

**HIGH PRODUCTION VOLUME (HPV) CHEMICAL CHALLENGE PROGRAM**

**GAS OILS CATEGORY ANALYSIS DOCUMENT AND HAZARD  
CHARACTERIZATION**

**Submitted to the US EPA**

**by**

**The American Petroleum Institute (API) Petroleum HPV Testing Group**

**[www.petroleumhpv.org](http://www.petroleumhpv.org)**

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## EXECUTIVE SUMMARY

The Gas Oil Category includes 28 members comprised of 4 finished products (distillate fuels) and 24 refinery streams with similar carbon ranges. The category members are complex substances, containing variable amounts of alkanes, cycloalkanes, olefins, and aromatics. Gas oil streams are produced either by atmospheric distillation or by secondary processing of the materials derived from the vacuum distillation of the residuum from the atmospheric distillation of crude oil. Materials from this secondary processing have higher aromatic and olefin contents than straight run gas oils. The distillate fuels may be straight run or a blend of various gas oil streams (both straight run and cracked). In comparison to gas oil refinery streams and fuel oils that do not have product specifications and can contain a range of 1-7 ring polyaromatic compounds (PAC), however Fuel oil No. 2 and the ultralow sulfur diesel (ULSD) fuels must meet stringent ASTM and EPA standards for commercialization. The boiling point specifications for these fuels essentially limit the aromatics to 1, 2, 3-ring compounds with minimal if any 4-ring PACs. Key parameters when analyzing this category for environmental hazards are the distribution of aromatic and saturated hydrocarbons, and for some mammalian endpoints (repeated-dose, developmental, reproduction, and mutagenicity) the content and distribution of 1-7 ring PAC are important.

**Physical-Chemical Properties:** Gas oils are variable and complex substances of hydrocarbons, predominantly having carbon chains from C<sub>9</sub> to C<sub>30</sub>, and boiling over the temperature range of approximately 150°C to 450°C. Vapor pressures are within a measurable range, with values of 0.4 kPa and 2 kPa being reported. Partition coefficients of constituent hydrocarbons range from 3.3 to >6. Water solubility values for components of these substances have been reported to range from 2.0 mg/L to 8.7 mg/L for dissolved hydrocarbons.

**Environmental Fate:** If gas oils are released to the environment, individual components will disperse and partition according to their individual physical-chemical properties. Based on modeling individual structures encompassing the different types and molecular weights of hydrocarbons, volatilization to the atmosphere is an important process for the low molecular weight fractions. Residence times in the atmosphere are relatively short due to indirect photodegradation reactions. In water, hydrolysis is not likely to occur, as the chemical linkages of hydrocarbons do not allow for these reactions. Rates of biodegradation of gas oils can be high, and these substances are considered to be inherently biodegradable. Rates for some individual gas oil samples may be sufficient to pass the criterion for ready biodegradability in 28-day tests

**Environmental Effects:** Available information includes studies of acute and chronic toxicity to fish and aquatic invertebrates (i.e. daphnids) and toxicity to aquatic plants (i.e. algae) expressed as growth inhibition. Testing of commercial distillate fuels used for heating and transportation (e.g., No. 2 fuel oil and diesel fuel) using water accommodated fractions of the gas oils showed moderate toxicity to aquatic life. LL<sub>50</sub> values for fish ranged from 3.2 to 65 mg/L and EL<sub>50</sub> values for invertebrates ranged from 2.0 to 210 mg/L. EL<sub>50</sub> values for inhibition of algal growth rate and biomass ranged from 1.9 to 78 mg/L. While there were no obvious differences in acute toxicity between fish and daphnids to the substances that were tested, daphnids appeared to have a greater sensitivity compared to fish for chronic toxicity. While the chronic data were limited to one test substance and one test per species, the NOELR for fish (1.2 mg/L) compared to daphnids (0.15 mg/L) suggests a sizeable difference in the chronic toxicity to gas oils for these two species.

**Human Health Effects:** This Interim Category Assessment Document (CAD) addresses health effects endpoints by evaluating the toxicology database for the gas oil related refinery streams and products and using read-across information whenever possible among category members, and other API HPV categories. In the final CAD, modeling data based on PAC profile for repeat dose,

developmental toxicity, and *in vitro* genetic toxicity endpoints will be employed to predict toxicity of untested streams for these endpoints.

Gas Oil streams and fuels induce minimal acute toxicity by the oral, dermal and inhalation routes. Moderate to severe skin irritation has been reported from studies involving 24 hour exposure periods, but skin irritation would more likely be mild to moderate if these substances were tested under the 4 hour exposure conditions recommended for classification purposes. No dermal sensitization has been reported. Eye irritation was minimal to slight.

Representative gas oil streams and distillate fuels generally induce gene mutation in bacterial and mammalian cells as demonstrated in both standard *in vitro* assays and the Optimized Ames Test. Overall, the weight of evidence from studies for chromosome aberrations or micronucleus formation indicate that gas oils generally do not cause cytogenetic damage in animals

Repeated dose 13-week rat dermal studies on gas oil streams indicate LOAEL values of 125mg/kg and NOAEL values of 25-30mg/kg with the exception of a light coker gas oil (CAS RN 64741-82-8 sample 87213) for which the LOAEL was 30mg/kg, the lowest dose tested. The effects were likely exacerbated by severe skin irritation at all dose levels. Skin irritation produced by other gas oils generally ranged from slight to moderate. In all studies effects were seen primarily on liver and thymus weights and hematologic endpoints. The 4 week duration rat dermal studies showed slight to moderate skin irritation and minimal systemic toxicity. No significant adverse effects were seen in reproductive organs in any rat dermal study. Supplemental studies of the effects of repeated dermal exposure in rabbits focused on irritation and mortality and are provided as supplementary information.

For developmental toxicity the substances tested in the Gas Oil Category had developmental LOAELs ranging from 125 – 500mg/kg and NOAELs ranging from 30 – 500mg/kg, attributed primarily to fewer live offspring at delivery and lower fetal or pup body weight at delivery or Lactation days 0-4. Fetal malformations were reported only for CAS RN 64741-43-1 [an intermediate gas oil] and CAS RN 64741-49-7 [Vacuum Tower Overheads]. Developmental toxicity was seen primarily at doses that were maternally toxic. Some gas oils showed no developmental toxicity at the highest doses tested even in the presence of maternal toxicity.

Reproductive parameters in developmental toxicity studies addressing fertility, successful insemination and implantation demonstrate that in general these endpoints are not adversely affected by treatment with gas oil streams. Three studies in which females were treated dermally for a week prior to mating through mating and gestation demonstrated that exposure to high concentrations of several gas oils did not adversely affect mating and establishment of pregnancy but did affect successful completion of pregnancy and pup viability at maternally toxic doses of 250mg/kg and above. 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, no abnormal histopathology or no effects on sperm at doses ranging up to 500-820mg/kg/day. The NOAELs for reproductive toxicity are not expected to be lower than the NOAELs for developmental toxicity because the most sensitive endpoints identified in the developmental and reproductive toxicity studies have been developmental effects, specifically reductions in fetal survival and growth resulting from *in utero* exposure.

Inhalation Studies: Two 4 week repeat dose inhalation studies with samples of hydrodesulfurized distillates administered at single concentrations of 25mg/m<sup>3</sup> and one developmental toxicity study of

a marketplace sample of diesel fuel [CAS RN 68476-34-6] administered at 100 or 400ppm daily on gestation days 6-15 did not result in any toxicologically important substance induced effects.

Dermal carcinogenesis studies indicate that Gas oils and distillate fuels are potential skin carcinogens after repeated skin application but are not associated with the induction of systemic tumors. The skin carcinogenicity of the petroleum streams with high boiling ranges has been found to correlate with 3-7 ring PAC content. Skin tumors produced by substances in this category containing low or no PAC are likely due to a non-genotoxic promotion effect and only observed in the presence of sustained severe skin irritation.

### **Human Exposure**

Because the No. 2 distillate fuels have widespread use in transportation and industrial and residential heating applications, both occupational and consumer exposures are possible. Exposure to children is not anticipated. The other substances in the Gas Oil Category are only used in industrial applications.

In conclusion, the information provided in this Interim Gas Oils Category Assessment Document is sufficient to characterize physiochemical properties and to evaluate the environmental and human health hazards of gas oil refinery streams and distillate fuels.

## 1. DESCRIPTION OF THE GAS OILS CATEGORY

### 1.1. Nomenclature, Use, and Manufacture

The Gas Oils category includes both finished products (distillate fuels) and the refinery streams (gas oils) from which they are blended. The specific CAS numbers and descriptions of category members are detailed in Appendix A.

