased body wt, weight gain at 50, 250 mg/kg. No adverse effect on gonadal function, estrous cycles, mating. NOAEL reproductive > 250mg/kg	Hoberman et al, 1995a
F-179 Catalytically cracked clarified oil [64741-62-4] Sample # 091645	Female rats only treated from 7 days premating + mating and GD0-20, litters maintained to LD4	0, 0.05, 10, 250	Maternal decreased body wt, weight gain and food consumption at 10, 250mg/kg. Increased vaginal discharge and decreased thymus wt at 250mg/kg. NOAEL maternal = 0.05mg/kg No litters at 250mg/kg. No adverse reproductive/developmental effects at 0.05 or 10mg/kg. NOAEL developmental = 10mg/kg	ARCO, 1994e ATX 91-0155
68410-00-4 Crude Oil Distillates				
F-125 [68410-00-4]	Refer to Table 21		NOAEL fetal = 500mg/kg [highest dose tested]	ARCO, 1993a ATX 92-0155
Gas Oil Intermediate C11-C25 F-215 [68410-00-4]	Refer to Table 21		NOAEL maternal/ developmental = 50mg/kg	ARCO 1994j ATX 91-0263
F-194 VDF Diesel [68410-00-4]	Refer to Table 21		Decreased pup weight at all doses NOAEL = not established, <125mg/kg	ARCO, 1994i ATX 91-1028
68471-81-7 Heavy Thermal Cracked Distillates				
Heavy Coker Gas Oil F-200 [68471-81-7] Sample # 091653	Female rats only treated from 7 days premating + mating and GD0-20, litters maintained to LD4	0. 0.1, 50, 250	Maternal decreased body wt, weight gain at 50 and 250mg/kg. Increased vaginal discharge, decreased food consumption and thymus weight at 250mg/kg. Only 1 litter at 250mg/kg; pups did not survive to LD4. At 50mg/kg decreased total/live pups per litter at LD0, decreased pup weights at LD0 and 4. NOAEL maternal/developmental = 0.1mg/kg	ARCO, 1994f ATX 91-0134
Heavy Coker Gas Oil [64741-81-7]	Refer to Table 21		NOAEL maternal/developmental = 30 mg/kg.	Mobil 1987g
68783-08-4 Heavy Atmospheric Gas Oil				
Full range gas oil [68783-08-4]	Refer to Table 21		NOAEL maternal = 50mg/kg; NOAEL developmental = 50mg/kg	ARCO, 1994h ATX93-0071

Category/Subgroup [CAS RN]	Sex/Duration	Dose/ mg/kg/day	Results	References
Supplemental data from Gas Oils Category Assessment Document **Heavy Atmospheric Gas Oil** [68915-97-9] Sample #086271	Refer to Table 21		NOAEL maternal/fetal = 30mg/kg	Mobil 1991 Study 64146

6.2 Health Effects Other

6.2.1. Carcinogenicity: Dermal

Several dermal carcinogenicity studies on samples of catalytic cracked clarified oils have been reported (API, 1989a; McKee et al., 1990). Although carcinogenicity is not a required endpoint of the HPV program the results are useful to complete the toxicity profile of the Heavy Fuels Category. A tabulation of these studies and a summary table from a study by Bingham et al., 1980 can be found in the Robust Summaries (separate document).

Table 26. Summary of Mouse Skin Painting studies with Heavy Fuel Oil

Material Tested	Dosing Regime (No. of animals)	Duration	Result	Mean latency (weeks)	References
Catalytic-cracked clarified oil (CAS RN 64741-62-4)	25 µl 3 X week (40)	> 2 years	36/40 tumors	17	McKee et al, 1990
Catalytic-cracked clarified oil (CAS RN 64741-62-4) API 81-15. 10% in toluene	50µl 2 X day (100)	> 2 years	49/50 tumors (48 malignant; 1 benign)	22	API,1989a
Catalytic-cracked clarified oil (CAS RN 64741-62-4) API 81-15, 1% in toluene	50µl 2 X day (100)	> 2 years	45/50 tumors (44 malignant; 1 benign)	72	API,1989a
Catalytic-cracked clarified oil (CAS RN 64741-62-4) API 81-15. 0.1% in toluene	50µl 2 X day (100)	> 2 years	2/50 tumors (2 benign)	113	API,1989a

CONCAWE 1998

Catalytic cracked clarified oil [aka. clarified slurry oil] and diluted samples were tested in lifetime mouse [C3H/HeJ] skin painting studies and produced significant increases in tumor frequency at concentrations as low as 1.0%. The latency period required for appearance of tumors increased with greater dilution. Only the sample diluted to 0.01% did not induce tumors at higher frequency than control animals.

Parallel skin painting studies were performed with two vacuum residuum samples considered to read-across representatives of CAS RN 70913-85-9 [See Asphalt Category Assessment Document, API 2009]. One sample, API 81-13 was only weakly carcinogenic inducing tumors in 5/50 mice with a long latency period of 113 weeks and the other sample API 81-14 did not produce tumors in greater frequency than those of negative controls, 2/50 mice with a latency of 120 weeks (API, 1989a).

Initiation/Promotion: To identify the mechanism by which catalytic cracked clarified oil [API 81-15] caused skin tumors an initiation promotion study was performed. The test material was applied at concentration of 1.0% in toluene to the shaved backs of CD-1mice. In the initiation phase 30 mice were treated dermally, once a day for 5 consecutive days with 50 µl of 1.0% test material in toluene. After a 2-week rest period, all mice were treated twice weekly with phorbol-12-myristate-13-acetate (PMA) a known tumor promoter for 25 weeks. Significant tumor initiating activity was detected in 26/30 mice with a mean latency of 16 days. In the promotion phase, catalytic cracked clarified oil did not increase the incidence of animals with histologically confirmed tumors but a

significant increase in the number of animals with masses and shortened latency times suggested possible weak promotion activity (API 1989b).

In a parallel initiation promotion studies performed with the vacuum residual samples API 81-13 and 81-14 diluted to 50% in toluene did not demonstrate either initiating or tumor promoting activity (API, 1989b)

Conclusions: Skin painting studies of the cracked residuum material, clarified slurry oil demonstrated that materials with a high content of PACs are dermal carcinogens and act primarily by initiating tumor development. Results from vacuum residuum samples in the Asphalt Category Assessment Document indicated these materials with a different distribution of - PAC were not dermal carcinogens. Although the entire weight % of DMSO extractable aromatics is usually measured in dermal carcinogenesis studies in mice results of the Optimized Ames assay described in Section 6.1.3 combined with analytical profile of 1-7 ring PAC can be used to predict the likelihood of tumor formation in skin painting studies.

7.0 HUMAN EXPOSURE SUMMARY

7.1 Occupational Exposure

Manufacture and transport of HFOs and residual fuel oil products is done in closed systems and typically at elevated temperatures thus limiting worker exposure. However, storage of HFO under these same conditions can result in formation and accumulation of hydrogen sulfide in enclosed spaces. An enforceable occupational exposure limit of 20 ppm (ceiling value) for hydrogen sulfide has been established (OSHA, 2011). A voluntary standard for occupational exposure to hydrogen sulfide of 1 PPM (8-hour time weighted average) and 5 PPM (15-minute short term exposure) has been recommended by ACGIH (2010).

The long history of petroleum refining has resulted in the development of recommended practices (RP) and standards (STD) to improve safety within the facilities. API has been a leader in developing these standards for both Upstream and Downstream operations. Listed below are groups of STDs and RPs that help ensure safe operation of the plant and reduce exposures to workers and the surrounding community.

API PERSONNEL SAFETY SET

PERSONNEL SAFETY INCLUDES THE FOLLOWING API STANDARDS: STD 2217A, RP 2016, STD 2220RP 2221, RP 54, RP 74, STD 2015

API PROCESS SAFETY SET

PROCESS SAFETY INCLUDES THE FOLLOWING API STANDARDS: PUBL 770, PUBL 9100, RP 751 RP 752

API SAFETY & FIRE SET

SAFETY AND FIRE - INCLUDES THE FOLLOWING API STANDARDS: 54, 74, 751, 752, 770, 2001, 2003, 2009, 2015, 2016, 2021, 2021A, 2023, 2026, 2027, 2028, 2030, 2201, 2207, 2210, 2214, 2216, 2217A 2218, 2219, 2220, 2221, 2350, 2510A, 9100

There are many specific laws and regulations are in place to limit occupational exposure and environmental release of HFO substances and residual fuel oil products. These include;

1. Occupational Safety and Health Act (29 CFR 1910)
2. Marine Occupational Safety and Health Standards (46 CFR 197)
    a. International Convention for the Safety of Life at Sea (74 Fed. Reg. 30, 612 -June 26, 2009)
3. Hazardous Materials Transportation Act (49 CFR 171)
4. Clean Water Act
    a. Oil Spill Prevention, Notification and Cleanup
        i. 30 CFR 250.203, 250.204, 254 Oil Spill Contingency Plan
        ii. 33 CFR Part 153 Control of Pollution by Oil and Hazardous Substances
        iii. 33 CFR Part 154 Facilities Transferring Oil or Hazardous Material in Bulk
        iv. 33 CFR Part 156 Oil and Hazardous Material Transfer Operations
        v. 40 CFR 110 Discharge of Oil
        vi. 40 CFR 112 Oil Pollution Prevention
5. Clean Air Act
    b. National Emission Standards for Hazardous Air Pollutants
        i. 40 CFR Part 63, Subpart Y National Emission Standards for Marine Tank Vessel Loading Operations

HFOs are used mainly as marine fuel for large diesel engines or boilers. They are also used for industrial and commercial heating as well as in the production of steam and electricity in power plants. Skin and inhalation exposures to HFOs may occur during its production, storage, distribution and use and during maintenance of the equipment. Due to the physicochemical properties of HFOs, the dermal route is the primary route of exposure. A method for measuring dermal exposure was recently developed using wipe sampling and measuring phenanthrene and naphthalene as markers of HFO exposure (Yvette et al., 2011). In that study, measurement surveys were carried out in four different types of facilities: oil refineries, distribution terminals, energy providers, and an engine building and repair company. Dermal wipe samples were collected from different anatomical regions: neck, hands, and forearms. The publication reported that, “The frequency of tasks with potential for dermal HFO exposure was generally low at these facilities, with the exception of the distribution terminals and the engine building and repair site. The geometric mean (GM) dermal load on the hands was ~0.1 μg cm−2 for both the left and right hand and 0.013 and 0.019 μg cm−2 for the left and right forearm, respectively. With one exception, all results from the neck samples were below the limit of detection. The highest dermal loads for the hands and forearms were found in the engine building and repair facility (hands: GM = 1.6 μg cm−2; forearms: GM = 0.41 μg cm−2). The tasks with the highest dermal loads were the maintenance (hands: GM = 1.7 μg cm−2) and cleaning tasks (hands: GM = 0.24 μg cm−2).” In characterizing the overall results of their study, Yvette et al., stated that, “Actual dermal loads were low when compared with workplace dermal exposure measurements reported by other researchers for similar scenarios with other substances. This may be explained by high compliance of gloves use by workers during HFO handling tasks and likely avoidance of contact with HFO due to its high viscosity and the requirement to keep HFO at elevated temperatures during storage, transport, and use.”

7.2 Consumer Exposure

There are no direct consumer uses of HFOs or residual fuel oils.

7.3 Exposure to Children

There are no anticipated exposures to children.

8. CATEGORY ANALYSIS CONCLUSIONS

The Heavy Fuel Oils (HFOs) category includes two finished products (residual fuels) and the primary refinery streams from which they are blended. The residual fuels are low-grade fuels primarily used in industrial boilers and other direct source heating applications (e.g., blast furnaces) and as a fuel for large marine diesel engines. The residual fuels are products that consist primarily of the residuum of the refining process after virtually all of the higher-quality hydrocarbons have been removed from crude oil feedstock. Members of the heavy fuel oils category are a diverse group of substances that encompass hydrocarbons with a wide range of molecular weights, with carbon numbers ranging from C7 to ≥C50 and boiling points between 250 – 1112 °F (121 - 600 °C) [EPA, 2004] or 350-650^{0}C [CONCAWE, 1998]. Data from over 50 HFO samples submitted by US companies for the HPV Challenge program had a boiling range from 152 ≥ 1327^{0}F (67 ≥ 719^{0}C). However, "typical" heavy fuel oils are C7 to > C50 with the low carbon numbers and boiling temperatures being associated with lighter weight "cutter" streams (CONCAWE, 1998). Because they are complex substances composed of relatively high molecular weight compounds, the materials in this category are typically not defined by detailed compositional information but instead by process history, physical properties, and product use specifications (ASTM, 2003).

Physical-Chemical Properties: Members of the Heavy Fuel Oil Category do not have sharply-defined melting points, but are viscous substances with pour points typically <30°C. Their individual constituents generally fall in the C20 to ≥C50 range, but this is influenced by refinery practices and the blending of these residuals with gas oils or similar low viscosity fractions to enhance the flow characteristics. Therefore, small quantities of low-end molecular weight hydrocarbons for some category member have been reported as low as C7. However, flash point specifications for heavy fuel oil products (>60°C or >140°F) would restrict the amount of these C7 hydrocarbons. This blending practice influences the physical-chemical characteristics and creates a diverse group of petroleum streams. The total vapor pressure of heavy fuel oils would normally be below measurable limits, but individual constituents representing the low molecular weight fractions may show measurable vapor pressures in their pure state. For blended fuels the vapor pressure of two samples were measured at < 0.013 kPa and 2.0 kPa. Partition coefficients representing the majority of compounds in the C7 to > C50 range are >6, but individual hydrocarbons representing the low-end molecular weight constituents may range from 1.7 to >6. Water solubility would be expected to be low for these substances, and studies have reported total dissolved hydrocarbons from <1 mg/L to approximately 6 mg/L in aqueous preparations of heavy fuel oils.

Environmental Fate: When heavy fuel oil enters the environment the individual constituents partition to various environmental compartments in accordance with their own physical-chemical properties. Fractions of heavy fuel oil < C20 may dissolve in water or evaporate to the atmosphere. Heaviest fractions may float or sink depending on density relationships, and become incorporated into soils/sediments. Some compounds may engage in direct photolytic reactions if they receive sufficient energy from sunlight to effect the chemical reactions. Others may undergo indirect photodegradation with photosensitized oxygen compounds in the troposphere with reaction rates from <0.1 days for volatile components to 5.2 days for components with higher carbon number distribution. Components of heavy fuels are stable to hydrolysis and this reaction is not a fate pathway for dissolved fractions. However, constituents of heavy fuel oils that dissolve become

available for biodegradation. Biodegradation rates are related to molecular weight and structural conformation, with the lower fractions being first to be utilized by microbes due to their bioavailability. From spill events, biodegradation of the different molecular species follows a specific order and is influenced by temperature, dispersion, and available nutrients.