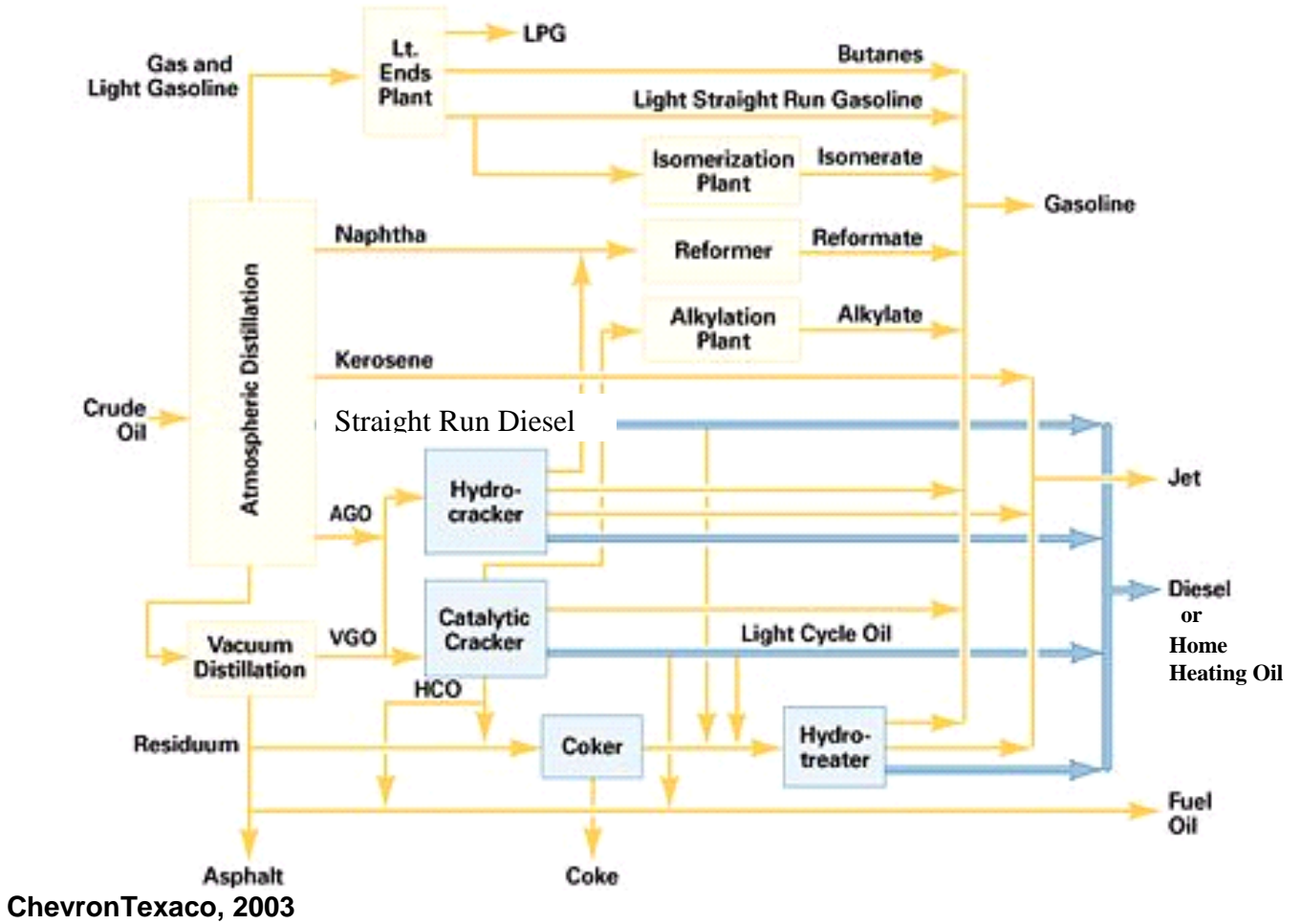
The distillate fuels covered in this category are used primarily as heating oils and as fuels in compression-ignition engines. Because they are manufactured to meet performance specification limits (and not specific chemical compositions), the chemical compositions of distillate fuels can vary since products with the desired fuel properties can be formulated in a number of ways. Distillate fuels are distinguished from each other based primarily on their boiling point ranges, chemical additives, and uses. However, whether straight run or blended, distillate fuels are produced to meet the ASTM specifications for either Fuel Oils (ASTM D396) or Diesel Fuel Oils (ASTM D975). The ASTM specification for diesel fuels limits the aromatic content of No. 1 D and No. 2-D low sulfur diesel fuels to a maximum 35% by volume (ASTM, 2002).

The boiling range of No. 2 Diesel Fuel and No. 2 Fuel Oil are limited to a maximum T90 of 338 °C (640 °F). That specification essentially limits the aromatics to 1, 2, or 3-ring compounds. Four-ring aromatic compounds are possible, but are rarely found in commercial on-road diesel fuel no. 2 (Table 16 – ULSD samples). This is not the case with Fuel oil No. 4 which does not have a specification for boiling range and could contain significant amounts of aromatics with 4+ rings. While Fuel oil No. 4 is sponsored in the Gas Oil Category, no member of the Petroleum HPV Testing Group actually makes the substance and therefore no samples were available to analyze.

Diesel fuel No. 2 is used for automotive diesel engines while No. 4 diesel fuel is used for low and medium speed diesel engines in non-automotive applications. Fuel Oil No. 4 has been used in commercial and industrial burners to generate steam, for space and water heating, pipeline pumping, and gas compression (ASTM, 2001; 2002). Two other classes of fuel oils, Fuel Oil No. 1 (also known as kerosene) and Fuel Oil No. 6 (heavy fuel oil) are covered in separate API HPV Category Closure Documents.

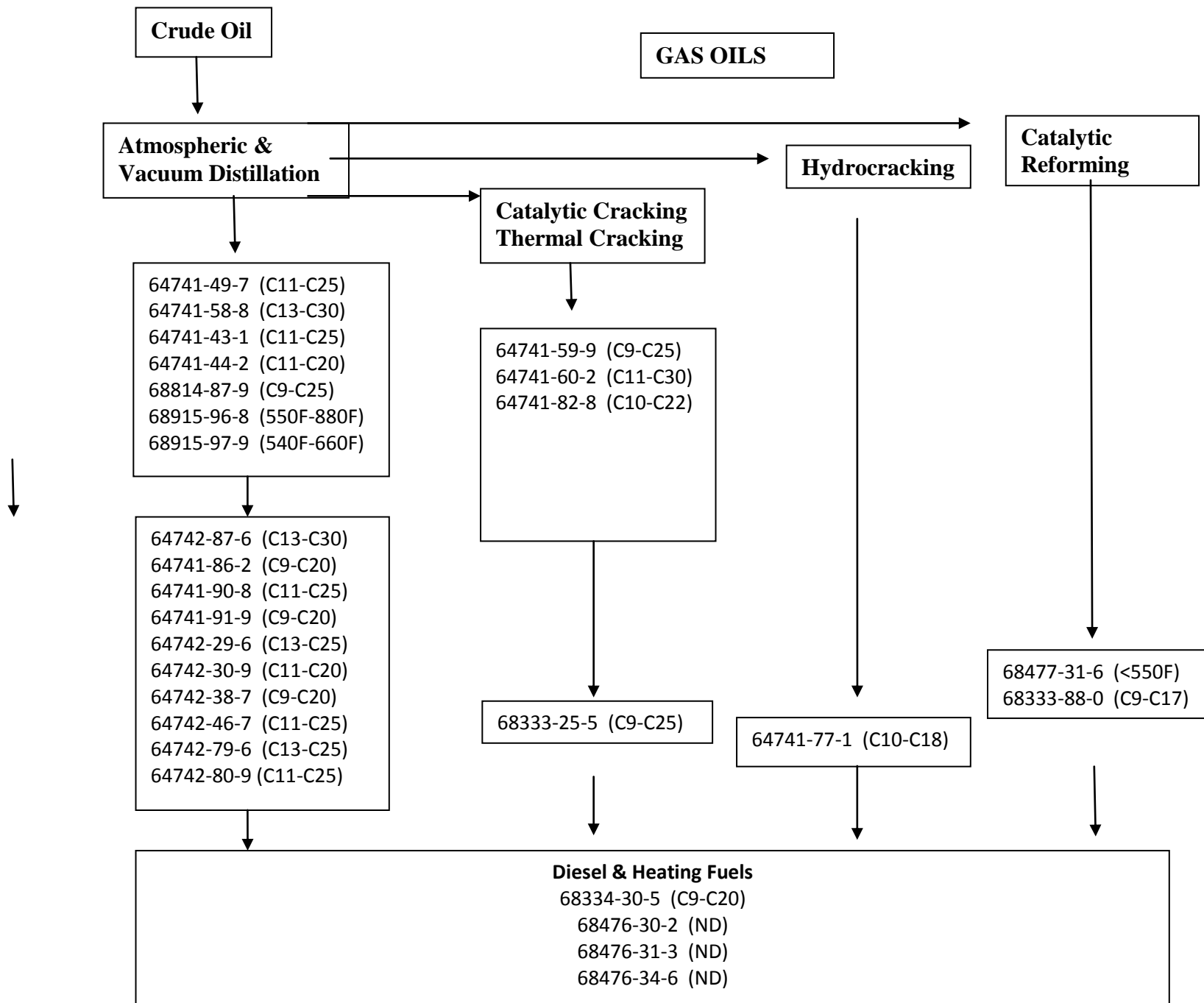
As shown in Figure 1, gas oil streams are produced either by atmospheric distillation or by secondary processing of the materials derived from the vacuum distillation of the residuum from the atmospheric distillation of crude oil. Materials from this secondary processing have higher aromatic and olefin contents than straight run gas oils. Distillate fractions that require only minor or no additional processing are known as “straight run” gas oils. The distillate fuels may be straight run or a blend of various gas oil streams (both straight run and cracked). Historically, straight-run gas oils are the major components of the distillate fuels, but rising demand has made it necessary to use increasing volumes of streams derived from the secondary processing of heavier fractions. 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. Thermal cracking uses heat to break molecular bonds and catalytic cracking uses a catalyst and heat to facilitate the cracking process. Figure 1b illustrates the distribution of CAS RNs in this category by process

**Figure 1. Gas Oils Process Diagram**



Note: AGO = atmospheric gas oil  
 VGO = vacuum gas oil  
 HCO = heavy cycle oil

**Figure 1b. Gas Oil Process Diagram by CAS RN distribution**

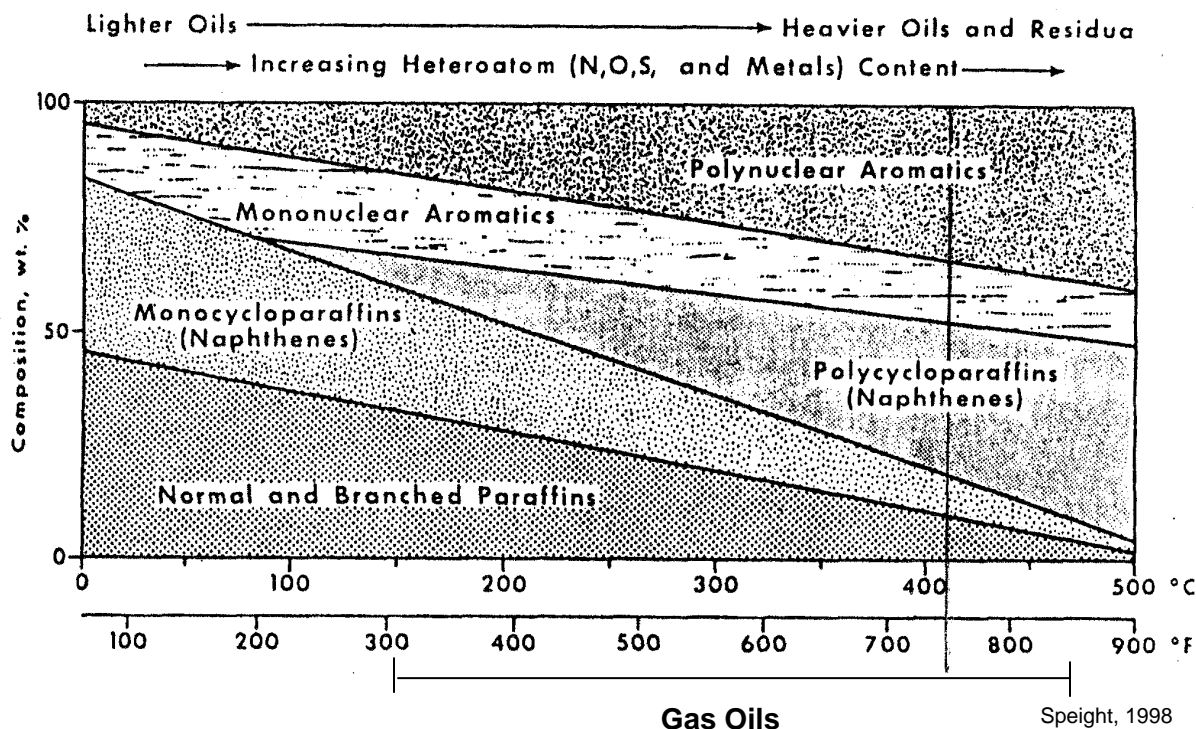


## 1.2 Analytical Characterization

The materials in this category are complex substances that boil over a range of approximately 300 to 880°F (150 to 471°C) and are composed primarily of saturated and/or aromatic hydrocarbons with carbon numbers ranging from C9 to C30. Gas oils contain straight and branched chain alkanes (paraffins), cycloalkanes (naphthenes), aromatic hydrocarbons and mixed aromatic cycloalkanes. As the boiling ranges of the fractions increase, the levels of polycyclic aromatic compounds (PACs), polycycloparaffins and heteroatoms (Nitrogen, Oxygen, and Sulfur) increase, while the levels of paraffins decrease (Figure 2, Speight, 1998). Most commercial gas oils contain PACs. In straight-run gas oils these are mainly 2 and 3-ring aromatic compounds, with relatively low concentrations of 4 to 7-ring PACs. The heavier atmospheric, vacuum or cracked gas oil components may contain increased levels of 4 to 7-ring PACs, some of which are carcinogenic (CONCAWE, 1996). Blended distillate fuels, in addition to containing the hydrocarbons from their blending stocks, may also contain low concentrations of performance additives such as flow improvers, corrosion inhibitors, defoamers, dyes/markers, anti-oxidants, stability improvers, cetane improvers, detergents and anti-static additives.

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

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



Because they are complex substances, 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 2001, 2002). Whereas detailed compositional information may be limited, general compositional information can be inferred from the gas oil's physical

properties and the type of processing it has undergone, e.g. the higher the boiling temperature range of a fraction, the higher the molecular weight of the oil's components. Similarly, streams that have been "cracked" have higher olefinic and aromatic hydrocarbon content while straight run gas oil streams that have undergone a limited amount of additional processing are composed predominantly of saturated hydrocarbons.

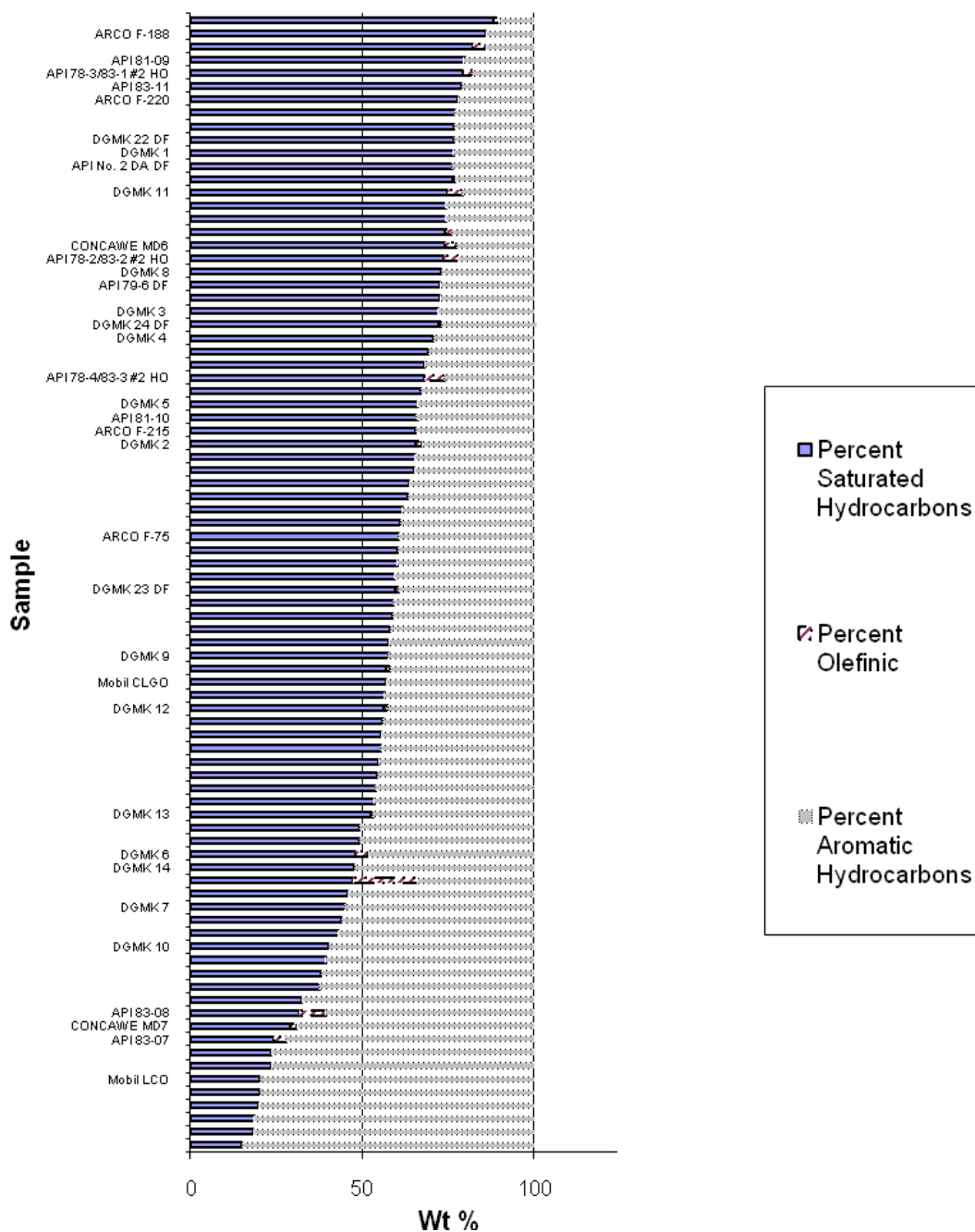
Compositional information on 86 gas oil samples (representing 15 of the CAS numbers in this category) showed that the range of hydrocarbon types was:

Saturates: 18 - 86%

Aromatics: 14 - 82 %

As shown in Figure 3, the saturate and aromatic hydrocarbon content of the Gas Oil category members forms a continuum from high saturate content to high aromatic content.

**Figure 3. Composition of Representative Samples of Gas Oils and Distillate Fuels**



Note: Samples shown with a descriptive title (i.e. ARCO F-188) are from studies described in the Robust summaries (Separate appendix). Compositional information for 86 samples of gas oils and distillate fuels was obtained from publications and company reports.