Environmental Effects: When the acute aquatic toxicity values for heavy fuel oil and heavy fuel oil blending streams were compared on the basis of the loading rates of water accommodated fractions, acute toxicity endpoints were always >100 mg/L. In some instances, no adverse effects were observed at the maximum loading rate of 1000 mg/L. Based on the limited data for the category members, algae appeared to be the more sensitive aquatic species. The lowest EL50 values for algae fell within the range of 10 to 30 mg/L when evaluated on the basis of growth biomass. Since members of the Heavy Fuel Oils category are commonly blended with lower molecular weight petroleum substances, ecotoxicity data from the gas oil and kerosene categories were also considered. Gas oil and kerosene streams typically show greater toxicity due to the higher solubility of their constituent compounds with values in the range of 1 to 100 mg/L on the basis of loading rates. Using the range of 1 to 100 mg/L for read-across to all members of the heavy fuel oil category may overestimate the aquatic toxicity of the category members, but conservatively reflects a potential toxicity based on consideration of the variable nature of these substances. For chronic aquatic toxicity, test data on gas oils may be used as read-across for the heavy fuel oil category because many of the heavy fuel oil streams are blended with middle distillates or by definition overlap with middle distillates at the low-end range of their molecular weight hydrocarbons. The lowest NOELR and LOELR were 0.05 mg/L and 0.10 mg/L, respectively, for a 21-day *D. magna* reproduction study.

Human Health Effects: Substances in the Heavy Fuel Oil Category demonstrate low oral and dermal toxicity, minimal eye irritation, minimal to moderate skin irritation with single exposures and are not skin sensitizers.

Genetic toxicity: *In vitro* studies demonstrate that streams in the heavy fuel oil category are generally mutagenic when tested in specifically modified Salmonella assays. The level of activity is related to PAC content over a continuum from low activity in streams containing less biologically active PAC to high activity in streams derived from cracked stocks with higher aromaticity. *In vivo* studies evaluating cytogenetic damage in a selection of streams in the Heavy Fuel Oil category indicate most of these materials, often those with substantial PAC and regardless of processing do not induce significant increases in chromosome damage or increased micronuclei in bone marrow cells regardless of exposure route. This conclusion is further supported by extensive testing of other PAC category petroleum-derived streams (aromatic extracts, asphalt, crude oils and gas oils) in bone marrow chromosome and micronucleus assays that demonstrated that these substances did not induce significant cytogenetic damage in these test systems regardless of route of exposure (McKee et al, 2010 abst.; McKee et al, 2012).

Repeat Dose and Developmental Toxicity endpoints have been evaluated using both animal toxicity studies and modeling based on PAC distribution profiles to assess biological effects.

Repeated Dose dermal studies of heavy fuel oils indicate that toxicity induced by these streams when present affected essentially the same organ systems (liver, spleen, thymus and bone marrow). Overall LOAEL range for 13 week studies are 5-500mg/kg and NOAELs of 1.06 – 125mg/kg. The most severe toxicity was observed with clarified slurry oils (CAS RN 64741-62-4) with LOAELs of 5 -10.6 and NOAELs of 1.06 to <8mg/kg. None of the heavy fuel oil streams

tested induced adverse histological changes in reproductive organs or sperm number or morphology when these parameters were evaluated. In general, cracked substances had the greatest toxic potential compare to other substances in the category.

Results of Developmental toxicity studies for heavy fuel oils indicate that the most severe adverse fetal effects appear in the cracked residuum, clarified slurry oil [CAS RN 64741-62-4] with a range of values of NOAEL = 0.05 to 10mg/kg and LOAEL = 1.0 to 10mg/kg. Less severe fetal toxicity was seen in developmental LOAELs ranging in general from 30mg/kg for a heavy coker gas oil Table 14 illustrates how modeled data can be used to rank and compare severity of biological activity for streams with a PAC aromatic ring distribution profile whether or not animal data are available [CAS RN 64741-81-7] to 1000mg/kg for an atmospheric tower residual [CAS RN 64741-81-7]. All developmental toxic effects were associated with maternal toxicity. One sample of crude oil distillate CAS RN 68410-00-4 (F215) caused no fetal toxicity at doses as high as 500mg/kg with maternal toxicity at 250mg/kg. Overall these data indicate that streams derived from cracked stocks tend to induce greater developmental and maternal toxicity. However fairly wide dose ranges sometimes produce overlapping results and make it difficult to fully define non-toxic levels.

Results from a reproductive function assay and assessment of reproductive parameters in developmental toxicity studies addressing fertility, successful insemination and pregnancy as well as evaluation of reproductive organs and sperm in 13 week studies demonstrate that these are not the most adversely affected endpoints by treatment with heavy fuel streams. Studies of several vacuum distillates in which females were treated for a week prior to mating through mating and gestation to GD20 demonstrated that exposure to high concentrations did not adversely affect mating and pregnancy but did adversely affect successful completion of pregnancy and pup viability in a dose related manner at doses in the range of 250mg/kg – 1000mg/kg doses at which maternal toxicity was also present. These values are generally higher than affected dose levels seen in developmental studies. Since the most sensitive endpoints for developmental or reproductive toxicity are expected to be effects on fetal survival and growth resulting from in utero exposure the NOAEL for reproductive toxicity are not expected to be lower than the NOAEL for developmental toxicity.

Modeled data based on PAC aromatic ring distribution profile of streams has been developed for repeated dose and developmental toxicity evaluation. The PDR_{10} value is the dose level at which a 10% change in response from control value for a given endpoint is seen for a specific sample. For heavy fuel oils, the PDR10 values correlate reasonably well with the LOAEL and NOAEL derived from animal data and indicate that cracked stocks with higher 3-7 ring aromatic content have the greatest toxic potential. We believe that use of this method can prove valuable in estimating potential and comparative biological activity for materials for which animal data are not available or where dose levels are very widely spaced.

Dermal carcinogenicity studies performed with catalytically cracked clarified oil [CAS RN 64741-62-4] demonstrated that materials with a high content of PACs are dermal carcinogens and act primarily by initiating tumor development. Read-across results from whole vacuum residuum samples in the Asphalt Category Assessment indicated these materials with a different distribution of PAC were not dermal carcinogens. Thus, the PAC content and aromatic ring distribution profiles play a significant role in skin cancer in mice.

Overall, the materials in the Heavy Fuel Oil Category are not acutely toxic but can induce levels of systemic and developmental toxicity with repeated doses that are linked to the concentration and distribution profiles of 1-7 ring polycyclic aromatic compounds. These distributions and

concentrations vary by crude oil basestocks and processing steps within and between CAS RNs. Animal studies provide toxicity data on a limited number of samples but identification of definitive toxic and non-toxic doses can be limited by the range of doses selected for each study. Modeling of dose levels for sensitive endpoints employing the PAC profile for each sample will provide a method of predicting the dose-response and allow estimation of relative toxicity for CAS RNs for which animal data are not available. Thus, heavy fuel oils are considered a single category. Mammalian repeat dose and developmental toxicity of HFO members depends on their PAC profile. There is a recognizable distinction between straight-run and cracked HFOs in the amount of DMSO extractable PAC and toxicity values (NOAEL/PDR10s) with cracked HFOs generally showing greater toxicity. However there is no difference in the risk management of HFOs based on PAC content. . For EU global hazard communication purposes all CAS RNs in the Heavy Fuel Oil Components category carry the same hazardous classifications (EC 1272/2008, 2008; CONCAWE, 2012).

Human exposure: Manufacture and transport of HFOs and residual fuel oil products is done in closed systems and typically at elevated temperatures thus limiting worker exposure. However, storage of HFO under these same conditions can result in formation and accumulation of hydrogen sulfide in enclosed spaces. An enforceable occupational exposure limit of 20 ppm (ceiling value) for hydrogen sulfide has been established (OSHA, 2011). A voluntary standard for occupational exposure to hydrogen sulfide of 1 PPM (8-hour time weighted average) and 5 PPM (15-minute short term exposure) has been recommended by ACGIH (2010).

HFOs are used mainly as marine fuel for large diesel engines or boilers, in industrial and commercial heating and in the production of stream and electricity in power plants. Due to the physicochemical properties of heavy fuel oils, the dermal route is considered the primary route of exposure. Results of a recent dermal wipe study conducted in oil refineries, distribution terminals, energy providers and an engine building and repair company concluded that actual dermal loads [neck, hands, forearms] were low when compared with workplace dermal exposure measurements reported by other researchers with other substances under similar conditions. The authors suggested that these findings may be explained by high compliance of glove use by workers and likely avoidance of contact with HFO due to its high viscosity and maintenance at elevated temperature during storage, transport and use. Specific laws and regulations to limit occupational exposure and environmental release of HFO substances and residual fuel oil products are cited in Section 8.1 above.

There is no direct consumer use of heavy fuel oils or residual fuel oils and exposures to children are not anticipated.

In conclusion, the information provided in this Heavy Fuel Oils Category Assessment Document is sufficient to characterize physicochemical properties and evaluate the environmental and human health hazards of heavy fuel oil substances and residual fuel oil products in accordance with the mandate of the EPA HPV voluntary testing program.

9.1 Data Matrix for Heavy Fuel Oils: Physical Chemical Properties, Environmental Fate and Environmental Effects

Endpoint		Measured Results	Predicted Results
Physical Chemical Properties			
Melting Point (°C)		No sharply defined melting points	
Pour Point (°C)		-2^0C to 35^0C	Exist at ambient temperature as dense, viscous oils
Freezing Point (°C)		NA	NA
Boiling Point (°C)		237^0C to 611^0C Actual mean initial to mean final BP for 54 API samples	Boiling range of 350 to 650°C is typical for heavy fuel oils having constituent compounds in the C20 to C50 range [CONCAWE, 1998] By their CAS definitions, the boiling point distribution ranges from 121 to 600°C [EPA, 2004]. The initial and/or final boiling points of constituent streams could be higher or lower than the typical range due to the manufacturing processes used.
Vapor Pressure		<0.013 kPa and 2.0 kPa measured at 20 or 21°C.	Vapor pressures of individual constituent compounds in heavy are extremely low and below measurable levels using standard guideline methods. Estimated vapor pressures that would be representative for compounds of those carbon chain lengths of C20 –C50 ranged from $1x10^{-8}$ kPa to $5x10^{-20}$ kPa. Estimated vapor pressures of lower molecular weight compounds that are representative of potential cutter stock streams ranged from 0.007 kPa to 9 kPa.
Partition Coefficient Log Kow			Modeled estimates of log Kow values for carbon chain lengths of C7 to C50 covering representative structural hydrocarbon and non-hydrocarbon compounds expected to exist in heavy fuel oils fell within a range from 1.7 to 25. For typical heavy fuel oil constituents covering carbon numbers C20 to C50, standard guidelines for measuring log Kow would not produce accurate measurements.
Water Solubility[1] (mg/L)		<1 – 6mg/L	A range of total dissolved hydrocarbons in the aqueous fraction of heavy fuel oil:water mixtures has been reported as <1 to approximately 6 mg/L. The dissolved hydrocarbon concentration is affected by the oil:water ratio, the carbon number distribution of the heavy fuel oil, and the composition of the hydrocarbons in the heavy fuel oil.
Environmental Fate			

Endpoint		Measured Results	Predicted Results
Photodegradation, OH^- reaction $T_{1/2}$ (h or d)			Substances in heavy fuel oil category would not persist in the atmosphere should conditions exist whereby they partition to the air. Reaction rates calculated for indirect photodegradation ranged from <0.1 days to approximately 5.2 days for a variety of hydrocarbon and heterocyclic compounds covering carbon numbers from C7 to C50.
Stability in Water			Substances in this category will be stable and not react with water
Transport between Environmental Compartments			Individual compounds of a heavy fuel oil will partition in accordance with their own physical-chemical properties. For the low molecular weight hydrocarbon fractions of heavy fuel oil, the atmosphere is the principal environmental compartment to which they will partition. Some of the heterocyclic compounds that have significant water solubility values will partition to the water. As the molecular weights of the individual components increase to the range considered typical of heavy fuel oil (i.e., C20 to >C50), the low volatility and low water solubility prevent these constituents from entering the atmosphere or dissolving in water at greater than minimal levels.
Biodegradation classification			Heavy fuel oils would not be expected to pass the criteria for ready biodegradability when assessed using standard guideline protocols. However, hydrocarbon and many heterocyclic compounds have been shown to be utilized by microbial communities as an energy source. These constituents in heavy fuel oils may be considered inherently biodegradable. Their rates of consumption by microbes depends upon physical factors associated with weathering to aid in dispersion as well as the availability of nutrients and oxygen for the microbial communities.
Environmental Effects			
Acute Fish LL50 (mg/L WAF loading rate)		CAS RN 68476-33-5 light Rainbow trout WAF 96-h LL50 >1000 CAS RN 68476-33-5 heavy Rainbow trout WAF 96-h LL50 >100 < 1000 No. 6 fuel oil Bluegill OWD	Using a toxicity range of 1 to 100 mg/L on the basis of loading rate for read-across to all category members provides a conservative assessment of the acute ecotoxicity of these substances to fish based on the potential contribution of low-end molecular weight hydrocarbons originating in some HFO streams or cutter stocks added to finished fuels.

Endpoint		Measured Results	Predicted Results
		96-h LL50 >10,000	
Acute Daphnia EL50 (mg/L WAF loading rate)		CAS RN 68476-33-5 light Daphnia magna WAF 48-h EL50 >1000 CAS RN 68476-33-5 heavy D. magna WAF 48-h EL50 >220 < 460 No. 6 fuel oil D. magna OWD 48-EL50 >10,000	Using a toxicity range of 1 to 100 mg/L on the basis of loading rate for read-across to all category members provides a conservative assessment of the acute ecotoxicity of these substances to *Daphnia magna* based on the potential contribution of low-end molecular weight hydrocarbons originating in some HFO streams or cutter stocks added to finished fuels
Algae EL50 (mg/L WAF loading rate) Raphidocelis subcapitata		CAS RN 68476-33-5 light WAF 96-h ELr50 >100 <300 96-h ELb50 >3 <10 CAS RN 68476-33-5 heavy WAF 96-h ELr50 >30 <100 96-h ELb50 >30 <100 No. 6 fuel oil OWD 96-h ELb50 > 5,000	Using a toxicity range of 1 to 100 mg/L on the basis of loading rate for read-across to all category members provides a conservative assessment of the acute ecotoxicity of these substances to algae based on the potential contribution of low-end molecular weight hydrocarbons originating in some HFO streams or cutter stocks added to finished fuels.
Chronic toxicity to aquatic invertebrates (mg/L WAF loading rate)			For heavy fuel oil streams consisting of hydrocarbon compounds having principal carbon chain lengths ≥C15, the NOELR is expected to be 1000 mg/L. For category members that may be blended with cutter stocks of middle distillates and for heavy fuel oil streams having a large proportion of their hydrocarbon constituents below C15, chronic toxicity to aquatic invertebrates may be read across from studies on middle distillates (gas oils). For those heavy fuel oil streams, the chronic NOELR is 0.05 mg/L.