An important compositional characteristic of gas oils is the presence of varying amounts of polycyclic aromatic compounds (PACs). PACs are a subset of the aromatic compounds presented in Figure 3 above. Although similar to polycyclic aromatic hydrocarbons (PAHs) that contain two or more fused-aromatic rings consisting only of carbon and hydrogen, PACs are a broader group of compounds that also includes heteroatomic compounds in which one or more of the carbon atoms in the PAH ring system are replaced by nitrogen, oxygen, or sulfur atoms. The distribution of PACs is dependent on the crude oil source and the nature and severity of refining processes and includes a complex variety of parent (i.e., unsubstituted) and alkylated structures. The alkyl-substitutions are usually one to four carbons long and can include non-carbon compounds such as sulfur. Multiple alkyl and cycloparaffin substitutions of the parent structure are also common, especially in higher boiling fractions of petroleum. The relative abundance of the alkylated polycyclic aromatics (C1-C4) in petroleum far exceeds the abundance of the parent compound (C0) (Speight, 2007). The fact that the levels of alkylated polycyclic aromatics are much greater than the parent polycyclic aromatics is the main feature of the PACs found in petroleum substances (Altgelt and Boduszynski, 1994).

Tables 1 to 3 summarize the composition of On Road Diesel Fuel No. 2 illustrating the limited aromatics content and profile of generally 1, 2, or 3-ring compounds and low sulfur content. In order to meet ASTM standards, commercial diesel fuels are much less variable in composition than refinery streams from which they are derived. The boiling point specifications for ultra low sulfur diesel fuels (ULSD) limit the PAC content, minimizing the amount of 4-ring PAC present. Comparison of the PAC analytical profiles of ULSD (CAS RN 68476-34-6) samples in Table 16 with refinery stream samples without product specifications further illustrates these differences.

**Table 1. Typical Properties of On-Road Diesel Fuel No. 2 (Ultra Low Sulfur, <15 PPM)<sup>a</sup>**

TEST DESCRIPTION	#2 REGULAR DIESEL S15		
	MINIMUM	MAXIMUM	AVERAGE
Number of Fuel Samples = 111			
Relative Density, 60/60 F	0.8239	0.8652	0.8458
Distillation, Deg F			
IBP	334	423	361
5 % rec.	367	447	396
10 % rec.	376	467	414
20 % rec.	402	488	440
30 % rec.	425	506	462
40 % rec.	446	527	484
50 % rec.	464	545	504
60 % rec.	483	564	525
70 % rec.	506	583	548
80 % rec.	534	604	574
90 % rec.	563	638	608
95 % rec.	586	669	637
EP	615	687	656
Kinematic Viscosity, @ 40 Deg C, cSt.	1.98	3.29	2.59
Cloud Point, Deg. F	-24	20	4
Nitrogen, Wt. %	<0.001	0.014	<0.002
Sulfur (D-5453), ppm wt.	<1	10	<6

Mono Aromatics Content (SFC)	14.9	28.5	21.7
Poly Aromatics (SFC)	0.8	8.5	3.9
Total Aromatics (SFC)	15.7	35.3	25.7

<sup>a</sup> Alliance of Automobile Manufacturers 2009 summer survey

**Table 2. Hydrocarbon Composition of On-Road Diesel Fuel No. 2 (Low Sulfur, <500 PPM)<sup>a</sup>**

Number of Fuel Samples = 12		Average	Min	Max
Extended FIAM by HPLC, Vol %				
	Aromatics, Vol %	29.3	11.9	46.6
	Olefins, Vol %	0.0	0.0	0.0
	Paraffins, Vol %	70.7	53.4	88.1
Total Aromatics, SFC		27.6	11.6	43.4
Monoaromatics, SFC		21.6	9.3	35.8
Polycyclic Aromatics, SFC		5.9	1.5	17.5
D2425 Mass Spec Group Type, Wt %				
	Paraffins	42.1	31.0	61.8
	Monocycloparaffins	20.6	14.8	31.0
	Dicycloparaffins	6.7	3.7	12.3
	Tricycloparaffins	1.2	0.6	2.9
	Benzenes	10.8	4.1	18.7
	Indans/Tetralins	8.4	2.1	13.0
	CnH2n-10	3.5	1.8	5.2
	Naphthalene	0.7	0.3	1.5
	Naphthalenes	2.8	0.5	9.0
	CnH2n-14	1.8	0.7	2.9
	CnH2n-16	1.3	0.2	2.8
	CnH2n-18	0.0	0.0	0.1
	Total Saturates	70.7	53.4	88.1
	Total Aromatics	29.3	11.9	46.6
D5769 Aromatics, Wt%				
	Benzene	0.008	0.000	0.025
	Toluene	0.062	0.000	0.178
	Ethylbenzene	0.047	0.016	0.070
	M,P-XYLENE	0.193	0.075	0.711
	1,2-DIMETHYLBENZENE	0.077	0.026	0.224
	ISOPROPYL-BENZENE	0.024	0.005	0.059
	PROPYL-BENZENE	0.075	0.011	0.285
	1-METHYL-3-ETHYLBENZENE	0.172	0.038	0.430
	1-METHYL-4-ETHYLBENZENE	0.042	0.006	0.099
	1,3,5-TRIMETHYLBENZENE	0.077	0.008	0.292
	1-METHYL-2-ETHYLBENZENE	0.070	0.000	0.173
	1,2,4-TRIMETHYLBENZENE	0.224	0.008	0.658
	1,2,3-TRIMETHYLBENZENE	0.074	0.008	0.209
	INDAN	0.040	0.007	0.102
	ALKYL INDANS	0.366	0.068	0.765
	1,4-DIETHYL+ BUTYLBENZENE	0.109	0.029	0.245

	1,2-DIETHYLBENZENE	0.061	0.025	0.161
	1,2,4,5-TETRAMETHYLBENZENE	0.049	0.025	0.101
	1,2,3,5-TETRAMETHYLBENZENE	0.179	0.036	0.302
	C10 BENZENES	0.564	0.154	0.993
	C11 BENZENES	1.792	0.289	3.074
	C12 BENZENES	0.154	0.043	0.277
	NAPHTHALENE	0.060	0.021	0.179
	2-METHYL-NAPHTHALENE	0.275	0.040	1.426
	1-METHYL-NAPHTHALENE	0.171	0.028	0.824

<sup>a</sup> Unpublished data from Petroleum HPV Testing Group member company, 1997.

**Table 3. Analysis of Metals in On-Road Diesel Fuel No. 2 (Low Sulfur, <500 PPM)<sup>a</sup>**

	Average	Min	Max
Number of Fuel Samples = 12			
Al, PPM	0	< 1	0
As, PPM	0	< 0.5	0
Be, PPM	0	< 0.02	0
Ca, PPM	0	< 2	0
Trace Ca, PPM	0	< 0.020	0
Cd, PPM	0	< 0.03	0
Co, PPM	0	< 0.1	0
Cr, PPM	0	< 0.05	0
Cu, PPM	0	< 0.3	0
Cu, by GFAAS (PPM)	0	< 0.010	0
Hg, (NAA), PPM	0	< 0.009	0
K, PPM	0	< 3	0
Trace K, PPM	0.039	0.021	0.049
Li, PPM	0	< 1	0
Trace Li, PPM	0	< 0.020	0
Mn, PPM	0	< 0.02	0
Na, PPM	0	< 3	0
Trace Na, PPM	0	< 0.020	0
Ni, PPM	0	< 0.06	0
Pb, PPM	0	< 0.2	0
Pb, by GFAAS (PPM)	0	< 0.010	0
Sb, PPM	0	< 0.5	0
Se, PPM	0	< 1	0
Si, PPM	0	< 0.1	0
Sulfur, D 2622 PPM	302	63	671
V, PPM	0	< 0.2	0
V, by GFAAS (PPM)	0	< 0.030	0

<sup>a</sup> Unpublished data from Petroleum HPV Testing Group member company, 1997

## 2.0 CATEGORY DEFINITION AND JUSTIFICATION

The Gas Oil Category includes finished products (distillate fuels) and the refinery streams with similar carbon ranges. The category members are complex substances, containing variable amounts of alkanes, cycloalkanes, olefins, and aromatics. Because they are complex substances, the materials in this category are difficult to characterize in detail analytically. Consequently, they are not defined by compositional information but instead by physical properties, process history, and product use specifications (ASTM, 2003).

The carbon number range of Gas Oils is between C9 and C30 which determines the volatility, water solubility, and viscosity of these substances. These properties in turn determine their environmental fate and ecotoxicity. Because of the diversity of constituents in Gas Oils, it is not feasible to model the physicochemical and environmental fate endpoints for each substance. Where modeling was necessary to fulfill an endpoint, such estimates were made for common hydrocarbon structures (e.g., saturated, aromatic) and range of molecular weight hydrocarbons (i.e., number of carbon atoms) known to be represented in Gas Oil 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 Gas Oil Category.

The ecotoxicological hazard evaluation of the gas oil category is described on the basis of the water accommodated fractions (WAFs) that elicit toxicity in aquatic organisms. WAFs are the preferred means of exposing aquatic organisms to complex substances having limited solubility. Thus, substances can be compared on the basis of the amount of test substance applied during test medium preparation that caused the observed effect (Girling et al., 1992; OECD, 2000a).

In this interim document, only measured data is presented to estimate the range of mammalian toxicity for Gas Oil substances. However, the mammalian health effects of Gas Oils are correlated with their content of 1-7 ring polycyclic aromatic compounds or PAC profile (which does not affect their acute toxicity). The association between PAC profile and certain repeat-dose, developmental toxicity, 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). In a subsequent Category Assessment document, results from statistical models will be added for untested substances.