WAF = Water Accommodated fraction; OWD = Oil-water dispersion

9.2 Data Matrix for Heavy Fuel Oils: Human Health Effects

CAS RN	Acute Oral Rat (mg/kg)	Acute Dermal Rabbit (mg/kg}	Repeated Dose LOAEL/NOAEL (mg/kg)	Genetic Toxicity *In vitro*	Genetic Toxicity- *In vivo*	Developmental Toxicity Dermal LOAEL/NOAEL (mg/kg) [1]	Reproductive toxicity [2]
Read Across Values for Untested Substances	LD_{50} >5000	LC_{50} >2000	13 week studies LOAEL = 5 – 500 NOAEL = 1.06 - 125	All CAS RN are considered positive with metabolic activation unless testing of individual samples in Salmonella gives negative results.	All CAS RN are considered negative for cytogenetic effects.	LOAEL = 1.0 – 1000 NOAEL = 0.05 - 500	Developmental toxicity values can be read across
64741-45-3	LD_{50} >5000	LC_{50} >2000	4 week study NOAEL = 928 [highest dose]			LOAEL = 1000 NOAEL = 333 23-200 [4 samples]	
64741-57-7		LC_{50} >2000	13 week study LOAEL =500 NOAEL =125			[4 samples] LOAEL <75 – 500 NOAEL = 50 – 125	
64741-61-3			4 week study LOAEL♂ =990; NOAEL♂= 99 LOAEL♀ = 99; NOAEL♀= 9.9			LOAEL = 50 NOAEL <50	
64741-62-4	LD_{50} 4320♀, 5270♂	LC_{50} >2000	13 week studies [4 samples] LOAEL = 5-10.6 NOAEL = 1.06 to <8.0			[5 samples] LOAEL = 1.0 – 50 NOAEL = 0.05 -10	NOAEL male and female = 250mg/kg
64741-75-9			4 week study NOAEL = 210 [highest dose]				
64741-80-6			13 week study LOAEL = 250; NOAEL = 60				
64741-81-7	LD_{50} >5000 [4 samples]	LC_{50} >2000 [4samples]	13 week studies [4 samples] LOAEL = 30-125;			[4 samples] LOAEL = 30 to >250 NOAEL = 1 – 250	

CAS RN	Acute Oral Rat (mg/kg)	Acute Dermal Rabbit (mg/kg}	Repeated Dose LOAEL/NOAEL (mg/kg)	Genetic Toxicity *In vitro*	Genetic Toxicity- *In vivo*	Developmental Toxicity Dermal LOAEL/NOAEL (mg/kg) [1]	Reproductive toxicity [2]
			NOAEL = 8-30				
64742-86-5						LOAEL = 333 NOAEL = 50	
68410-00-4						[3 samples] LOAEL = 125 to >500 NOAEL = 50 -500	
68476-33-5			4 week studies [2 samples] LOAEL = 480-496 [highest doses]			]	
68553-00-4	LD_{50} = 5.13 to >25ml/kg						
68783-08-4						LOAEL = 250 NOAEL = 50	

1-Read across for developmental effects reflects range of developmental LOAEL/NOAEL for studies which include treatment from GD 0-19 or 20, killed on GD20 or maintained untreated to Lactation day 4.

2 -The NOAEL for reproductive toxicity is not expected to be lower than the NOAEL for developmental toxicity because the most sensitive endpoints in either developmental or reproductive toxicity studies are expected to be effects on fetal survival and growth resulting from *in utero* exposure. One reproductive function study is presented

10. References

Ames, B.N., McCann, J., and Yamasaki, E. Methods for detecting carcinogens and mutagens with the *Salmonella*/mammalian-microsome mutagenicity test. Mutat Res. 31: 347 –364.

Anderson, J.W., J.M. Neff, B.A. Cox, H.E. Tatem, and G.M. Hightower. 1974. Characteristics of dispersions and water-soluble extracts of crude oil and refined oils and their toxicity to estuarine crustaceans and fish. Marine Biology. 27:75-88. [as cited in Jokuty et al., 2002]

API (American Petroleum Institute). 1980a. Acute toxicity tests API 78-6 #6 Heavy fuel oil (API gravity 11.7/2.7%S. API Med. Res. Publ. 27-32814, Washington D.C.

API (American Petroleum Institute). 1980b. Acute toxicity tests API 78-7 #6 Heavy fuel oil (API gravity 17.1/0.8%S. API Med. Res. Publ. 27-32774, Washington D.C.

API (American Petroleum Institute). 1980c. Acute toxicity tests API 78-8 #6 Heavy fuel oil (API gravity 23.1/0.2%S. API Med. Res. Publ. 27-32816, Washington D.C.

API (American Petroleum Institute). 1980d. Acute toxicity tests API 79-2 #6 Heavy fuel oil (API gravity 5.2/1.2%S. API Med. Res. Publ. 27-32813, Washington D.C.

API (American Petroleum Institute). 1982a. Acute toxicity studies catalytically cracked clarified oil Sample 81-15. API Med. Res. Publ. 30-31854, Washington D.C.

API (American Petroleum Institute). 1982b. Acute oral toxicity in rats, Acute dermal toxicity in rabbits, Eye and Skin irritation in rabbits from a vacuum residuum API 81-13. API Med. Res. Publ. 30-31987. Washington, DC

API (American Petroleum Institute). 1982c. Acute oral toxicity in rats, Acute dermal toxicity in rabbits, Eye and Skin irritation in rabbits from a vacuum residuum API 81-14. API Med. Res. Publ. 30-31989. Washington, DC

API (American Petroleum Institute). 1983a Subchronic dermal toxicity in rabbits exposed to vacuum residuum API 81-13 for 4 weeks. API Med. Res. Publ. 30-32852. Washington, DC

API (American Petroleum Institute). 1983b. Subchronic dermal toxicity in rabbits exposed to vacuum residuum API 81-14 for 4 weeks. API Med. Res. Publ. 30-32853. Washington, DC

API (American Petroleum Institute. 1983c. *In vitro* L5178Y Mouse lymphoma mutagenesis assay and *in vivo* oral bone marrow cytogenetics assay in Sprague Dawley rats of a vacuum residuum API 81-13. API Med Res. Publ. 31-30614. Washington, DC

API (American Petroleum Institute). 1983d. *In vitro* L5178Y Mouse lymphoma mutagenesis assay and *in vivo* oral bone marrow cytogenetics assay in Sprague Dawley rats of a vacuum residuum API 81-14. API Med. Res. Publ. 31-30615. Washington, DC

API (American Petroleum Institute). 1984. Dermal sensitization study in guinea pigs closed patch technique Catalytic cracked clarified oil API sample 81-15. API Med. Res. Publ. 31-31417, Washington D.C.

API (American Petroleum Institute). 1985a. CHO/HGPRT Mammalian cell forward gene mutation assay of API 81-15. API Med. Res. Publ. 32-32118, Washington D.C.

API (American Petroleum Institute). 1985b. Evaluation of the potential of RO-1, 81-15 and PS8-76D5-SATto induce unscheduled DNA synthesis in primary rat hepatocyte cultures. API Med. Res. Publ. 32-32407, Washington D.C.

API (American Petroleum Institute). 1985c. Evaluation of the potential of RO-1, 81-15, and PS8-76D-SATto induce unscheduled DNA synthesis in the in vivo-in vitro hepatocyte DNA repair assay. API Med. Res. Publ. 32-32406, Washington D.C.

API (American Petroleum Institute). 1985d. In vivo sister chromatid exchange assay API 81-15, catalytically cracked clarified oil (CAS 64741-62-4). API Med. Res. Publ. 32-32254, Washington D.C.

API (American Petroleum Institute). 1985e. Mutagenicity evaluation studies in the rat bone marrow cytogenetic assay and in the mouse lymphoma forward mutation assay catalytic cracked clarified oil API sample 81-15. API Med. Res. Publ. 32-30534, Washington D.C.

API (American Petroleum Institute). 1985f. Sister chromatid exchange assay in Chinese Hamster Ovary (CHO) cells. Catalytic cracked clarified oil; API sample 81-15 CAS 64741-62-4. API Med. Res. Publ. 32-32750, Washington D.C.

API (American Petroleum Institute). 1986a. Morphological transformation of BALB/3T3 Mouse embryo cells API 81-15, Catalytically cracked clarified oil (CAS 64741-62-4). API Med. Res. Publ. 33-32638, Washington D.C.

API (American Petroleum Institute). 1986b. Salmonella/Mammalian-microsome plate incorporation mutagenicity assay (Ames test) with API 81-15, Catalytically cracked clarified oil. API Med. Res. Publ. 33-30599, Washington D.C.

API (American Petroleum Institute). 1987. Comprehensive Analytical Analysis of API generic petroleum streams. American Petroleum Institute, Washington, DC.

API (American Petroleum Institute). 1989a. Lifetime dermal carcinogenesis/chronic toxicity screening bioassay of refinery streams in C3H/HeJ mice (AP-135r). API Med. Res. Publ. 36-31364, Washington D.C.

API (American Petroleum Institute). 1989b. Short-term dermal tumorigenesis study of selected petroleum hydrocarbons in male CD-1 mice. Initiation and promotion phases. API Med. Res. Publ. 36-32643. Washington, D.C.

API (American Petroleum Institute). 2003a. Test Plan for HPV Category: Kerosene/Jet Fuel. Submitted to the U. S. Environmental Protection Agency for the High Production Volume (HPV) program. API, Washington, DC.

API (American Petroleum Institute). 2003b. Test Plan for HPV Category: Gas Oils. Submitted to the U. S. Environmental Protection Agency for the High Production Volume (HPV) program. API, Washington DC

API (American Petroleum Institute). 2003c. Test Plan for HPV Category: Lubricating oil basestocks. Submitted to the U. S. Environmental Protection Agency for the High Production Volume (HPV) program. API, Washington DC

API (American Petroleum Institute). 2003d. Test Plan for HPV Category: Aromatic extracts. Submitted to the U. S. Environmental Protection Agency for the High Production Volume (HPV) program. API, Washington DC

API (American Petroleum Institute). 2008. PAC Analysis Task group. The relationship between the aromatic ring class content and selected endpoints of repeat-dose and developmental toxicity of high-boiling petroleum substances. http://www.petroleumhpv.org.

API (American Petroleum Institute). 2008. Category Assessment Document and Hazard Charaxterization: Gasoline Blending Streams. Submitted to the U. S. Environmental Protection Agency for the High Production Volume (HPV) program. August 26, 2008 At www.petroleumhpv.org

API (American Petroleum Institute). 2009. Category Assessment Document and Hazard Characterization: Asphalt. Submitted to the U. S. Environmental Protection Agency for the High Production Volume (HPV) program. August 3, 2009 At www.petroleumhpv.org

API (American Petroleum Institute). 2010. Category Assessment Document and Hazard Charaxterization: Kerosene/Jet Fuel. Submitted to the U. S. Environmental Protection Agency for the High Production Volume (HPV) program. September 21, 2012. At www.petroleumhpv.org

API. (American Petroleum Institute). 2011a. Category Assessment Document and Hazard Characterization Lubricating oil basestocks:. Submitted to the U.S. Environmental Protection Agency, April 5, 2011. At www.petroleumhpv.org

API. (American Petroleum Institute). 2011b. Category Assessment Document and Hazard Characterization Waxes and repated materials:. Submitted to the U.S. Environmental Protection Agency, January 21, 2011. At www.petroleumhpv.org

API. (American Petroleum Institute). 2012a. Category Assessment Document and Hazard Characterization: Aromatic extracts:. Submitted to the U.S. Environmental Protection Agency, May 21, 2012. At www.petroleumhpv.org

API. (American Petroleum Institute). 2012b. Category Assessment Document and Hazard Characterization Gas Oils: Submitted to the U.S. Environmental Protection Agency, October 1, 2012. At www.petroleumhpv.org

ARCO. 1986a. Dermal sensitization study in guinea pigs administered heavy fuel oil {F74-01]. Report No. ATX-85-0158. performed at UBTL (Utah Biomedical Testing Laboratory Inc.), Salt Lake City. UT.

ARCO. 1986b. 28 day dermal toxicity study in rats on Heavy Fuel Oil [F-92-01]. Report No. ATX-86-0090. performed at UBTL (Utah Biomedical Testing Laboratory Inc.), Salt Lake City UT.

ARCO. 1987a. 28 day dermal toxicity study in rats on Carbon Black oil]. Report No. ATX-86-0007. performed at UBTL (Utah Biomedical Testing Laboratory Inc.), Salt Lake City UT.

ARCO. 1987b. 28 day dermal toxicity study in rats on Watson Heavy Fuel Oil [F-74-01]. Report No. ATX-86-0008. performed at UBTL (Utah Biomedical Testing Laboratory Inc.), Salt Lake City UT.

ARCO. 1988. Acute oral toxicity study in rats administered F-97-01. Report No. ATX-88-0086, study No. 64707. performed at UBTL (Utah Biomedical Testing Laboratory Inc.), Salt Lake City, UT

ARCO. 1989a. Acute dermal toxicity study (limit test) in rabbits administered test article F-97-01. Study No. 64834. Report No. ATX-88-0087. performed at UBTL (Utah Biomedical Testing Laboratory Inc.), Salt Lake City, UT

ARCO. 1989b. Dermal sensitization study in guinea pigs administered test article F-97-01 (Coker heavy gas oil). Study No. 64838. Report No. ATX-88-0090. performed at UBTL (Utah Biomedical Testing Laboratory Inc.), Salt Lake City UT.

ARCO. 1989c. Dermal sensitization study in guinea pigs administered test article F-98-01 (Vacuum tower bottoms. Study No. 65066. Report No. ATX-88-0097. performed at UBTL (Utah Biomedical Testing Laboratory Inc.), Salt Lake City UT.

ARCO. 1989d. Primary dermal irritation study in rabbits administered test article F-97-01 (Coker heavy gas oil). Study No. 64782. Report No. ATX-88-0089. performed at UBTL (Utah Biomedical Testing Laboratory Inc.), Salt Lake City UT.

ARCO 1989e. Primary dermal irritation study in rabbits administyered test article F-98-01 (Vacuum tower bottoms). Study No. 65054. Report No. ATX-88-0096. performed at UBTL (Utah Biomedical Testing Laboratory Inc.), Salt Lake City UT.

ARCO. 1989f. Primary eye irritation study in rabbits administered test article F-97-01 (Coker heavy gas oil). Study No. 64831. Report No. ATX-88-0088. performed at UBTL (Utah Biomedical Testing Laboratory Inc.), Salt Lake City UT.

ARCO 1989g. Primary eye irritation study in rabbits administered test article F-98-01 (Vacuum tower bottoms). Study No. 65042. Report No. ATX-88-0095. performed at UBTL (Utah Biomedical Testing Laboratory Inc.), Salt Lake City UT.

ARCO 1989h. Developmental Toxicity (Embryo-Fetal Toxicity and Teratogenic Potential) Study of F-115-01 administered Percutaneously to Crl:CD®BRK VAF/Plus® Presumed Pregnant Rats. Report ATX-89-005

ARCO. 1990a. Acute oral toxicity study in rats administered test article F-132. Report No. ATX-90-0059. performed at UBTL (Utah Biomedical Testing Laboratory Inc.), Salt Lake City, UT.