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, the ASTM and EPA specifications for No. 2 Diesel Fuel and No. 2 Fuel Oil limit the spectrum of PAC that will be found in those finished products.

The Gas Oils Category contains 28 gas oil petroleum streams, four of which are finished, distillate fuels. A list of category members by CAS RN and full substance definition is provided in Appendix A. The rationale for combining these 28 refinery substances into the Gas Oil Category was based upon the similarity of production processes within the refinery and the resultant similarity of physical and chemical characteristics among category members.

- The materials included in the Gas Oils category are related from both process and physical-chemical perspectives;
- The saturated and aromatic hydrocarbon content of the category members forms a continuum from high saturate content to high aromatic content;

- Key parameters when analyzing this category for environmental hazards are the distribution of aromatic and saturated hydrocarbons, and for some mammalian endpoints (repeated-dose, developmental, and mutagenic) the content and distribution of 1-7 ring PAC are important.

### **3. PHYSICAL-CHEMICAL PROPERTIES**

Substances in the gas oil category are multi-constituent complex hydrocarbon substances with carbon number distributions in the range of C<sub>9</sub> to C<sub>30</sub>. Although their compositions are highly variable, the streams and finished products consist of components from the principal classes of hydrocarbon types which vary in relative proportions but fall within the cited range of carbon numbers. This similarity among the streams in this category allows the characterization of physical-chemical properties to be given as ranges of values for the different endpoints. When the physical-chemical properties are compared across the various substances that are characterized and described in the robust summaries, it is evident that these attributes are similar across the category.

#### **3.1 Physical-Chemical Endpoints**

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

Melting Point

Boiling Point

Vapor Pressure

Octanol/Water Partition Coefficient

Water Solubility

For complex substances such as gas oils, it is not possible to measure or calculate a single numerical value for some of the physicochemical properties. For example, a complex substance does not have a single boiling point. Instead, the boiling point is described as a range of values reflective of the values of the individual components as described in Section 3.1.2.

Although some measured physical-chemical data for category members exist, not all of these endpoints are defined and a consensus database for chemicals that represent products in this category does not exist. For the physical-chemical properties that cannot be provided as single values, ranges of endpoint values were reported for constituent hydrocarbons covering the principal hydrocarbon types and molecular weight ranges in these streams. When available, measured data were reported. In the absence of measured data, physical-chemical properties were estimated using the EPI-Suite™ computer subroutines (US EPA, 2000).

When estimated data were provided, the individual compounds were chosen from detailed hydrocarbon analyses of representative gas oil streams. Since molecular weight and structural conformation determine in large part the solubility and vapor pressure characteristics of the hydrocarbons, representative isomeric structures of the lower (C<sub>9</sub>) and higher molecular weight (C<sub>30</sub>) hydrocarbons of each group of the chemical species found in these materials (paraffinic, naphthenic, olefinic and aromatic) were modeled for relevant physicochemical and fate processes. This provided a range of values that were considered to encompass the majority of the compounds in the gas oil category.

### 3.1.1 Melting Point

To better describe the physical phase or flow characteristics of petroleum products, 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). The pour point temperature increases as the viscosity increases. The pour points of two samples of a light catalytic cracked gas oil (60.8% - 79.8% aromatic hydrocarbons) were measured by API (1987d) to be  $-15^{\circ}\text{C}$  and  $-12^{\circ}\text{C}$ . The maximum pour points of three types of distillate fuels were reported by CONCAWE (1996) to range from  $-6^{\circ}\text{C}$  to  $0^{\circ}\text{C}$ . These fuels included an automotive gas oil (diesel), a heating oil, and a marine distillate fuel. The pour point values for four commercial diesel fuels (Alaska, Canada, and Southern USA) reported by Jokuty et al. (2002) ranged from  $-50^{\circ}\text{C}$  to  $-14^{\circ}\text{C}$ . The wide range in pour point values for commercial fuels may be attributed to fuel additives (e.g., flow improvers) to meet market specifications for particular regions.

**Conclusion:** The pour point values of gas oils fall within the approximate range of  $-50^{\circ}\text{C}$  to  $0^{\circ}\text{C}$ .

### 3.1.2 Boiling Point

Gas oils do not have a single numerical value for boiling point, but rather a boiling or distillation range that reflects the individual components in the complex hydrocarbon substance. CONCAWE (1996) provided a boiling range of  $150^{\circ}\text{C}$  to  $450^{\circ}\text{C}$  ( $302^{\circ}\text{F}$  to  $842^{\circ}\text{F}$ ) as a general distribution for this category. Ranges for specific streams or products vary depending on the refinery processes used and sources of the feedstocks. CONCAWE (1996) listed representative ranges for three fuel types, an automotive gas oil ( $160^{\circ}\text{C}$  to  $390^{\circ}\text{C}$ ), a heating oil ( $160^{\circ}\text{C}$  to  $400^{\circ}\text{C}$ ), and a distillate marine fuel ( $170^{\circ}\text{C}$  to  $420^{\circ}\text{C}$ ). Jokuty et al. (2002) also provided boiling point ranges for several fuels from commercial retailers from different geographical region in Canada and the U.S. They reported boiling point distributions for samples taken from the southern U.S., Alaska, and Canada of  $174^{\circ}\text{C}$  to  $355^{\circ}\text{C}$ ,  $141^{\circ}\text{C}$  to  $320^{\circ}\text{C}$ , and  $246^{\circ}\text{C}$  to  $388^{\circ}\text{C}$ , respectively. Some variability in the ranges was attributed to the manner in which these values were reported. Some of the boiling point limits were given as initial and final values, while others were reported for a given weight percent, typically 5% and 90-95%.

With respect to several individual gas oil streams, API (1987d) reported low end and high end distillation temperatures for a hydrodesulfurized middle distillate ( $172$  to  $344^{\circ}\text{C}$ ), a straight-run middle distillate ( $185^{\circ}\text{C}$  to  $391^{\circ}\text{C}$ ), and a light catalytic cracked distillate ( $185^{\circ}\text{C}$  and  $372^{\circ}\text{C}$ ). No substantial differences the boiling ranges were apparent for gas oils with high concentrations of either aromatic (catalytic cracked stock) or saturated hydrocarbons (straight run stock).

**Conclusion:** The boiling point distributions of gas oils can be expected to fall approximately within the range  $150^{\circ}\text{C}$  to  $450^{\circ}\text{C}$  ( $302^{\circ}\text{F}$  to  $842^{\circ}\text{F}$ ).

### 3.1.3 Vapor Pressure

Gas oils are expected to have low but measurable vapor pressure due to their boiling range ( $150$  to  $450^{\circ}\text{C}$ ) and the molecular weights of the constituent hydrocarbons ( $\text{C}_9 - \text{C}_{30}$  carbon atoms). Measured values according to ASTM Method D2889 for an automotive gas oil (diesel fuel) and a heating oil were approximately  $0.4\text{ kPa}$  at  $40^{\circ}\text{C}$  (CONCAWE, 1996), while the vapor pressure of a No. 2 fuel oil and a diesel oil measured according to the Reid Method (ASTM,

D323) were reported as 2 kPa at 38°C (Jokuty et al., 2002). Because the physical-chemical characteristics of distillate fuels reflect the gas oil streams from which they were produced, these vapor pressure measurements are expected to approximate the vapor pressures of individual gas oils. However, estimated vapor pressure values of constituent hydrocarbons in gas oil streams were made using EPI-Suite™ (EPA, 2000). These estimates were determined for representative low (C<sub>9</sub>), middle (C<sub>15</sub>), and high (C<sub>30</sub>) molecular weight hydrocarbon constituents in gas oils. Because the vapor pressure of a mixture is dependent on the vapor pressure of each chemical component and the mole fraction of the component present (Raoult's law) and gas oils typically contain small amounts of large numbers of constituents, no single constituent would be expected to contribute substantially to the overall vapor pressure. Vapor pressure estimates of low molecular weight hydrocarbons (e.g. C<sub>9</sub>) of varying isomeric structures fell within a range of 0.03 to 0.8 kPa, with higher molecular weight hydrocarbons (e.g. C<sub>30</sub>) showing very low vapor pressures (e.g., 10<sup>-8</sup> to 10<sup>-10</sup> kPa).

**Conclusion:** The vapor pressures of gas oils can be expected to approximate the range of 0.4 kPa to 2 kPa when measured at approximately 40°C.

#### 3.1.4 Partition Coefficient

Standard tests for partition coefficient are intended for mono-constituent substances and are not appropriate for complex substances such as gas oils. Therefore it is not possible to determine a single log K<sub>ow</sub> value for these materials. Instead, partition coefficients have been calculated for individual component hydrocarbons with known hydrocarbon composition (CONCAWE, 1996). The percent distribution of the hydrocarbon groups (i.e., paraffins, olefins, naphthenes, and aromatics) and the carbon chain lengths of hydrocarbon constituents in gas oils largely determine the partitioning characteristics of the mixture. Generally, hydrocarbon chains with fewer carbon atoms tend to have lower partition coefficients than those with higher carbon numbers (CONCAWE, 2001). The calculated range reported by CONCAWE (1996) for hydrodesulfurized middle distillates, straight-run middle distillates, and catalytic cracked middle distillates fell within the range of 3.9 to >6.0. That range is in agreement with a range of log K<sub>ow</sub> values of 3.3 to >6 determined by the Testing Group using EPI-Suite™ (EPA, 2000) for various C<sub>9</sub> to C<sub>30</sub> hydrocarbon components in gas oils. There are no apparent differences in the range of K<sub>ow</sub> values determined for gas oils with high concentrations of either aromatic or saturated hydrocarbons.

**Conclusion:** The partition coefficients of individual constituent hydrocarbons found in gas oils can be expected to fall within the range of 3.3 to >6.

#### 3.1.5 Water Solubility

Individual components of complex petroleum substances have specific and differing water solubility characteristics that are related to their molecular weights and hydrocarbon structures. For example, solubility decreases with increasing molecular weight, and aromatic hydrocarbons typically have greater solubility than saturated hydrocarbons of equal molecular weight. When addressing the aqueous solubility of complex and variable composition of petroleum substances, the amount dissolving in the aqueous phase is a function of: 1) the loading rate (i.e., ratio of petroleum substance to water), 2) log K<sub>ow</sub> of the component hydrocarbons, 3) the amount of component present, and 4) the maximum water solubility of each component. Initially, as the complex petroleum substance is added to water in amounts below the solubility limit of

the least soluble component, the aqueous concentration increases proportionally until the least soluble component reaches its saturation concentration. As more of the test substance is added to water, only the more soluble components continue to dissolve until they reach their own solubility limits, resulting in a two phase system. Further addition of the complex petroleum substance results in an aqueous concentration that is a non-linear function of the amount added.

The middle distillate streams are complex substances that follow this pattern of component dissolution in an aqueous medium, which has been shown by analysis of hydrocarbon components in the dissolved phase. Shiu et al. (1990) demonstrated the effect of loading rate required to maximize the amount of total hydrocarbons in the aqueous phase for a variety of petroleum fractions. It was shown that the water-to-oil ratio should be  $\leq 40$  to create a consistent saturated solution. For a No. 2 fuel oil (density:  $0.862 \text{ g/cm}^3$  @  $20^\circ\text{C}$ , viscosity:  $3.64 \text{ cp}$  @  $20^\circ\text{C}$ ), Shiu et al. (1990) measured the total dissolved hydrocarbons by purge-and-trap GC for water-to-oil loading rates of 5-10:1. Measurements were taken at two temperatures (5 and  $20^\circ\text{C}$ ) and for distilled and salt water (3% NaCl). Under those conditions, the solubility levels of the No. 2 fuel oil in distilled water at 5 and  $20^\circ\text{C}$  were 2.7 and 3.2 mg/L, respectively. For saltwater, at the same two temperatures, the solubility levels were 2.05 and 2.5 mg/L, respectively. Anderson et al. (1974) measured the aqueous fraction of a 10:1 ratio of seawater to No. 2 fuel oil using infrared analysis. Total petroleum hydrocarbons in the aqueous fraction was 8.7 mg/L.

For individual hydrocarbon constituents in gas oils, water solubility values vary by orders of magnitude. Water solubility of component hydrocarbon molecules was estimated using the WSKOW V1.40 subroutine of the EPI-Suite™ computer model (EPA, 2000). Water solubility ranged from essentially insoluble (approximately  $10^{-8} \text{ mg/L}$ ) for the higher molecular weight fractions (e.g.,  $\text{C}_{30}$  paraffin) within gas oil to approximately 52 mg/L for a  $\text{C}_9$  alkylbenzene (propylbenzene).

**Conclusions:** Precise measurements of water solubility for complex substances such as gas oils are complicated by factors such as the sensitivity of the analytical method and the water-to-oil ratio. When the ratio is optimized to achieve maximum hydrocarbon concentrations, measurements have ranged from 2.05 mg/L to 8.7 mg/L. Solubility values of individual constituents in gas oils vary widely due to the wide range of molecular weights. Individual water solubility may range from essentially insoluble (e.g.,  $<0.001 \text{ mg/L}$ ) to 52 mg/L, depending on the molecular structure.

### 3.2 Assessment Summary for Physical-Chemical Endpoints

Gas oils are variable and complex substances of hydrocarbons, predominantly having carbon chains from  $\text{C}_9$  to  $\text{C}_{30}$ , and boiling over the temperature range of  $150^\circ\text{C}$  to  $450^\circ\text{C}$ . Vapor pressures are within a measurable range, with values of 0.4 kPa and 2 kPa being reported. Partition coefficients of constituent hydrocarbons range from 3.3 to  $>6$ . Water solubility values for these substances have been reported from 2.0 mg/L to 8.7 mg/L for dissolved hydrocarbons.

## 4.0 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. The environmental fate endpoints include the following:

- Photodegradation
- Stability in water [Hydrolysis]
- Transport Between Environmental Compartments [Fugacity/Distribution]
- Biodegradation

In determining these fate characteristics for constituents in gas oils, the US EPA's collection of physical-chemical and environmental fate models in EPI-Suite™ (US 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 be used for microbial metabolism.

#### **4.1.1 Photodegradation**

##### **4.1.1.1 Direct**

The direct aqueous 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 (Harris, 1982a). 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, on the other hand, have shown absorbance of the 290 to 800 nm range of light energy and could potentially undergo photolysis reactions (Fasnacht and Blough, 2002). The degree and rate at which these compounds photodegrade depends upon whether conditions allow penetration of light with sufficient energy to effect a change.

##### **4.1.1.2 Indirect**

Constituents of gas fuel oils that volatilize to the troposphere have the potential to undergo gas-phase oxidation reactions with photochemically produced hydroxyl radicals (OH) as well as other oxygen containing radicals (e.g., NO<sub>3</sub>) and ozone (O<sub>3</sub>). Atmospheric oxidation as a result of these types of reactions is not direct photochemical degradation but 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) reports that reactions with OH and NO<sub>3</sub> radicals can be important for alkanes, whereas reactions with O<sub>3</sub> are negligible. Additionally, nighttime reactions with NO<sub>3</sub> occur at rates approximately two orders of magnitude less than daytime OH radical reactions. Olefins may react with OH and NO<sub>3</sub> radicals and O<sub>3</sub>, with OH and O<sub>3</sub> 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, 2000). 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<sub>3</sub>, but as described by Atkinson (1990), these rates tend to be substantially less than for 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) compounds in gas 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 gas oils. Therefore, the estimated values identify a potential range of half-lives for substances in the gas oil category. The half-lives for representative constituents of gas oils were determined to range from 0.1 days to approximately 1.5 days. This range spans isomeric structures for representative paraffinic, olefinic, naphthenic, and aromatic compounds in gas oils that cover the molecular weights of C<sub>9</sub> to C<sub>30</sub> carbon chain lengths. For the majority of the thousands of compounds constituting gas oils, the low vapor pressures of the majority of the compounds 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:** Direct photodegradation is not likely to be an important fate process for gas oils due to their relatively low concentrations of photosensitive constituents. However, indirect photodegradation will be an important degradation pathway for constituents that volatilize to the atmosphere. Reaction rates calculated for indirect photodegradation ranged from 0.1 days to approximately 1.5 days for a variety of hydrocarbon and heterocyclic compounds covering carbon numbers from C<sub>9</sub> to C<sub>30</sub> and show that these substances would not persist in the atmosphere.

#### 4.1.2 Stability in Water

Chemicals that have a potential to hydrolyze include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters (Harris, 1982b). Because gas oils do not contain significant levels of these functional groups, materials in the gas oils category are not subject to hydrolysis.

**Conclusion:** Gas oils will be stable and not react with water. Constituent compounds do not contain chemical moieties that undergo hydrolysis.

#### 4.1.3 Transport and Distribution in the Environment (Fugacity)

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. A widely used fugacity model is the EQC (Equilibrium Criterion) model (Mackay et al., 1996, 1997). 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. The model assumes the chemical becomes instantaneously distributed to an equilibrium condition using physical-chemical properties to quantify the chemical's behavior. The model does not include degrading reactions, advective processes or inter-media transport between compartments. 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 (US EPA, 1999).

Results of Level I models are basic partitioning data that allow for comparisons between chemicals and indicate the compartment(s) to which a chemical is likely to partition in the environment. One drawback of these and higher level models is their inability to predict the environmental distribution of all the constituents comprising complex petroleum streams. To gain an understanding of the potential environmental distribution for these complex substances, modeling was performed on a representative range of molecular weight compounds covering the different isomeric hydrocarbon structures. Specific compounds were selected on the basis of carbon number and hydrocarbon type as identified in the description of the category substances and detailed hydrocarbon analyses. The resulting distribution characteristics represent the potential ranges of distribution to environmental media for those hydrocarbon constituents found in these streams.