ARCO. 1990b. Dermal sensitization study in albino guinea pigs administered test article F-113-01 (Heavy Vacuum Gas Oil). Report No. ATX-89-0035. performed at UBTL (Utah Biomedical Testing Laboratory Inc.), Salt Lake City UT

ARCO. 1990c 28 day dermal toxicity study in rats on Coker heavy gas oil [F-97-01]. Report No. ATX-88-0092. performed at UBTL (Utah Biomedical Testing Laboratory Inc.), Salt Lake City UT.

ARCO. 1991. Primary eye irritation study in rabbits administered test article F-132 (Atmospheric tower bottoms). Study No. 65833. Report No. ATX-90-0061. performed at UBTL (Utah Biomedical Testing Laboratory Inc.), Salt Lake City UT.

ARCO. 1992a. Acute dermal toxicity study (limit test) in rabbits administered test article F-136. Study No. 65989. Report No. ATX-90-0092. performed at UBTL (Utah Biomedical Testing Laboratory Inc.), Salt Lake City, UT.

ARCO. 1992b. Acute dermal toxicity study in rabbits administered test article F-132.. Study No. 65893. Report No. ATX-90-0060. performed at UBTL (Utah Biomedical Testing Laboratory Inc.), Salt Lake City, UT.

ARCO. 1992c. Dermal sensitization study in guinea pigs administered test article F-132 (Atmospheric tower bottoms). Study No. 65849. Report No. ATX-90-0063. performed at UBTL (Utah Biomedical Testing Laboratory Inc.), Salt Lake City UT.

ARCO. 1992d. 28 day dermal toxicity study in rats on heavy paraffinic vacuum distillate [F-128]. Report No. ATX-90-0034. performed at UBTL (Utah Biomedical Testing Laboratory Inc.), Salt Lake City UT.

ARCO. 1992e. 28 day dermal toxicity study in rats on Hydrocracker recycle Oil [F-127]. Report No. ATX-90-0026. performed at UBTL (Utah Biomedical Testing Laboratory Inc.), Salt Lake City UT.

ARCO 1992f. 28 day dermal toxicity study in rats on Coker heavy gas oil [F-136]. Report No. ATX-90-0098 performed at UBTL (Utah Biomedical Testing Laboratory Inc.), Salt Lake City. UT.

ARCO. 1992g. Screening test for reproductive toxicity of F-179 administered percutaneously to Crl: CD®BR VAF/Plus® male rats. Protocol 1001-002. Report No. ATX 91-0040. performed at Argus Research Laboratory, Horsham, PA.

ARCO, 1992h. Critical Period Developmental toxicity (Embryo-Fetal Toxicity and Teratogenic Potential) Study of F-179 Administered Percutaneously to Crl:CD®BRK VAF/Plus® Presumed Pregnant Rats. Report ATX91-0042. published as Hoberman et al, 1995b

ARCO 1992i. 28 day dermal toxicity study in rats on an Atmospheric Residuum [Atmospheric Tower Bottoms F-132]. Report No. ATX-90-0066. performed at UBTL (Utah Biomedical Testing Laboratory Inc.), Salt Lake City. UT.

ARCO. 1992j. 28 day dermal toxicity study in rats on Heavy Cycle oil [F-134]. Report No. ATX-900082 performed at UBTL (Utah Biomedical Testing Laboratory Inc.), Salt Lake City UT.

ARCO 1992k Primary dermal irritation study in rabbits administered test article F-132 (Atmospheric tower bottoms) Study No. 65841. Report No. ATX-90-0062 performed at UBTL (Utah Biomedical Test Laboratory, Inc.), Salt Lake City UT

ARCO. 1993a. Developmental Toxicity (Embryo-Fetal Toxicity and Teratogenic Potential) Study of F-215 Administered Percutaneously to Crl:CD®BRK VAF/Plus® Presumed Pregnant Rats. Report ATX-92-0155.

ARCO. 1993b. Developmental Toxicity (Embryo-Fetal Toxicity and Teratogenic Potential) Study of F-196 Administered Percutaneously to Crl:CD®BRK VAF/Plus® Presumed Pregnant Rats. Report ATX-92-0012.

ARCO. 1993c. Developmental Toxicity (Embryo-Fetal Toxicity and Teratogenic Potential) Study of F-197 Administered Percutaneously to Crl:CD®BRK VAF/Plus® Presumed Pregnant Rats. Report ATX-92-0154.

ARCO 1993d. Ninety day (90) dermla toxicity study in rats administered test article F-179. Report No. ATX-91-0012

ARCO. 1993e. 28 day dermal toxicity study in rats on FCCU Clarified oil [F-115-01]. Report No. ATX-89-0077. performed at UBTL (Utah Biomedical Testing Laboratory Inc.), Salt Lake City UT.

ARCO 1993f. 28 day dermal toxicity study in rats administered test article F-113-01. Report No. ATX -89-0011. performed at UBTL (Utah Biomedical Testing Laboratory Inc.), Salt Lake City UT.

ARCO. 1994a. A Developmental Toxicity Screen in Female Sprague-Dawley Rats Administered F-201 Dermally During GD -7 to 20. Report ATX-913-0135.

ARCO. 1994b. A Developmental Toxicity Screen in Female Sprague-Dawley Rats Administered F-276 Dermally During GD -7 to 20. Report ATX-93-0073.

ARCO. 1994c. A Developmental Toxicity Screen in Female Sprague-Dawley Rats Administered F-197 Dermally During Gestation Days -7 to 20. Report ATX-91-0131.

ARCO. 1994d. A Developmental Toxicity Screen in Female Sprague-Dawley Rats Administered F-196 Dermally During GD -7 to 20. 1994. Report ATX-91-0130.

ARCO. 1994e. A Developmental Toxicity Screen in Female Sprague-Dawley Rats Administered F-179 Dermally During GD -7 to 20. 1994. Report ATX-91-0155

ARCO. 1994f. A Developmental Toxicity Screen in Female Sprague-Dawley Rats Administered F-200 Dermally During Gestation Days -7 to 20. Report ATX-91-0134.

ARCO. 1994g. A Developmental Toxicity Screen in Female Sprague-Dawley Rats Administered F-228 Dermally During GD 0 to 20. Report ATX-91-0267.

ARCO, 1994h A Developmental Toxicity Screen in Female Sprague-Dawley Rats Administered F-275 Dermally During GD 0 to 20. 1994. Report ATX-93-0071.

ARCO. 1994i. A Developmental Toxicity Screen in Female Sprague-Dawley Rats Administered F-194 Dermally During Gestation Days 0 to 20. Report ATX-91-0128

ARCO. 1994j. A Developmental Toxicity Screen in Female Sprague-Dawley Rats Administered F-215 Dermally During GD 0 to 20. Report ATX-91-0263.

ARCO. 1994k. A Developmental Toxicity Screen in Female Sprague-Dawley Rats Administered F-225 Dermally During GD 0 to 20. Report ATX-91-0270.

ARCO. 1994l. A Developmental Toxicity Screen in Female Sprague-Dawley Rats Administered F-227 Dermally During GD 0 to 20. Report ATX-91-0266

ARCO. 1994m. A Developmental Toxicity Screen in Female Sprague-Dawley Rats Administered F-229 Dermally During GD 0 to 20. Report ATX-91-0268.

ARCO. 1994n. A Developmental Toxicity Screen in Female Sprague-Dawley Rats Administered F-274 Dermally During GD 0 to 20. Report ATX-93-0069.

ARCO. 1994o. A Developmental Toxicity Screen in Female Sprague-Dawley Rats Administered F-222 Dermally During GD 0 to 20. Report ATX-91-0270.

ASTM (American Society for Testing and Materials). 1999. Standard Test Method for Pour Point of Petroleum Oils. ASTM D97, Volume 05.01. West Conshohocken, PA.

ASTM (American Society for Testing and Materials). 2002. Standard Specification for Fuel Oils. ASTM D396. West Conshohocken, PA.

ASTM (American Society for Testing and Materials). 2003. Liquid fuels - Fuel oils - Part 3: Fuel oil S; Minimum requirements. West Conshohocken, PA.

Atkinson, R. 1990 Gas-phase tropospheric chemistry of organic compounds: a review. Atmos. Environ. 24A(1):1-41.

Bartha, R. and R.M. Atlas. 1977. The microbiology of aquatic oil spills. Adv. Appl. Microbiol. 22:225-266.

Bingham, E., Trosset, R. P. and Warshawsky, D. (1980) Carcinogenic potential of petroleum hyrocarbons A critical review of the literature J. Env. Pathology and Toxicology, Vol 3, pp 483-563

CONCAWE. 1998. Heavy fuel oils. Product dossier No. 98/109. Brussels. 48 pp.

CONCAWE. 2001. Environmental Classification of Petroleum Substances – Summary Data and Rationale. Report no. 01/54. Brussels. 134 pp.

CONCAWE. 2010 Hazard Classification and Labeling of Petroleum Substances in the European Economic Area – 2012.
http://www.concawe.be/DocShareNoFrame/docs/1/LFJNNIDDAIMKAEGCBIEECGGGVEVCWY9W9YBYP3B1W1B3/CEnet/docs/DLS/Rpt_12-8-2012-05150-01-E.pdf

CONSCI (Consolidated Sciences, Inc.). 1992a. Certificate of Analysis No. 21012010. Pasadena, Texas.

CONSCI (Consolidated Sciences, Inc.). 1992b. Certificate of Analysis No. 21012014. Pasadena, Texas.

CONSCI (Consolidated Sciences, Inc.). 1993a. Certificate of Analysis No. 30330004. Pasadena, Texas.

CONSCI (Consolidated Sciences, Inc.). 1993b. Certificate of Analysis No. 30330008. Pasadena, Texas.

CONSCI (Consolidated Sciences, Inc.). 1993c. Certificate of Analysis No. 30330013. Pasadena, Texas.

CONSCI (Consolidated Sciences, Inc.). 1993d. Certificate of Analysis No. 30330016. Pasadena, Texas.

Crump, K. 1984. A new method for determining allowable daily intakes. Fund. Appl. Toxicol. 4: 854-871.

Cruzan, G., Low, L. K., Cox, G. E., Meeks, J. R., Mackerer, C. R., Craig, P. H., Singer, E. J. and Mehlman, M. A. 1986. Systemic toxicity from subchronic dermal exposure, chemical characterization, and dermal penetration of catalytically cracked clarified slurry oil. Tox. and Ind. Health Vol 2, No. 4, pp 429-444.

DataChem Laboratories. 1990. Characterization of Test Article F-92-01. Task Order No. 86-010. Salt Lake City, UT.

ECB (European Chemicals Bureau). 2000. European Chemical Substances Information System (ESIS), IUCLID Dataset, Residual Fuel Oils (CAS No. 64741-62-4). Web version URL: http://ecb.jrc.it/.

EPA (U.S. Environmental Protection Agency). 1999. Guidance for Assessing Adequacy of Existing Data, **http://www.epa.gov/chemrtk/guidocs.htm**.

EPA (U.S. Environmental Protection Agency). 2000. EPI (Estimation program interface) Suite Version 3.10. Office of Pollution Prevention and Toxics, Washington, DC.

EPA (U.S. Environmental Protection Agency). 2001. EPI (Estimation Programs Interface) Suite, V3.10, Subroutine AOPWIN, V1.90. Office of Pollution Prevention and Toxics, Washington, DC.

EPA (U.S. Environmental Protection Agency). 2004. Substance registry system (SRS) Database U.S. Environmental Protection Agency. http://www.epa.gov/srs/index.htm.

EU Classification, Labelling and Packaging regulation. 2008. Regulation (EC) Number 1272/2008 of the European Parliament and of the Council'
http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:353:0001:1355:en:PDF

Fasnacht, M.P. and Blough, N.V. 2002. Aqueous photodegradation of polycyclic aromatic hydrocarbons. Environ. Sci. Technol. 36:4364-4369.

Feuston, M. H., Low, L. K., Hamilton, C. E. and Mackerer, C. R. 1994. Correlation of systemic and developmental toxicities with chemical component classes of refinery streams. Fundamental and Applied Toxicolgy Vol 22 pp 622-630.

Feuston, M.H., and Mackerer, C.R. 1996. Developmental toxicity of clarified slurry oil, syntower bottoms, and distillate aromatic extract administered as a single oral dose to pregnant rats. J. Toxicol. Environ. Hlth. 49:45-66

Garrett, R.M., Haith, C.E., Prince, R.C., and Pickering, I.J. 1998. Photooxidation of polycyclic aromatic hydrocarbons in crude oils. In: Proceedings of the 21st Arctic and Marine Oil Spill Program. (AMOP) Technical Seminar. Environment Canada, Ottawa, Ont., pp. 99-114.

Garrett, R.M., Rothenburger, S.J., and Prince, R.C. 2003. Biodegradation of fuel oil under laboratory and arctic marine conditions. Spill Sci. Technol. Bull. 8(3): 297-302.

Gary, J. H. and Handwerk. G. E. 1994. Petroleum Refining Technology and Economics, Third Ed. Chapter 10 p.202.

Gray, T., Simpson, B., Nicolich, M., Murray, J., Verstuyft, A, Roth, R., McKee, R. 2012. Assessing the Mammalian Toxicity of High Boiling Petroleum Substances under the Rubric of the HPV Program. Regulatory Toxicol Pharmacol. In press.

Harris, J.C. 1982. Rate of Hydrolysis. In Handbook of Chemical Property Estimation Methods. Lyman, Reehl and Rosenblatt, eds. McGraw-Hill Book Co., New York.

Hoberman, A. M., Christian, M. S., Lovre,S., Roth, R. And Koschier, F. 1995a. Reproductive toxicity study of clarified slurry oil in the rat. J Amer College of Toxicol 14: 119-128

Hoberman, A. M., Christian, M. S., Lovre,S., Roth, R. And Koschier, F. 1995b. Developmental toxicity study of clarified slurry oil (CSO) in the rat. Fundamental and Applied Toxicology, vol. 28, pp 34-40

Houston Refining. 2006a. MSDS No. AP0701, Carbon Black Oil, Version 6.1, November 1, 2006. Houston Refining, Houston, Texas.

Houston Refining. 2006b. MSDS No. AP0881, Heavy Cycle Oil, Version 4.1, November 1, 2006. Houston Refining, Houston, Texas.

IARC (International Agency for Research on Cancer). 1989. Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 45: Occupational exposures in petroleum refining; crude oil and major petroleum fuels. Lyon, France

Irwin, R.J., M. Van Mouwerik, L. Stevens, M.D. Seese, and W. Basham. 1997. Environmental Contaminants Encyclopedia. National Park Service, Water Resources Division, Fort Collins, Colorado

Jézèquel, R., L. Menot, F. X. Merlin, and R.C. Prince. 2003. Natural cleanup of heavy fuel oil on rocks: an in situ experiment. Mar. Pollut. Bull. 46: 983-990.

Jokuty, P., Whiticar S., Wang Z., Fingas M., Fieldhouse B., Lambert P., and Mullin J. 2002. Properties of Crude Oils and Oil Products. Environmental Protection Service, Environment Canada, Ottawa, Ontario. Internet Version 2002, URL: http://www.etcentre.org/spills.

Keizer, P.D., Ahern, T.P., Dale, and Vandermeulen, J.H. 1978. Residues of Bunker C oil in Chedabucto Bay, Nova Scotia, 6 years after the Arrow Spill. J. Fish. Res. Board Can. 35:528-535.

Leahy, J.G., And R.R. Colwell. 1990. Microbial degradation of hydrocarbons in the environment. Microbiol. Rev. 54:305-315.

Lee, K., R.C. Prince, C.W. Greer, K.G. Doe, J.E.H. Wilson, S.E. Cobanli, G.D. Wohlgeschaffen, D. Alroumi, T. King, and G.H. Tremblay. 2003. Composition and toxicity of residual Bunker C fuel oil in intertidal sediments after 30 years. Spill Sci. Technol. Bull. 8(2): 187-199.

MacLean, M.M. and Doe, K.G. 1989. The comparative toxicity of crude and refined oils to Daphnia magna and Artemia. Manuscript Report EE-111, Environment Canada, Ottawa, On. 72 pp.

Mc Kee, R.H. , Nicolich, M.J., Scala, R. A., and Lewis, S.C. 1990. Estimation of epidermal carcinogenic potency. Fundamental and Applied Toxicology, vol. 15, pp 320-328.

McKee, R.H., Schreiner, C.A., Nicolich, M.J., and Gray, T.M. 2010. Assessment of the *in vivo* cytogenetic potential of petroleum-derived substances. 49th Annual Meeting of the Society of Toxicology, Salt Lake City, Utah, March 7-11. The Toxicologist, Suppl to Toxicological Sciences 114 (1). Abst 1122.

McKee, R.H., Schreiner, C.A., Nicolich, M.J. and Gray, T.M. 2012 Genetic toxicity of high boiling petroleum substances. Reg Toxicol Pharmacol. In press

Mobil. 1985. Thirteen-week toxicity study by dermal application of clarified slurry oil (CSO) to rats. Study No. 20525. Mobil Environmental and Health Science Laboratory, Princeton, NJ.

Mobil. 1986. Micronucleus assay of bone marrow red blood cells from rats treated via dermal administration of Heavy Coker Gas Oil - Beaumont. Study No. 50392. Mobil Environmental and Helath Science Laboratory, Princeton, NJ.

Mobil. 1987a. A Static 96-hour Acute Toxicity Study of Process Oil to Bluegill Sunfish. Mobil Environmental and Health Science Laboratory, Pennington, NJ.

Mobil. 1987b. A Static 48-hour Acute Toxicity Study of Process Oil to Daphnia magna. Mobil Environmental and Health Science Laboratory, Pennington, NJ.

Mobil. 1987c. A Static 96-hour Acute Toxicity Study of Process Oil to *Selenastrum capricornutum*. Mobil Environmental and Health Science Laboratory, Pennington, NJ.

Mobil. 1987d. Developmental toxicity screen in rat exposed dermally to Heavy coker gas oil-2. Report of study No. 50431. Mobil Environmental and Health Science Laboratory, Princeton, NJ.

Mobil. 1987e. Metaphase analysis of Chinese hamster ovary (CHO) cells treated in vitro with a DMSO extract of heavy vacuum gas oil (a screening assay). Study No. 52262. Mobil Environmental and Health Science Laboratory, Princeton, NJ. [Cited in CONCAWE (2000) IUCLID data set]

Mobil. 1987f. Micronucleus assay of bone marrow red blood cells from rats treated via dermal administration of heavy vacuum gas oil. Study No. 61591. Mobil Environmental and Health Science Laboratory, Princeton, NJ.

Mobil. 1987g. Developmental Toxicity Screen in Rats Exposed Dermally to Heavy Coker Gas Oil. Mobil Environmental and Health Sciences Laboratory Report 50431.

Mobil. 1987h. Clarified Slurry Oil Developmental Toxicity Study in Rats. Mobil Environmental and Health Sciences Laboratory Report 50541.

Mobil. 1987i. Developmental toxicity screen in rats exposed dermally to heavy vacuum gas oil (HVGO): Final report. Study No. 61801. Mobil Environmental and Health Sciences Laboratory, Princeton, NJ.

Mobil. 1988a. Consolidated acute test report on heavy vacuum gas oil. Study Nos. 62443, 62444, 62445. Mobil Environmental and Health Science Laboratory, Princeton, NJ.

Mobil. 1988b. Consolidated acute test report on V/breaker HGO. Study Nos. 62496, 62497, 62498, 62499. Mobil Environmental and Health Science Laboratory, Princeton, NJ.

Mobil. 1988c. Consolidated acute test report on vis gas oil VIBRA. Study Nos. 62500, 62501, 62502, 62503. Mobil Environmental and Health Science Laboratory, Princeton, NJ.

Mobil. 1988d. Thirteen-week dermal administration of heavy vacuum gas oil to rats. Study No. 61590. Mobil Environmental and Health Science Laboratory, Princeton, NJ.

Mobil. 1988e. Developmental Toxicity Screen in Rats Exposed Dermally to Heavy Vacuum Gas Oil. Mobil Environmental and Health Sciences Laboratory Report 61801.

Mobil.1988f. Teratology Study Rats Exposed Dermally to Clarified Slurry Oil [GD9-12 dermal]. Mobil Environmental and Health Sciences Laboratory Report 62492.

Mobil, 1988g. Thirteen-Week Dermal Administration of Syntower Bottoms to Rats. Mobil Environmental and Health Science Laboratory, Report 62710.Princeton, NJ.

Mobil. 1989a. Developmental Toxicity Study in Rats Exposed Dermally to Ferndale Syntower Bottoms. Mobil Environmental and Health Sciences Laboratory Report 62934.

Mobil. 1989b Micronucleus assay of bone marrow red blood cells from rats treated via dermal administration of Syn Tower Bottoms. Study No. 62711. Mobil Environmental and Helath Science Laboratory, Princeton, NJ.

Mobil. 1990a. Developmental Toxicity Study in Rats Exposed Orally to a Single Dose of Syntower Bottoms. Mobil Environmental and Health Sciences Laboratory Report 63123.

Mobil. 1990b. Developmental Toxicity Study in Rats Exposed Orally to a Single Dose of Clarified Slurry Oil. Mobil Environmental and Health Sciences Laboratory Report 63122. 12.

Mobil. 1990c. Micronucleus assay of bone marrow red blood cells from rats treated via dermal administration of Visbreaker Gas Oil. Study No. 63238. Mobil Environmental and Helath Science Laboratory, Princeton, NJ.

Mobil. 1991a. Micronucleus assay of bone marrow red blood cells from rats treated via dermal administration of Heavy Coker Gas Oil - Torrance. Study No. 64185. Mobil Environmental and Helath Science Laboratory, Princeton, NJ.

Mobil. 1991b. Developmental toxicity study in rats exposed dermally to heavy atmospheric gas oil. Study No. 64146. Mobil Environmental and Health Science Laboratory, Princeton, NJ.

Mobil. 1992a. Consolidated acute test report on V.B. Mittelol. Study Nos. 64635, 64636, 64637, 64638. Mobil Environmental and Health Science Laboratory, Princeton, NJ.

Mobil. 1992b. Thirteen-week dermal administration of visbreaker gas oil to rats. Study No. 63237. Mobil Environmental and Health Sciences Laboratory, Princeton, NJ.

Mobil. 1992c. Thirteen-week dermal administration of visbreaker residual to rats. Study No. 64002. Mobil Oil Corporation Environmental and Health Sciences Laboratory, Princeton, NJ.

Mobil. 1992d. Thirteen-week dermal administration of heavy atmospheric gas oil to rats. Study No. 63456. Mobil Oil Corporation Environmental and Health Sciences Laboratory, Princeton, NJ.

Mobil. 1993 Micronucleus assay of bone marrow red blood cells from rats treated via dermal administration of Heavy Coker Gas Oil - Joliet. Study No. 64166. Mobil Environmental and Helath Science Laboratory, Princeton, NJ.

Mobil. 1994a. Thirteen-week dermal administration of Joliet heavy coker gas oil to rats. Study No. 64165. Mobil Environmetal and Health Science Laboratory, Princeton, NJ.

Mobil. 1994b. Developmental Toxicity Study in Rats Exposed Dermally to V.B. Mittelol. Mobil Environmental and Health Sciences Laboratory Report 64643.

Mobil. 1994c. Developmental Toxicity Study in Rats Exposed Dermally to Heavy Coker Gas Oil. Mobil Environmental and Health Sciences Laboratory Report 64168.

Mobil. 1994d. Thirteen-week toxicity study by dermal application of heavy coker gas oil (Paulsboro) to rats. Study No. 50391. Mobil Environmental and Health Science Laboratory, Princeton, NJ.

Mobil. 1994e. Micronucleus assay of bone marrow red blood cells from rats exposed dermally to Heavy Coker Gas Oil Joliet in a developmental toxicity study. Study No 64169. Mobil Environmental and Health Science Laboratory, Princeton, New Jersey

Mobil. 1995. Thirteen-week dermal administration of Torrance heavy coker gas oil to rats – 3. Study No. 64184. Mobil Environmental and Health Sciences Laboratory, Princeton, NJ.

Mulkins-Phillips, G.J., and J.E. Stewart. 1974. Effect of environmental parameters on bacterial degradation of Bunker C oil, crude oils and hydrocarbons. App. Microbiol. 28(6): 915-922.

Murray, F.J. Roth, R., Nicolich, M., Gray, T., and Simpson, B. 2012a. The relationship between developmental toxicity and aromatic-ring class content of high-boiling petroleum substances. Regulatory Toxicol Pharmacol. In press

Murray, F.J., Gray, T.M., Roberts, L.G., Roth, R.N., Nicolich, M.J. and Simpson, B.J. 2012b. Evaluating the male and female reproductive toxicity of high-boiling petroleum substances. Regulatory Toxicol Pharmacol. In press.

NIcolich, M.J., McKee, R.H., Schreiner, C.A. and Gray, T.M. 2010. Predicting the outcome of Optimized Salmonella Assays. 49th Annula Meeting of the Society of Toxicology, Salt Lake City, Utah, March 7-11. The Toxicologist, Suppl to Toxicological Sciences 114 (1). Abst. 698.

Nicolich, M.J, Simpson, B.J., Murray, F.J., Roth, R.N., Gray, T.M. 2012.. The development of statistical models to determine the relationship between aromatic-ring class profile and repeat-dose and developmental toxicities onf high-boiling petroleum substances. Regulatory Toxicol Pharmacol. In press.

NIPER (National Institute for Petroleum and Energy Research). 1993a. Analyses of ARCO Petroleum Stream Samples. Bartlesville, Oklahoma.

NIPER (National Institute for Petroleum and Energy Research). 1993b. Analyses of ARCO Petroleum Stream Samples: Set II. Bartlesville, Oklahoma.

NOAA (National Oceanic and Atmospheric Administration). 2004. Fact Sheet: Number 6 Fuel Oil (Bunker C) Spills. Office of Response and Restoration, National Ocean Service, NOAA. Web URL: http://response.restoration.noaa.gov/oilaids/reports.html#fact

NOVA Chemicals. 2004. MSDS No. NOVA-009, Revision 2.00, Vacuum Gas Oil, January 13, 2004. NOVA Chemicals (Canada) Ltd., Sarnia, Ontario, Canada.

OECD (Organization for Economic Cooperation and Development). 1989. Guideline No. 117: Partition Coefficient (n-octanol/water): High performance liquid chromatography (HPLC) method, adopted 30 March 1989. In: OECD Guideline for Testing of Chemicals, Paris.

OECD (Organization for Economic Cooperation and Development). 1995. Guideline No. 107: Partition Coefficient (n-octanol/water): Shake flask method, adopted 27 July 1995. In: OECD Guideline for Testing of Chemicals. Paris.

OECD. (Organization for Economic Cooperation and Development)1995. OECD guideline for testing of chemicals, Guideline 104, Vapour Pressure, Adopted 27 July 1995. OECD, Paris.

OECD (Organization for Economic Cooperation and Development). 2000. Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures. ENV/JM/MONO (2000) 6. Environmental Health and Safety Publications Series on Testing and Assessment No. 23. Paris, September.

OECD. (Organization for Economic Cooperation and Development) 2007. Manual for Investigation of HPV Chemicals. Available through the Environment Directorate, OECD. URL: http://www.oecd.org/document/7/0,3343, en_2649_34379_1947463_1_1_1_1,00.html

Peterson, D.R. 1994. Calculating the aquatic toxicity of hydrocarbon mixtures. Chemosphere. 29(2): 2493-2506.

Potter, T.L. and Simmons K.E. 1998. Total petroleum hydrocarbon criteria working group series, Volume 2. Composition of petroleum mixtures. Amherst Scientific Publishers, Amherst, Massachusetts. 114 pp.

Prince, R.C. 2002. Petroleum and other hydrocarbons, biodegradation of. In: Bitton, G. (ed.), Encyclopedia of Environmental Microbiology. John Wiley & Sons, New York, pp. 2402-2416.

Prince, R.C., R.M. Garrett, R.E. Bare, M.J. Grossman, T. Townsend, J.M. Suflita, K. Lee, E.H. Owens, G.A. Sergy, J.F. Braddock, J.E. Lindstrom, and Lessard R.R.. 2003. The roles of photooxidation and biodegradation in long-term weathering of crude and heavy fuel oils. Spill Sci. Technol. Bull. 8(2): 145-156.

Przygoda, R.T., Mckee, R.H., Amoruso, M.A., and Freeman, J.J. 1999. Assessment of the utility of the micronucleus test for petroleum-derived materials. Mutation research 438: 145 – 153

Quann, R.J. and S.B. Jaffe. 1992. Structure-oriented lumping: Describing the chemistry of comples hydrocarbon mixtures. Ind. Eng. Chem. Res. 31(11):2483-2497.

Rashid, M.A. 1974. Degradation of Bunker C oil under different coastal environments of Chedabucto Bay, Nova Scotia. Est. and Coastal Mar. Sci. 2:137-144.

Richmond, S.A., J.E. Lindstrom, and J.F. Braddock. 2001. Effects of chitin on microbial emulsification, mineralization potential, and toxicity of Bunker C fuel oil. Mar. Poll. Bull. 42(9): 773-779.

Roth, R., Simpson, B., Nicolich, M., Murray, F.J. and Gray, T. 2012 The relationship between repeat –dose toxicity and and aromatic-ring class content of high-boiling petroleum substances. Regulatory Toxicol Pharm: In press

Saeger, R.B. and Jaffe S.B. 2002. Petroleum stream compositional modeling for the petroleum HPV testing group program. ExxonMobil Process Research Laboratories, Paulsboro, NJ.

Schwarzenbach, R.P., Gschwend, P.M., and Imboden, D.M., eds. 2003. Chapter 16: Indirect Photolysis: Reactions with Photooxidants in Natural Waters and in the Atmosphere. In: Environmental Organic Chemistry, 2nd Edition. John Wiley and Sons, Inc.