The range of properties of gas oil components is such that the components cannot be considered as a single group with respect to environmental distribution. Because of the varied properties of the individual constituents, when a gas oil enters the environment, the individual compounds 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 gas oil can potentially distribute. To gain an understanding of the potential distribution of the constituent compounds in gas oil, the EQC model was used to characterize the environmental distribution of representative hydrocarbon and heterocyclic compounds in gas 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 gas oils (Potter and Simmons, 1998). In so doing, an understanding of the potential environmental distribution of components in gas oil may be gained. Distribution patterns determined by the EQC model for the different constituents are shown in Table 4

**Table 4. Estimated Percent Distribution of Constituent Compounds Represented in Gas Oils.**

Compound Type/ Carbon Chain	Air	Water	Soil	Sediment	Suspended Sediment	Biota
<b>n-alkanes</b>						
C9	99	<0.1	1	<0.1	<0.1	<0.1
C15	13	<0.1	85	2	<0.1	<0.1
C30	<0.1	<0.1	98	2	<0.1	<0.1
<b>iso-alkanes</b>						
C9	99	<0.1	0.5	<0.1	<0.1	<0.1
C15	68	<0.1	31	0.7	<0.1	<0.1
C30	0.1	<0.1	98	2	<0.1	<0.1

<b>straight olefins</b>						
C9	99	<0.1	0.7	<0.1	<0.1	<0.1
C15	17	<0.1	81	2	<0.1	<0.1
C30	<0.1	<0.1	98	2	<0.1	<0.1
<b>cyclic olefins</b>						
C9	99	<0.1	0.7	<0.1	<0.1	<0.1
C15	49	<0.1	50	1	<0.1	<0.1
C30	<0.1	<0.1	98	2	<0.1	<0.1
<b>1-ring naphthenes</b>						
C9	99	<0.1	0.9	<0.1	<0.1	<0.1
C15	0.4	<0.1	97	2	<0.1	<0.1
C30	0.1	<0.1	98	2	<0.1	<0.1
<b>2-ring naphthenes</b>						
C9	99	0.2	1	<0.1	<0.1	<0.1
C15	51	<0.1	48	1	<0.1	<0.1
C30	0.1	<0.1	98	2	<0.1	<0.1
<b>1-ring aromatics</b>						
C9	97	1	2	<0.1	<0.1	<0.1
C15	18	<0.1	79	2	<0.1	<0.1
C30	<0.1	<0.1	98	2	<0.1	<0.1
<b>2-ring aromatics</b>						
C10	77	8	15	0.3	<0.1	<0.1
C15	0.7	0.2	97	2	<0.1	<0.1
C30	<0.1	<0.1	98	2	<0.1	<0.1

Regardless of chemical structure, hydrocarbons having nine carbon atoms showed a tendency to partition to air (up to 99%). As molecular weight increases, partitioning shifts to soil, which accounts for 98% of the distribution of the C<sub>30</sub> components. Few of the representative structures partitioned to water or other environmental compartments.

**Conclusion:** The low molecular weight constituents in gas oils will tend to partition to the air. As molecular weight increases, partitioning shifts to the soil compartment.

#### 4.1.4 Biodegradation

On the basis of the biodegradability characteristics of other petroleum substances such as kerosene and lubricating oil basestocks, gas oils are not likely to pass the criteria for ready biodegradability. However, most hydrocarbon species present in gas oils are known to be ultimately degraded by aerobic microorganisms (Connell and Miller, 1980; CONCAWE, 1996). Lower molecular weight compounds may be expected to be degraded relatively quickly in aerobic conditions, while higher molecular weight compounds, particularly polycyclic aromatics, will degrade slower. Much of this evidence is based on bioremediation studies of contaminated soils, which have shown that hydrocarbon components in gas oils are degraded in the presence of oxygen (Hoeppe et al., 1991; Miethe et al., 1994). Bioremediation of a diesel fuel spill also has been demonstrated under Arctic conditions (Liddell et al., 1994).

Biodegradation data were available for a solvent-refined gas oil (CAS no. 64741-90-8; Exxon, 1994) and two samples of a blended diesel fuel (Clark, et al., 2003; Mobil, 1999). A fourth study was cited in CONCAWE (1996) for an undisclosed gas oil sample. The data show that these

substances are inherently biodegradable. For the solvent-refined gas oil, an inherent biodegradability study (method ISO 14593) using adapted inoculum achieved 36% biodegradation by day 7 of the test. However, degradation could not be prolonged, as a maximum of only 41% was attained between day 7 and day 28 (Exxon, 1994). In a ready biodegradability test following the manometric respirometry method (OECD 301F), Clark et al. (2003) measured 60% biodegradation at the end of 28 days for a commercial diesel fuel. This test did not attain the 60% biodegradation level within the 10-day window criterion that is required for pure chemicals. However, for ready biodegradability classification of mixtures of structurally similar chemicals such as petroleum substances, the 10-day window should not be applied. For such substances where the 60% biodegradation level is achieved by day 28, then that substance may be considered readily biodegradable (OECD, 2006). Following the same respirometry method, Mobil (1999) achieved a similar biodegradation rate of 57.5% for a commercial diesel fuel. CONCAWE (1996) reported on a study by Battersby et al. (1992), who observed approximately 40% biodegradation for a gas oil in a 28-day modified Sturm procedure. Collectively, these four studies show that gas oils may not pass ready biodegradability status, but biodegradation rates can be high and these substances are considered inherently biodegradable. Some individual gas oil samples may meet the criterion for ready biodegradability.

Under anaerobic conditions, such as anoxic sediments, rates of biodegradation of gas oils components are negligible and the gas oils may persist under those conditions for some time (CONCAWE, 1996; Brown 1989). Degradation then will be dependent on bioturbation or resuspension to provide microbes with access to oxygen.

**Conclusion:** Rates of biodegradation of gas oils can be high, and these substances are considered to be inherently biodegradable. Biodegradation rates for some individual gas oil samples may be sufficient to pass the criterion for ready biodegradability in 28-day tests

#### **4.2 Assessment Summary for Environmental Fate**

If gas oils are released to the environment, individual components will disperse and partition according to their individual physical-chemical properties. Their final disposition is shaped by both abiotic and biotic processes. Based on modeling individual structures encompassing the different types and molecular weights of hydrocarbons, volatilization to the atmosphere is an important process for the low molecular weight fractions. Residence times in the atmosphere are relatively short due to indirect photodegradation reactions. In water, hydrolysis is not likely to occur, as the chemical linkages of hydrocarbons do not allow for these reactions. Components in gas oils will biodegrade, and moderate to rapid rates of biodegradation were measured in standard tests. Gas oils are considered to be inherently biodegradable, and for some individual gas oil samples, biodegradation rates may be high enough to achieve ready biodegradability classification.

### **5.0 ENVIRONMENTAL EFFECTS**

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 substances such as petroleum products, the generally accepted procedure is to report results expressed in terms of the "loading rate" (OECD, 2000a). The loading rate is defined as the amount of the substance 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  $LL_{50}$  or  $EL_{50}$  define the loading rate of the test substance lethal to or producing a specific effect in 50% of the test organisms. Exposures 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 product to be expressed in terms of the amount of that product required to produce a particular effect (OECD, 2000). Such results are not comparable to results obtained under WAF or OWD preparation methods.

## **5.1 Aquatic Toxicity**

Hydrocarbon constituents in gas oils elicit acute aquatic toxicity through non-polar narcosis, whose mechanism of action is disruption of biological membrane function (van Wezel and Opperhuizen, 1995). Therefore, gas oil streams share a common mode of action, and their acute toxicities would be expected to fall within a relatively narrow range. Any differences between toxicities (i.e., LC/ $LL_{50}$ , EC/ $EL_{50}$ ) can be explained by the differences between the target tissue-partitioning behavior of the individual chemicals (Verbruggen et al., 2000). For example, the existing fish toxicity database for hydrophobic neutral chemicals supports a critical body residue (CBR, the internal concentration that causes mortality) of approximately 2-8 mmol/kg fish (wet weight) (McCarty and Mackay, 1993; McCarty et al., 1991). When normalized to lipid content, the CBR is approximately 50  $\mu\text{mol/g}$  of lipid for most organisms (Di Toro et al., 2000).

### **5.1.1 Aquatic Endpoints – Acute Toxicity**

The acute aquatic toxicity of gas oils to fish, invertebrates, and algae is described below, and an overall range of acute toxicity values is provided for each trophic level. The referenced data are studies conducted using the WAF or OWD methods of preparing exposure solutions. Other studies using dilutions of WSFs are also discussed, although these are not considered reliable studies for characterizing aquatic hazard. The aquatic toxicity data are represented by tests on blended commercial fuels (e.g., diesel and/or No. 2 fuel oil). No data were available for individual gas oil streams.

#### **5.1.1.1 Acute Toxicity to Aquatic Vertebrates**

The results of the studies described in detail in the robust summaries for the hazard of gas oils to fish are provided in the following table.

**Table 5. Acute Toxicity Values for Gas Oils to Fish.**

Test Substance	Test Species and Type (WAF or OWD)	Toxicity Endpoint	Endpoint Value, mg/L	Reference
CAS No. 68334-30-5, diesel oil	<i>Onchorynchus mykiss</i> WAF	96-h LL <sub>50</sub> NOELR	21 10	Shell, 1995a
CAS No. 68334-30-5, diesel oil	<i>O. mykiss</i> WAF	96-h LL <sub>50</sub> NOELR	65 10	Shell, 1995b
CAS No. 68476-30-2, No. 2 fuel oil	<i>O. mykiss</i> WAF	96-h LL <sub>50</sub> BPH critical <sup>1</sup>	6.6 155 nmol/mg C	EBSI, 1998a
CAS No. 68476-30-2, no. 2 fuel oil	<i>Cyprinodon variegatus</i> WAF	96-h LL <sub>50</sub> BPH critical	57 202 nmol/mg C	EBSI, 1998b
CAS No. 68476-30-2, no. 2 fuel oil	<i>Menidia beryllina</i> WAF	96-h LL <sub>50</sub> BPH critical	3.2 72 nmol/mg C	EBSI, 1998c
CAS No. 68476-30-2, No. 2 fuel oil	<i>Pimephales promelas</i> WAF	96-h LL <sub>50</sub> BPH critical	57 388 nmol/mg C	EBSI, 1999
No. 2 fuel oil (no CAS No. cited)	<i>C. variegates</i> OWD	96-h LL <sub>50</sub>	93	Anderson, et al., 1974
No. 2 fuel oil (no CAS No. cited)	<i>M. beryllina</i> OWD	48-h LL <sub>50</sub>	125	Anderson, et al., 1974
No. 2 fuel oil (no CAS No. cited)	<i>Fundulus similis</i> OWD	96-h LL <sub>50</sub>	33	Anderson, et al., 1974
No. 2 fuel oil (no CAS No. cited)	<i>Jordanella floridae</i> OWD	96-h LL <sub>50</sub>	51	Hedtke and Puglisi, 1982 <sup>2</sup>
No. 2 fuel oil (no CAS No. cited)	<i>P. promelas</i> OWD	96-h LL <sub>50</sub>	33	Hedtke and Puglisi, 1982 <sup>2</sup>

<sup>1</sup> The BPH critical represents an estimate of the bioavailable petroleum hydrocarbons (BPH) corresponding to a threshold total body residue in an aquatic organism. Acute toxicity is predicted once the BPH critical is exceeded.