Shell. 1997a. Light fuel oil: Acute toxicity of water accomodated fractions to *Oncorhynchus mykiss*. Study OP.97.47001, Shell Research and Technology Centre, Thornton, UK.

Shell. 1997b. Heavy fuel oil: Acute toxicity of water accomodated fractions to *Oncorhynchus mykiss*. Study OP.97.47002. Shell Research and Technology Centre, Thornton, UK.

Shell. 1997c. Light fuel oil: Acute toxicity of water accomodated fractions to *Daphnia magna*. Study OP.97.47001. Shell Research and Technology Centre, Thornton, UK.

Shell. 1997d. Heavy fuel oil: Acute toxicity of water accomodated fractions to *Daphnia magna*. Study OP.97.47002. Shell Research and Technology Centre, Thornton, UK.

Shell. 1997e. Light fuel oil: Acute toxicity of water accomodated fractions to *Raphidocelis subcapitata*. Study OP.97.47001. Shell Research and Technology Centre, Thornton, UK.

Shell. 1997f. Heavy fuel oil: Acute toxicity of water accomodated fractions to *Raphidocelis subcapitata*. Study OP.97.47002. Shell Research and Technology Centre, Thornton, UK.

Shiu, W.Y., M. Bobra, A.M. Bobra, A. Maijanen, L. Suntio, and Mackay D. 1990. The water solubility of crude oils and petroleum products. Oil & Chem. Poll. 7:57-84.

Simpson, B.J., Nicolich,M.J., Roth, R.N., Murray, F.J., and Gray, T.M. 2012. Application of statistical models to characterize the repeat-dose and developmental toxicity of high-boiling petroleum substances. Regulatory Toxicol Pharmacol. In press.

Speight, J. G. 1998. Petroleum Chemistry and Refining. Applied Energy Technology Series. Taylor and Francis, Washington, D.C.

Suntio, I., W.Y. Shiu, and D. Mackay. 1986. Analyses of water soluble fractions of crude oils and refined products: a study of solubility of selected oils in water, Contract No. 0164, Environment Canada, Ottawa, On. [as cited in Jokuty et al., 2002]

Trent University. 1999. Level 1: Fugacity-based environmental equilibrium partitioning model. Environmental Modeling Centre, Trent University, Peterborough, Ontario.

Valero. 2006. MSDS No. 203, Fuel Oil No. 6, July 26, 2006. Valero Marketing and Supply Company, San Antonio, Texas

Van Wezel, A.P. and A. Opperhuizen. 1995. Narcosis Due to Environmental Pollutants in Aquatic Organisms: Residual-Based Toxicity, Mechanisms, and Membrane Burdens. Critical Reviews in Toxicology 25:255-279.

Walker, J.D., L. Petrakis, and R.R. Colwell. 1976. Comparison of the biodegradability of crude and fuel oils. Can. J. Microbiol. 22:598-602.

WIL Laboratories 2012a. A 90-Day Repeat-Dose Dermal Toxicity Study Utilizing Clarified Oils, Catalytic Cracked in Sprague Dawley Rats. WIL Study # 402023. WIL Research Laboratories, LLC. 1407 George Road, Ashland, OH 44805-8946

WIL Laboratories 2012b. A Dermal Prenatal Developmental Toxicity Study of Clarified Oils, Catalytic Cracked in Rats. WIL Study # 402016. WIL Research Laboratories, LLC. 1407 George Road, Ashland, OH 44805-8946

Yvette, C., Van Tongeren, M., Urbanus, J. And Cherrie, J.W. 2011. An assessment of dermal exposure to heavy fuel oil (HFO) in occupational settings. Ann Occup Hyg 55(3): 319-328.

11. LIST OF APPREVIATIONS AND ACRONYMS

API – American Petroleum Institute
BOD – biological oxygen demand
AUGC – area under the growth curve
CAS RN/CAS #/CAS No. - Chemical Abstract Service Registry Number
^{o}C – degrees Celsius
CIR – Cosmetics Ingredients Review Panel
CONCAWE – Conservation of Clean Air and Water in Europe
d - day
DMSO – Dimethyl sulfoxide
EINECS – European Inventory of Existing Commercial Chemical Substances
EL_{50} – effective loading rate lethal to 50% of the test population
E_bL_{50} – effective loading rate that causes 50% reduction in algal cell biomass
E_rL_{50} – effective loading rate that causes 50% reduction in algal growth rate
EPA/US EPA – United States Environmental Protection Agency
g/cm^3 – grams per cubic centimeter
h - hour
HLS – Huntingdon Life Sciences
HPV – High Production Volume
HSDB – Hazardous Substances Data Bank
IRDC – International Research and Development Corporation
^{o}K – degrees Kelvin
kPa - kilopascal
LC_{50} – lethal concentration for 50% of the test population
LC_{50}– lethal dose level for 50% of the test population
LL_{50} – lethal loading rate for 50% of the test population
Loading Rate – total amount of test substance added to dilution water to prepare water accommodated fractions (WAFs) for ecotoxicity testing
LOAEL – lowest observable adverse effect level
mg/kg – milligrams per kilogram
mg/L – milligrams per liter
mg/m^3 – milligrams per cubic meter
mL - milliliter
mm - millimeter
nm - nanometer
NOAEL – no observable adverse effect level
NOEC – no observable effect concentration
NOELR – no observable effect loading rate
NTP – National Toxicology Program
OECD – Organization for Economic Cooperation and Development
OPPTS – US EPA Office of Prevention, Pesticides and Toxic Substances
PAC - Polycyclic aromatic compound
PAH – polycyclic aromatic hydrocarbon
PNA – polynuclear aromatic
ppm – part per million
SIDS – Screening Information Data Set
UNEP – United Nations Environment Program
US EPA – United States Environmental Protection Agency
UV - ultraviolet
WAF – water accommodated fraction
wt% - weight percent

μg - microgram
μg/L – microgram/liter
> greater than
< less than

12. GLOSSARY

NOTE: The following terms are used in this document. To the extent possible, definitions were taken from relevant authoritative sources such as EPA, OECD, ASTM and IUPAC.

Acute Toxicity: The adverse effects occurring within a short time-frame of administration of a single dose of a substance, multiple doses given within 24 hours, or uninterrupted exposure over a period of 24 hours or less. Exposure may be via oral, dermal or inhalation routes as described in OECD Guidelines 401, 402, 403, and 420 in OECD Guidelines for the Testing of Chemicals.

Alga, Growth Inhibition Test: In a three-day exposure, growth inhibition is defined by the EC_{50}, the concentration of test substance in growth medium which results in a 50% reduction in either alga cell growth or growth rate relative to a control group. Test methodology is described in OECD Guideline 201, in OECD Guidelines for the Testing of Chemicals.

ARC: Aromatic ring class that reflects the weight percent of PACs that have a given number of aromatic rings (1 through 7) within the total analyzed sample.

Bioavailability: The state of being capable of being absorbed and available to interact with the metabolic processes of an organism. Typically a function of chemical properties, physical state of the material to which an organism is exposed, and the ability of the individual organism to physiologically take up the chemical. Also, the term used for the fraction of the total chemical in the environmental which is available for uptake by organisms. (AIHA, 2000)

Biodegradation: Breakdown of a substance catalyzed by enzymes *in vitro* or *in vivo*. As an endpoint in EPA's HPV program, biodegradation is measured by one of six methodologies described in OECD Guidelines 301A-F, in OECD Guidelines for the Testing of Chemicals.

BMD: The Benchmark Dose is the dose producing a predetermined change in response and is calculated from a dose-response model statistically fitted to experimental data. (Gephart, et al, 2001)

Category Member: The individual chemical or substance entities that constitute a chemical category.

Category: A chemical category, for the purposes of the HPV Challenge Program, is a group of chemicals whose physicochemical and toxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity. These structural similarities may create a predictable pattern in any or all of the following parameters: physicochemical properties, environmental fate and environmental effects, and/or human health effects. (US EPA, 2007)

***Daphnia* sp., Acute Immobilization Test:** In a one or two-day exposure, acute toxicity is defined by the EC_{50}, the concentration of test substance in water which causes immobilization to 50% of the test population of invertebrates. Test methodology is described in OECD Guideline 202, Part 1, in OECD Guidelines for the Testing of Chemicals.

Developmental Toxicity: Adverse effects on the developing organism that may result from exposure prior to conception (either parent), during prenatal development, or postnatally until the time of sexual maturation. The major manifestations of developmental toxicity include death of the developing organism, structural abnormality, altered growth, and functional deficiency. (US NLM, 2007)

Dose: The amount of a substance available for interactions with metabolic processes or biologically significant receptors after crossing the outer boundary of an organism. The **potential dose** is the amount ingested, inhaled, or applied to the skin. The **applied dose** is the amount presented to an absorption barrier and available for absorption (although not necessarily having yet crossed the outer boundary of the organism). The **absorbed dose** is the amount crossing a

specific absorption barrier (e.g., the exchange boundaries of the skin, lung, and digestive tract) through uptake processes. **Internal dose** is a more general term denoting the amount absorbed without respect to specific absorption barriers or exchange boundaries. The amount of the chemical available for interaction by an particular organ or cell is termed the delivered or **biologically effective dose** for that organ or cell (US EPA, 2002).

Dose-Response Relationship: The relationship between a quantified exposure (dose) and the proportion of subjects demonstrating specific biological changes in incidence or in degree of change (response) (US EPA, 2002).

Ecological Effects – all endpoints (OECD definitions)

Endpoint: In the context of the EPA High Production Volume Challenge Program, an endpoint is a physical-chemical, environmental fate, ecotoxicity, and human health attribute measurable by following an approved test methodology (e.g., OECD Guidelines for Testing of Chemicals). Melting point, biodegradation, fish acute toxicity, and genetic toxicity are examples of endpoints that are measured by an approved test method. (US EPA, 1999)

Environmental Fate Effects – all endpoints (OECD definitions)

Exposure: Contact made between a chemical, physical, or biological agent and the outer boundary of an organism. Exposure is quantified as the amount of an agent available at the exchange boundaries of the organism (e.g., skin, lungs, gut). (US EPA, 2002).

Feedstock: A refinery product that is used as the raw material for another process; the term is also generally applied to raw materials used in other industrial processes. (Speight, 2007).

Female Mating Index: Number of females with confirmed mating (sperm and/or vaginal plug)/number of females placed with males. (US EPA, 1996)

Fish, Acute Toxicity Test: In a four-day exposure, acute toxicity is defined by the LC_{50}, the concentration of test substance in water which kills 50% of the test population of fish. Test methodology is described in OECD Guideline 203, in OECD Guidelines for the Testing of Chemicals.

Genetic Toxicity *in vitro* (Gene Mutations): The assessment of the potential of a chemical to exert adverse effects through interaction with the genetic material of cells in cultured mammalian cells. Genotoxicity may be studies in cultured cells using methods described in OECD Guideline 476, in OECD Guidelines for the Testing of Chemicals.

Genetic Toxicity *in vivo* (Chromosomal Aberrations): The assessment of the potential of a chemical to exert adverse effects through interaction with the genetic material of cells in the whole animal. Genotoxicity may be studies in the whole animal using methods described in OECD Guideline 475, in OECD Guidelines for the Testing of Chemicals.

Hazard: A potential source of harm (US EPA, 2002).

Hazard Assessment: The process of determining whether exposure to an agent can cause an increase in the incidence of a particular adverse health effect (e.g., cancer, birth defect) and whether the adverse health effect is likely to occur in humans (US EPA, 2002).

Hazard Characterization: A description of the potential adverse health effects attributable to a specific environmental agent, the mechanisms by which agents exert their toxic effects, and the associated dose, route, duration, and timing of exposure (US EPA, 2002).

Health Effects: all endpoints (OECD definitions, unless otherwise specified)

Highly Refined: a descriptor for those lubricant oil basestocks that are not expected to be mutagenic or dermally carcinogenic based on knowledge of refining history or results from tests

such as the optimized Ames assay, IP346 assay, skin-painting tests in mice, and analysis of PAC content by GC (such as PAC-2 method).

Lowest-Observed-Adverse-Effect Level (LOAEL): The lowest exposure level at which there are statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control group (US EPA, 2002).

Modified Ames Test: A modification of the Ames test used for petroleum materials and designed to facilitate physical contact between the test substance and the bacteria as well as enhance the reactions among the bacteria. Also referred to as the Optimized Ames test.

Mutagenicity Index: The primary endpoint in the modified Ames test indicating the slope for the linear portion of the dose-response curve (number of revertant colonies vs dose of test substance per plate).

No-Observed-Adverse-Effect Level (NOAEL): The highest exposure level at which there are no biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control group; some effects may be produced at this level, but they are not considered adverse or precursors to adverse effects (US EPA, 2002).

Optimized Ames Test: See Modified Ames test.

PAC Profile: The listing of the weight percent of each of the DMSO-extractable 1- through 7-ring polycyclic aromatic compounds from a test material. (API, 2008)

PAC 2: A single analytical method that involves solvent extraction (DMSO) and an analysis of the DMSO-extracted concentrate of PACs by gas chromatography with an FID or MS detector. The DMSO extraction procedure is selective for the less polar PAC species, so that highly alkylated PACs are excluded from measurement. (API, 2008)

PDR_{10}: The Predicted Dose for a Response that is a 10% change from control. The prediction is based on models developed from a series of exposure-response studies. (API, 2008)

Photodegradation: The photochemical transformation of a molecule into lower molecular weight fragments, usually in an oxidation process. This process may be measured by Draft OECD Guideline, "*Phototransformation of Chemicals in Water – Direct and Indirect Photolysis*". This process also may be estimated using a variety of computer models.

Portal-of- Entry Effect: A local effect produced at the tissue or organ of first contact between the biological system and the toxicant (US EPA, 1994).

Read-Across: Read-across can be regarded as using data available for some members of a category to estimate values (qualitatively or quantitatively) for category members for which no such data exist. (OECD, 2007)

Repeated Dose Toxicity: The adverse effects occurring due to repeated doses that may not produce immediate toxic effects, but due to accumulation of the chemical in tissues or other mechanisms, produces delayed effects. Repeated dose toxicity may be studied following methods described in OECD Guidelines 407, 410, or 412 in OECD Guidelines for the Testing of Chemicals.

Reproductive Toxicity: The occurrence of biologically adverse effects on the reproductive systems of females or males that may result from exposure to environmental agents. The toxicity may be expressed as alterations to the female or male reproductive organs, the related endocrine system, or pregnancy outcomes. The manifestation of such toxicity may include, but not be limited to, adverse effects on onset of puberty, gamete production and transport, reproductive cycle normality, sexual behavior, fertility, gestation, parturition, lactation, developmental toxicity, premature reproductive senescence, or modifications in other functions that are dependent on the integrity of the reproductive systems. (US EPA, 1996)

Stability in Water: This environmental fate endpoint is achieved by measuring the hydrolysis of the test substance. Hydrolysis is defined as a reaction of a chemical RX with water, with the net exchange of the group X with OH at the reaction center. Test methodology for hydrolysis is described in OECD Guideline 111, in OECD Guidelines for the Testing of Chemicals.

Systemic Effects or Systemic Toxicity: Toxic effects as a result of absorption and distribution of a toxicant to a site distant from its entry point (US EPA, 2002).

Target Organ: The biological organ(s) most adversely affected by exposure to a chemical or physical agent (US EPA, 2002).

Transport Between Environmental Compartments: This endpoint describes the distribution of a chemical between environmental compartments using fugacity-based computer models. The results of the model algorithms provide an estimate of the amount of the chemical within a specific compartment. The environmental compartments included in many models are air, water, soil, sediment, suspended sediment, and aquatic biota.

APPENDIX A. CAS Numbers and Definitions of Category Members

The CAS numbers and definitions of refinery streams, including those in the heavy fuel oils category, were developed in response to Section 8(b) of the Toxic Substances Control Act. This section of TSCA required identification and registration with the Environmental Protection Agency before July 1979 of each "chemical substance" being manufactured, processed, imported or distributed in commerce. Due to analytical limitations and known variability in refinery stream composition, identification of every specific individual molecular compound in every refinery process stream under all processing conditions was impossible. Recognizing these problems, the American Petroleum Institute (API) recommended to the EPA a list of generic names for refinery streams consistent with industry operations and covering all known processes used by refiners. The list, including generic names, CAS numbers and definition of each stream, was published by the EPA as "Addendum I, Generic Terms Covering Petroleum Refinery Process Streams."

Because of the variability inherent in the processing of petroleum materials, the definitions API developed for the CAS numbers are qualitative in nature, written in broad, general terms. The definitions often contain only ranges of values for carbon numbers, with little if any quantitative analytical information or concern for possible compositional overlaps. As a result, the CAS descriptions are not useful in determining the exact composition of any specific refinery stream.

CAS RN	Definitions
64741-45-3	**Residuals (petroleum), atm. Tower** A complex residuum from the atmospheric distillation of crude oil. It consists of hydrocarbons having carbon numbers predominantly greater than C20 and boiling above approximately 350 °C (662°F). This stream is likely to contain 5 wt % or more of 4- to 6-membered condensed ring aromatic hydrocarbons.
64741-57-7	**Gas oils (petroleum), heavy vacuum** A complex combination of hydrocarbons produced by the vacuum distillation of the residuum from atmospheric distillation of crude oil. It consists of hydrocarbons having carbon numbers predominantly in the range of C20 through C50 and boiling in the range of approximately 350°C to 600°C (662°F to 1112°F). This stream is likely to contain 5 wt. % or more of 4- to 6-membered condensed ring aromatic hydrocarbons.
64741-61-3	**Distillates (petroleum), heavy catalytic cracked** A complex combination of hydrocarbons produced by the distillation of products from a catalytic cracking process. It consists of hydrocarbons having carbon numbers predominantly in the range of C15 through C35 and boiling in the range of approximately 260 °C to 500°C (500°F to 932°F). This stream is likely to contain 5 wt. % or more of 4- to 6-membered condensed ring aromatic hydrocarbons
64741-62-4	**Clarified oils (petroleum), catalytic cracked** (also listed in Olefins Panel Fuel Oils Category) A complex combination of hydrocarbons produced as the residual fraction from distillation of the products from a catalytic cracking process. It consists of hydrocarbons having carbon numbers predominantly greater than C20 and boiling above approximately 350°C (662°F). This stream is likely to contain 5 wt % or more of 4- to 6-membered condensed ring aromatic hydrocarbons.
64741-67-9	**Residuals (petroleum), catalytic reformer fractionator**

	A complex combination of hydrocarbons produced as the residual fraction from distillation of the product from a catalytic reforming process. It consists of predominantly aromatic hydrocarbons having carbon numbers predominantly in the range of C10 through C25 and boiling in the range of approximately 160 °C to 400°C (320°F to 725°F). This stream is likely to contain 5 wt. % or more of 4- or 6-membered condensed ring aromatic hydrocarbons.
64741-75-9	**Residuals (petroleum), hydrocracked** A complex combination of hydrocarbons produced as the residual fraction from distillation of the products of a hydrocracking process. It consists of hydrocarbons having carbon numbers predominantly greater than C20 and boiling above approximately 350°C (662°F).
64741-80-6	**Residuals (petroleum), thermal cracked** A complex combination of hydrocarbons produced as the residual fraction from distillation of the product from a thermal cracking process. It consists predominantly of unsaturated hydrocarbons having carbon numbers predominantly greater than C20 and boiling above approximately 350°C (662°F). This stream is likely to contain 5 wt % or more of 4- to 6-membered condensed ring aromatic hydrocarbons.
64741-81-7	**Distillates (petroleum), heavy thermal cracked** A complex combination of hydrocarbons from the distillation of the products from a thermal cracking process. It consists predominantly of unsaturated hydrocarbons having carbon numbers predominantly in the range of C15 through C36 and boiling in the range of approximately 260°C to 480°C (500°F to 896°F). This stream is likely to contain 5 wt. % or more of 4- to 6-membered condensed ring aromatic hydrocarbons.
64742-59-2	**Gas oils (petroleum), hydrotreated vacuum** A complex combination of hydrocarbons obtained by treating a petroleum fraction with hydrogen in the presence of a catalyst. It consists of hydrocarbons having carbon numbers predominantly in the range of C13 through C50 and boiling in the range of approximately 230°C to 600°C (446°F to 1112°F). This stream is likely to contain 5 wt % or more of 4- to 6-membered condensed ring aromatic hydrocarbons.
64742-78-5	**Residuals (petroleum), hydrodesulfurized atmospheric** A complex combination of hydrocarbons obtained by treating an atmospheric tower residuum with hydrogen in the presence of a catalyst under conditions primarily to remove organic sulfur compounds. It consists of hydrocarbons having carbon numbers predominantly greater than C20 and boiling above approximately 350°C (662°F). This stream is likely to contain 5 wt % or more of 4- to 6-membered condensed ring aromatic hydrocarbons.
64742-86-5	**Gas oils (petroleum), hydrodesulfurized heavy vacuum** A complex combination of hydrocarbons obtained from a catalytic hydrodesulfurization process. It consists of hydrocarbons having carbon numbers predominantly in the range of C20 through C50 and boiling in the range of approximately 350°C to 600°C (662°F to 1112°F). This stream is likely to contain 5 wt. % or more of 4- to 6-membered condensed ring aromatic hydrocarbons.
68187-58-6	**Pitch, petroleum, arom**

	The residual from the distillation of thermal cracked or steam-cracked residuum and/or catalytic cracked clarified oil with a softening point from 40 degree C to 180 degree C (104 degree F to 356 degree. F). Composed primarily of a complex combination of three or more membered condensed ring aromatic hydrocarbons**.**
68333-22-2	**Residuals (petroleum), atmospheric** A complex residuum from atmospheric distillation of crude oil. It consists of hydrocarbons having carbon numbers predominantly greater than C11 and boiling above approximately 200°C (392°F). This stream is likely to contain 5 wt.% or more of 4- to 6-membered condensed ring aromatic hydrocarbons.
68333-26-6	**Clarified oils (petroleum), hydrodesulfurized catalytic cracked** A complex combination of hydrocarbons obtained by treating catalytic cracked clarified oil with hydrogen to convert organic sulfur to hydrogen sulfide which is removed. It consists of hydrocarbons having carbon numbers predominantly greater than C20 and boiling above approximately 350°C (662°F). This stream is likely to contain 5 wt. % or more of 4- to 6-membered condensed ring aromatic hydrocarbons.
68333-27-7	**Distillates (petroleum), hydrodesulfurized intermediate catalytic cracked** A complex combination of hydrocarbons obtained by treating intermediate catalytic cracked distillates with hydrogen to convert organic sulfur to hydrogen sulfide which is removed. It consists of hydrocarbons having carbon numbers predominantly in the range of C11 through C30 and boiling in the range of approximately 205°C to 450°C (401°F to 842°F). It contains a relatively large proportion of tricyclic aromatic hydrocarbons.
68410-00-4	**Distillates (petroleum), crude oil** A complex combination of hydrocarbons produced by distillation of crude oil. It consists of hydrocarbons having carbon numbers predominantly in the range of C11 through C50 and boiling in the range of approximately 205°C to greater than 495°C (401°F to above 923°F).
68476-32-4	**Fuel oil, residuals-straight-run gas oils, high-sulfur** NONE
68476-33-5	**Fuel oil, residual** The liquid product from various refinery streams, usually residuals. The composition is complex and varies with the source of the crude oil.
68478-13-7	**Residuals (petroleum), catalytic reformer fractionator residual distn.** A complex residuum from the distillation of catalytic reformer fractionator residual. It boils approximately above 399°C (750°F).
68478-17-1	**Residuals (petroleum), heavy coker gas oil and vacuum gas oil** A complex combination of hydrocarbons produced as the residual fraction from the distillation of heavy coker gas oil and vacuum gas oil. It predominantly consists of hydrocarbons having carbon numbers predominantly greater than C13 and boiling above approximately 230°C (446°F).
68512-62-9	**Residuals (petroleum), light vacuum** A complex residuum from the vacuum distillation of the residuum from

	the atmospheric distillation of crude oil. It consists of hydrocarbons having carbon numbers predominantly greater than C13 and boiling above approximately 230°C.
68553-00-4	**Fuel oil, no. 6** A distillate oil having a minimum viscosity of 900 SUS at 37.7°C (100°F) to a maximum of 9000 SUS at 37.7°C (100°F).
68607-30-7	**Residuals (petroleum), topping plant, low-sulfur** A low-sulfur complex combination of hydrocarbons produced as the residual fraction from the topping plant distillation of crude oil. It is the residuum after the straight-run gasoline cut, kerosene cut and gas oil cut have been removed.
68783-08-4	**Gas oils (petroleum), heavy atmospheric** A complex combination of hydrocarbons obtained by the distillation of crude oil. It consists of hydrocarbons having carbon numbers predominantly in the range of C7 through C35 and boiling in the range of approximately 121°C to 510°C (250°F to 950°F),
68783-13-1	**Residuals (petroleum) coker scrubber condensed-ring-aromatic-containing** A very complex combination of hydrocarbons produced as the residual fraction from the distillation of vacuum residuum and the products from a thermal cracking process. It consists predominantly of hydrocarbons having carbon numbers predominantly greater than C20 and boiling above approximately 350°C (662°F). This stream is likely to contain 5 wt. % or more of 4- to 6-membered condensed ring
68955-27-1	**Distillates (petroleum), petroleum residuals vacuum** A complex combination of hydrocarbons produced by the vacuum distillation of the residuum from the atmospheric distillation of crude oil.
70592-76-6	**Distillates (petroleum), intermediate vacuum** A complex combination of hydrocarbons produced by the vacuum distillation of the residuum from atmospheric distillation of crude oil. It consists of hydrocarbons having carbon numbers predominantly in the range of C14 through C42 and boiling in the range of approximately 250°C to 545°C (482°F to 1013°F). This stream is likely to contain 5 wt.% or more of 4- to 6-membered condensed ring aromatic
70592-77-7	**Distillates (petroleum), light vacuum** A complex combination of hydrocarbons produced by the vacuum distillation of the residuum from atmospheric distillation of crude oil. It consists of hydrocarbons having carbon numbers predominantly in the range of C11 through C35 and boiling in the range of approximately 250°C to 545°C (482°F to 1013°F).
70592-78-8	**Distillates (petroleum), vacuum** A complex combination of hydrocarbons produced by the vacuum distillation of the residuum from atmospheric distillation of crude oil. It consists of hydrocarbons having carbon numbers predominantly in the range of C15 through C50 and boiling in the range of approximately 270°C to 600°C (518°F to 1112°F). This stream is likely to contain 5 wt.% or more of 4- to 6-membered condensed ring aromatic hydrocarbons
70592-79-9	**Residuals (petroleum), atm. tower, light**

	A complex residuum from the atmospheric distillation of crude oil. It consists of hydrocarbons having carbon numbers predominantly greater than C11 and boiling above approximately 200°C (392°F). This stream is likely to contain 5 wt % or more of 4- to 6-membered condensed ring aromatic hydrocarbons.
70913-85-8	**Residuals (petroleum), solvent-extd. vacuum distilled atm residuum** A complex residuum produced by the solvent extraction of the vacuum distillate of the complex residuum from the atmospheric distillation of crude oil.
70955-17-8	**Aromatic hydrocarbons, C12-20** A complex combination of hydrocarbons obtained from the distillation of biphenyl and naphthalene feedstocks. It consists predominantly of hydrocarbons having carbon numbers predominantly in the range of C12 through C20, such as alkylbenzenes, alkylnaphthalenes, indans, fluorenes, acenaphthalenes, phenanthrenes and anthracenes, and boiling in the range of approximately 282.degree.C to 427.degree.C (540.degree.F to 800.degree.F).

APPENDIX B. Heavy Fuel Oil Streams Processes

Atmospheric distillation

Heavy fuel oil related streams produced by atmospheric distillation comprise fractions of crude oil separated by heating (650-700°F [346-374^{0}C]) at atmospheric pressure. They include atmospheric distillates (heavy gas oils) and the heavier residual materials. The distillate HFO streams are similar to some of the refinery streams covered in the API HPV Gas Oils category, albeit of higher molecular weight. Some of these streams may be further hydrotreated or desulfurized to remove sulfur, nitrogen, and other impurities. Most atmospheric distillates undergo further processing in order to convert them into higher value fuels (diesel, kerosene).

Vacuum distillation

The residuum from the atmospheric distillation unit is distilled under vacuum to further separate heavier molecules without the use of high temperatures. This is done under reduced pressure to prevent thermal cracking. In addition to producing lube oils, various vacuum distillates (vacuum gas oils) and vacuum residuals are produced. Similar to the atmospheric distillates, some of the vacuum distillates may be hydrotreated or desulfurized to remove sulfur, nitrogen, and other impurities. Most vacuum distillates undergo further processing in order to convert them into higher value fuels (diesel, kerosene).

Portions of the heavier atmospheric or vacuum distillate streams may be used as blending stocks to reduce the viscosity of other residual streams. The atmospheric and vacuum residual refinery streams, each comprise a heterogeneous group of poorly defined, viscous, high boiling hydrocarbon streams that usually contain suspensions of resin/asphaltene complexes. These streams often have high levels of heterocyclic aromatic and naphthenic compounds. Varying percentages of sulfur, nitrogen, oxygen, and other elements are present as heterocyclic inclusions, primarily in the aromatics fraction. These residual streams often have a PAC content over 5%,

Cracking

Many of the distillate and residual streams used to blend heavy fuel oils are derived from cracking processes. Cracking is a process that breaks (“cracks”) the heavier, higher boiling petroleum streams produced by atmospheric or vacuum distillation into lighter molecular weight materials such as gasoline, diesel fuel, jet fuel and kerosene.

There are two basic types of cracking processes, those using heat (thermal cracking) to break molecular bonds, and those using a catalyst and heat (catalytic cracking) to facilitate the cracking process.

- **Thermal Cracking:** Visbreaking, coking and steam cracking are types of thermal cracking. In visbreaking, the heavy feedstock is heated under pressure to crack the molecules in the stream. Coking is a severe method of thermal cracking. In steam cracking, the hydrocarbon stream is diluted with steam and then briefly heated (>900 °C) in a furnace. Light hydrocarbon feeds produce streams rich in the lighter alkenes, including ethylene, propylene and butadiene. Heavier hydrocarbon feeds give some of these, but also give products rich in aromatic hydrocarbons. Petroleum pitch, sold as a product for various applications, is a high aromatic residual material produced from either thermal cracking or catalytic cracking.

- **Catalytic Cracking:** Catalytic cracking and hydrocracking are two types of catalytic cracking. Catalytic cracking is similar to thermal cracking except a catalyst facilitates

conversion of the heavier to lighter products and requires less severe operating conditions than thermal cracking. Catalytic cracking converts heavy paraffins to light paraffins and olefins, heavy naphthenes to light naphthenes and olefins, and heavy aromatics to light aromatics, naphthenes and olefins. As noted above, petroleum pitch is a high aromatic residual material from either catalytic cracking or thermal cracking.

- **Hydrocracking:** Hydrocracking is a combination of catalytic cracking and hydrogenation, using high pressure, high temperature, a catalyst, and hydrogen. It is typically used for feedstocks that are difficult to process by either catalytic cracking or reforming. When the feedstock has a high paraffin content, the primary function of hydrogen is to prevent formation of PACs. Hydrocracking converts sulfur and nitrogen compounds to hydrogen sulfide and ammonia.

The refinery streams produced by the various cracking processes represent a continuum in the severity of the cracking process. All the cracking processes produce refinery streams that are similar from a physical-chemical perspective, being differentiated from each other primarily by the ratio of their unsaturated and saturated hydrocarbon content. The saturated and aromatic hydrocarbons species are similar but may vary in ratio between streams. For instance, refinery streams that are produced by catalytic cracking have high levels of aromatics. In contrast, hydrocracked streams have relatively low amounts of aromatics, since hydrocracking introduces hydrogen into the cracking process resulting in saturation of aromatic compounds.

Reforming

Catalytic reforming employs a catalyst to facilitate the structural rearrangement of hydrocarbon molecules in order to increase the aromatic content of a refinery stream, ultimately producing higher octane gasoline blending stocks. During reforming, olefins are saturated to form paraffins, which are then converted to shorter paraffins, isoparaffins, and naphthenes. The naphthenes are converted to aromatics by dehydrogenation (Gary and Handwerk, 1994). As shown in Figure 1, there are two refinery streams in the heavy fuel oils category that are produced as residuals of reforming. See Appendix A for a more detailed description of each of these streams.

APPENDIX C. Links to Additional Resources

Refining Processes: General Descriptions

http://www.chevron.com/about/learning_center/refinery
http://www.lubrizol.com/lubetheory/default.htm
http://www.orionrefining.com/flow.htm
http://www.osha-slc.gov/dts/osta/otm/otm_toc.html
http://www.shellglobalsolutions.com/base_oils/library/library.htm
http://www.shell-lubricants.com/learningcenter/aboutoil.html
http://www.shellus.com/welcome/history/hist_oil_main.html
http://www.epa.gov/compliance/resources/publications/assistance/sectors/notebooks/petrefsnpt1.pdf
http://www.mts.net/~dbrad1/base_oil.htm

Petroleum Related Glossaries

http://www.caltex.com.au/products_glo.asp
http://www.citgo.com/CommunityInvolvement/Classroom/Glossary.jsp
http://www.epplp.com/gloss.html
http://www.prod.exxon.com/exxon_productdata/lube_encyclopedia/
http://www.hellenic-petroleum.gr/english/glossary/gl_main.htm
http://www.prod.exxon.com/exxon_productdata/lube_encyclopedia/
http://www.oilanalysis.com/dictionary
http://www.orionrefining.com/glossary.htm
http://www.gedolbear.com/glossary.htm
http://www.shellglobalsolutions.com/base_oils/glossary/a_g.htm
http://www.ursa-texaco.com/English/glossary_a.html
http://www.eia.doe.gov/pub/oil_gas/petroleum/data_publications/petroleum_marketing_annual/current/pdf/glossary.pdf

APPENDIX D. Correlation between PAC Profile and Selected Endpoints of Mammalian Toxicity

As indicated in the Heavy Fuel Oils Test Plan submitted to the EPA in 2003, the mammalian toxicity of crude oils is expected to be related to their PAC profiles; particularly the toxicity measured in repeat-dose, developmental, and *in vitro* mutagenicity studies. The PAC[1] profile is the weight percent of DMSO-extractable, aromatic compounds contained in the 1 to 7 aromatic ring classes.

The initial indication that PAC content could be used to predict the toxicity of untested petroleum-related materials including crude oils was based on the publication by Feuston et al. (1994). Their research, based on thirteen petroleum-derived refinery streams, examined the correlations between the weight percentage of several chemical classes of compounds and the magnitude of various effects produced in rats treated dermally with these substances in repeat-dose and developmental toxicity studies. In general, Feuston et al. found that the toxicity of the streams was correlated with the concentrations of the 3 to 7 ring PACs. The analyses were based on the ranks of several measures of toxicity and the individual PAC concentrations.

In 2004, the API Testing Group recognized the need to further evaluate the observations made by Feuston et al. (1994) and commissioned a Task Group (PAC Analysis Task Group, or TG) comprised of experts in the fields of petroleum chemistry, toxicology, and biostatistics. The TG issued a report describing the relationships between PAC profile and the repeat-dose and developmental toxicities of high-boiling petroleum-related substances, i.e. those with final boiling point approximately ≥650^{0}F [>343^{0}C] (API, 2008). Predictive models for seven selected repeat-dose and developmental dermal toxicity endpoints in the rat were reported (API, 2008). The report was reviewed in a peer consultation process and/are publicly available (TERA, 2008). Reports are in preparation on the relationship between PACs and reproductive and genetic toxicities of high-boiling petroleum substances.

Four potential sources of information were reviewed for the project: the publication by Feuston et al (1994); other published literature on the toxicity of individual PAH and PAC containing materials; studies sponsored by the American Petroleum Institute (API); and unpublished company laboratory reports. The unpublished laboratory reports consisted of: (1) reports of repeat-dose toxicity studies, (2) reports of developmental toxicity studies, (3) two reproductive toxicity screening studies, one each with treated males and females, on a single substance containing a high concentration of PAC, (4) an exploratory dose range-finding study in non-pregnant female rats, (5) reports of mutagenesis tests, primarily results of optimized Ames tests, and (6) reports of compositional data on the tested substances. All unpublished company laboratory reports (repeat-dose, developmental toxicity, and analytical) were judged to be either "reliable without restrictions" or "reliable with restrictions, i.e. reliability scores of 1 or 2 (Klimsch, et al. 1997).

The relationship between acute toxicity and PAC was not investigated statistically since the reported oral LD_{50} values for high-boiling petroleum substances are generally greater than the maximum doses tested, typically 5 g/kg and 2 g/kg for oral and dermal exposures, respectively (API 2001, 2002, 2003a, b, c & d, 2004). These data demonstrate that the respective petroleum-derived streams are not toxic, at least within the operational definitions of the regulatory testing guidelines.

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[1] Note that "polycyclic aromatic hydrocarbons" (PAH) refers to compounds of two or more fused-aromatic rings consisting of carbon and hydrogen only. Polycyclic aromatic compounds (PAC) is a more inclusive term than PAH since, in addition to the PAHs, PAC also includes compounds in which one or more atoms of nitrogen, oxygen or sulfur (a heteroatom) replaces one or more of the carbon atoms in a fused ring system and perhaps more importantly includes alkylated (methyl, ethyl, etc.) rings **(API, 2008)**.

To model the outcomes of repeat-dose and developmental studies, sets of matched data of PAC composition and biological effects were selected. Each biological endpoint had an average of about 80 data points. The seven biological endpoints that were selected for final statistical characterization were four repeat-dose measures, i.e. thymus weight, liver to body weight ratio, platelet count and, hemoglobin concentration, and three developmental measures, i.e. fetal weight, live fetal count, and percent resorptions. The endpoints selected for modeling are consistent with effects reported for both individual PACs and PAC containing substances (SCF, 2002, ATSDR, 1995; IPCS, 1998; IRIS 2007; RAIS, 2007). The endpoints selected are also supported by other studies on PAC-containing petroleum-related substances submitted by the Petroleum HPV Testing Group as robust study summaries to satisfy the USEPA HPV Challenge Program requirements for the Aromatic Extracts, Crude Oil, Gas Oils, Heavy Fuel Oils, Lubricating Oil Basestocks, and Waxes and Related Materials.

The PAC compositional data was developed using an analytical technique referred to as the "PAC-2 Method," or 'Mobil Oil PAC Method" or, simply "Method II" (Feuston et al., 1994; Roy et al., 1985; Roy et al., 1988), a variation of the Institute of Petroleum IP 346 method (IP, 1980). In the PAC-2 Method, the percent of sample mass is determined for each PAC ring class (1 through 7) contained in PAC-concentrated dimethyl sulfoxide (DMSO) extracts of the test material. The analysis was performed by gas chromatography with flame ionization detection (GC/FID) or mass spectrometry (GC/MS).

The dose-response relationships between the "PAC profile" and specific biologic effects were successfully predicted using linear regression models. The correlations between observed and model-predicted data were very high ($r > 0.90$). The predictive ability of the models was rigorously tested and the models were found to be accurate predictors when used with interpolated data. A test material that has its PAC profile and dose within the range of the PAC profiles and doses used to develop the model gives rise to an interpolated model prediction. Predictions from samples that do not meet this requirement are considered extrapolated predictions. Extrapolated predictions might not be accurate and are considered unreliable by the Testing Group.

Interpolated model results can be used to estimate the dose that would cause a 10% change in the response relative to the control group (PDR_{10}). The concept is similar to the Benchmark Dose (BMD) for continuous endpoints (Crump, 1984). Comparison of the PDR_{10} and BMD_{10} from a series of samples has shown a close agreement indicating the usefulness of the PDR_{10} when no biological endpoint testing data exists and only the PAC profile is available to assess toxicity.

While similar to the BMD, the PDR_{10} has several advantages:

- The PDR_{10} is based on one validated model, whereas the BMD can be developed from several competing models, making the BMD strongly dependent on the selected model (Gephardt et al, 2001).
- The PDR_{10} can be applied to untested materials for which there are compositional data (i.e., PAC profiles) but no response data, whereas the BMD cannot be used for untested materials.
- The PDR_{10} is based on the large amount of data accumulated over multiple studies, whereas the BMD is based on a single study, usually with only 3 to 5 data points.

A copy of the full report detailing the development and testing of the predictive models developed by the Testing Group can be obtained through either API or TERA (API, 2008; TERA, 2008). Publications of these methods are in press at Regulatory Toxicology and Pharmacology (Gray et al, 2012; Nicolich et al, 2012; Murray, et al., 2012a; Roth et al., 2012; Simpson et al., 2012)

Appendix E. Optimized Ames Test and Statistical Modeling

The Optimized Ames test was developed to improve the performance of the reverse mutation *Salmonella* assay for detecting mutagenic and potentially carcinogenic lubricant base stocks and related refinery streams (ASTM, 2002). The method involves concentration of polycyclic aromatic compounds (PAC) by extraction, employing the most consistently PAC- sensitive strain of *Salmonella* [TA98] and increasing the metabolic activation system to maximize metabolism of the streams being evaluated. These modifications allowed detection of positive bacterial gene mutation response identified as an increase of mutant colonies in treated groups at least 2-fold that of negative controls as in the Standard Ames Assay and allowed prediction of potential dermal carcinogenesis by calculation of a mutagenicity index (MI).

The mutagenicity index (MI) is the slope of the initial portion of the dose response curve expressed in units of revertants per microliter. The mutagenicity index was highly correlated with dermal carcinogenic potential, suggesting that oils with MI values < 1 were unlikely to be dermally carcinogenic, oils with MI values $\geq$ 1 but < 2 were indeterminate, and oils with MI values $\geq$ 2 would likely produce skin tumors if tested in mice. The test method was refined to provide the greatest predictive value of gene mutagenicity and potential carcinogenicity for the widest range of high boiling [final boiling point approximately $\geq 650^0$F $\geq 343^0$C (API, 2008)] PAC-containing streams and thus provides a more sensitive general *Salmonella* protocol for this class of petroleum substances. In 1995, the optimized Ames test was standardized as an ASTM method [ASTM E1687-95].

Correlation of Mutagenic Activity with PAC Profile

The relationship of the MI with the PAC profile of refinery streams with known dermal carcinogenic potential has been established. The method of quantifying PAC constituents in which the condensed ring aromatics are removed by DMSO extraction and analyzed for 3-7 ring PAC by gas chromatography (GC) was developed by Roy *et al*. (1985; 1988). Having demonstrated a strong correlation between analytical distribution of PAC and mutagenicity in the optimized Ames test for petroleum-derived substances which produce dermal tumors when tested in mice, the utility of this relationship for read-across to untested substances has been expanded by statistical modeling.

Statistical Modeling of Analytical Data with the Optimized Salmonella Assay (Ames Test)

A statistical model has been developed to predict MI scores for untested substances encompassing precision in the critical 0-2 range (McKee, et al., 2010 abst.; McKee et al, 2012). This model employs the 1-7 ring PAC profile for each sample to predict MI scores. This model separated the data from 193 samples of a range of PAC-rich petroleum streams into those with mutagenicity index values equal to or greater than 1.0 and those with MI values less than 1.0. This model was not designed to quantify mutagenic potency but to identify whether or not a substance had an MI value less than 1 or not; this result can be used as an indication of whether the material has the potential to induce gene mutations in the optimized *Salmonella* assay and thus, to potentially be active in dermal carcinogenesis assays as well.

The statistical model is based on a series of three steps each predicting if the test substance was above or below an MI cut-point using a binary logistic general additive model. Step 1 predicts the probability that the substance has an MI of 5 or larger. The second step used only the substances predicted to have an MI below 5 and tested for a split at an MI of 2 or larger (the samples from the first step that are predicted to be above 5 were set at 5 and were no longer in the model process). The third step uses only the substances predicted to have an MI below 2 and tested for a split at an MI of 1 or larger (again with the substances from the second step that were predicted to be greater than 2 were set to 2 and were no longer in the modeling process). At each step the probability for a decision is based on a value of 0.50. For example, in the first step, if the probability of the substance having an MI less than 5 was greater than 0.50 the substance was assigned a predicted

MI of 'less than 5.' The final result was the combination of the results from the 3 steps with each substance predicted as being either < 1 or ≥ 1.

The model predictions agreed with the experimentally determined results 98% of the time, with the majority of the incorrect predictions being at MI values that were close to 1.0. When the model was tested with 49 hold out samples, 94% of the predictions were in agreement with the experimentally determined values.

From this information it is apparent that the outcome of optimized Ames tests can be predicted from compositional information with an accuracy that seems comparable to that associated with variability inherent with either the experimental methods or the methods used to calculate mutagenicity index from the experimental data.