<sup>2</sup> Endpoint values in the Hedtke and Puglisi (1982) study were presented as µL/L. CONCAWE (1996) cited this work and recalculated the endpoints assuming a specific gravity of 0.85 g/cm<sup>3</sup>.

Based on the studies cited in Table 5 for WAF exposures, the range of fish acute LL<sub>50</sub> values (expressed as loading rates) was 3.2 – 65 mg/L for No. 2 fuel oil or diesel. The OWD studies (Hedtke and Puglisi, 1982) resulted in slightly higher LL<sub>50</sub> values, which may be expected due to the manner in which these exposure solutions are prepared. The dispersion technique can result in loss of volatile components from the dissolved fraction. Therefore, for blended middle distillate fuels such as No. 2 fuel oil or diesel, the range of toxicity values used for read across to other fuels of this type is 3.2 – 65 mg/L expressed as the loading rate.

**Conclusion:** The acute toxicity (LL<sub>50</sub>) of blended middle distillate fuels to fish is expected to fall within the range 3.2 to 65 mg/L based on WAF studies and expressed as the loading rate.

### 5.1.1.2 Acute Toxicity to Aquatic Invertebrates

The results of the studies described in detail in the robust summaries for the hazard of gas oils to aquatic invertebrates are provided in the following table.

**Table 6. Acute Toxicity Values for Gas Oils to Aquatic Invertebrates.**

Test Substance	Test Species and Type (WAF or OWD)	Toxicity Endpoint	Endpoint Value, mg/L	Reference
CAS No. 68334-30-5, diesel oil	<i>Daphnia magna</i> WAF	48-h EL <sub>50</sub> NOELR	13 3	Shell, 1994
CAS No. 68334-30-5, diesel oil	<i>D. magna</i> WAF	48-h EL <sub>50</sub> NOELR	68 46	Shell, 1995c
CAS No. 68334-30-5, diesel oil	<i>D. magna</i> WAF	48-h EL <sub>50</sub> NOELR	210 46	Shell, 1995d
CAS No. 68334-30-5, diesel oil	<i>D. magna</i> WAF	48-h EL <sub>50</sub> NOELR	>100, <300 100	Clark, et al., 2003
CAS No. 68476-30-2, No. 2 fuel oil	<i>D. magna</i> WAF	48-h EL <sub>50</sub> BPH critical	2.0 85.3 nmol/mg C	EBSI, 2001
CAS No. 68476-30-2, No. 2 fuel oil	<i>D. magna</i> WAF	48-h EL <sub>50</sub> NOELR	7.8 1.25	Fraunhofer-Institut, 2000
CAS No. 68476-30-2, No. 2 fuel oil	<i>D. magna</i> WAF	48-h EL <sub>50</sub> NOELR	5.3 1.25	Fraunhofer-Institut, 2000
CAS No. 68476-30-2, No. 2 fuel oil	<i>D. magna</i> WAF	48-h EL <sub>50</sub> NOELR	14 1.5	Fraunhofer-Institut, 2000
CAS No. 68476-30-2, No. 2 fuel oil	<i>D. magna</i> WAF	48-h EL <sub>50</sub> NOELR	42 7.5	Fraunhofer-Institut, 2000
CAS No. 68476-30-2, No. 2 fuel oil	<i>D. magna</i> WAF	48-h EL <sub>50</sub> NOELR	13 <6.25	Fraunhofer-Institut, 2000
CAS No. 68476-34-6, No. 2 fuel oil	<i>D. magna</i> WAF	48-h EL <sub>50</sub> NOELR	6.4 <1.9	Fraunhofer-Institut, 2000
CAS No. 68476-34-6, No. 2 fuel oil	<i>D. magna</i> WAF	48-h EL <sub>50</sub> NOELR	36 6.25	Fraunhofer-Institut, 2000

CAS No. 68476-34-6, No. 2 fuel oil	<i>D. magna</i> WAF	48-h EL <sub>50</sub> NOELR	9.6 3.1	Fraunhofer- Institut, 2000
No. 2 fuel oil (no CAS No. cited)	<i>Palaemonetes</i> <i>pugio</i> OWD	96-h EL <sub>50</sub>	3.0	Anderson, et al., 1974
No. 2 fuel oil (no CAS No. cited)	<i>Penaeus</i> <i>aztecus</i> OWD	96-h EL <sub>50</sub>	9.4	Anderson, et al., 1974

Based on the tests cited in Table 6 for WAF exposures, the range of EL<sub>50</sub> values (expressed as loading rates) was 2.0 – 210 mg/L for No. 2 fuel oil and diesel. The study by Clark et al. (2003) only reported the concentration boundaries within which the EC50 was expected to fall. The two OWD studies gave EL<sub>50</sub> values within the range for the WAF studies. Therefore, for blended middle distillate fuels such as No. 2 fuel oil or diesel, the range of toxicity values used for read across to other fuels of this type is 2.0 – 210 mg/L expressed as the loading rate.

**Conclusion:** The acute toxicity (EL<sub>50</sub>) of blended middle distillate fuels to invertebrates is expected to fall within the range 2.0 to 210 mg/L based on WAF studies and expressed as the loading rate.

### 5.1.1.3 Toxicity to Aquatic Plants

The results of the studies described in detail in the robust summaries for the hazard of gas oils to aquatic plants are provided in the following table.

**Table 7. Toxicity Values for Gas Oils to Aquatic Plants.**

Test Substance	Test Species and Type (WAF or OWD)	Toxicity Endpoint	Endpoint Value, mg/L	Reference
CAS No. 68334-30-5, diesel oil	<i>Raphidocelis subcapitata</i> ( <i>Selenastrum capricornutum</i> ) WAF	E <sub>b</sub> L <sub>50</sub> E <sub>r</sub> L <sub>50</sub> NOELR	10 22 3	Shell, 1995e
CAS No. 68334-30-5, diesel oil	<i>Raphidocelis subcapitata</i> ( <i>Selenastrum capricornutum</i> ) WAF	E <sub>b</sub> L <sub>50</sub> E <sub>r</sub> L <sub>50</sub> NOELR	25 78 3	Shell, 1995f
CAS No. 68334-30-5, diesel oil	<i>Selenastrum capricornutum</i> WAF	E <sub>b</sub> L <sub>50</sub> E <sub>r</sub> L <sub>50</sub> NOELR	≥10, ≤22 ≥22, ≤46 <1	Clark et al., 2003

CAS No. 68476-30-2, No. 2 fuel oil	<i>Selenastrum capricornutum</i> WAF	E <sub>b</sub> L <sub>50</sub> E <sub>r</sub> L <sub>50</sub> BPH critical	1.9 2.9 63 nmol/mg C	EBSI, 1998e
CAS No. 68476-30-2, No. 2 fuel oil	<i>Skeletonema costatum</i> WAF	E <sub>b</sub> L <sub>50</sub> E <sub>r</sub> L <sub>50</sub>	5.8 2.2	EBSI, 1998f

For the data in Table 7, endpoints based on algal biomass (E<sub>b</sub>L<sub>50</sub>) ranged from 1.9 – 25 mg/L. The range for the endpoints based on growth rate were somewhat wider, with values of 2.2 to 78 mg/L, expressed as loading rates. For blended middle distillate fuels, the range of toxicity values used for read across to other fuels of this types is 1.9 – 25 mg/L, expressed as the loading rate and based on algal biomass.

**Conclusion:** The toxicity (EL<sub>50</sub>) of blended middle distillate fuels to algae, when based on algal biomass, is expected to fall within the approximate range of 1.9 - 25mg/L when expressed as loading rate. When based on algal growth rate, E<sub>r</sub>L<sub>50</sub> values are anticipated to fall within the range 2.2 to 78 mg/L.

## 5.1.2 Aquatic Endpoints – Chronic Toxicity

### 5.1.2.1 Chronic Toxicity to Aquatic Vertebrates

The chronic toxicity of a fuel oil No. 2 to rainbow trout (*O. mykiss*) was measured following the OECD 215 guideline (OECD, 2000b). Survival and growth of juvenile trout were measured during a 28-day exposure to WAF preparations of the test substance. The results of this test are shown in the following table.

**Table 8. Chronic Toxicity of Gas Oils to Rainbow Trout.**

Test Substance	Test Species and Type (WAF or OWD)	Toxicity Endpoint	Endpoint Value (loading rate)	Reference
CAS No. 68476-30-2, No. 2 fuel oil	<i>O. mykiss</i> WAF	28-d LL <sub>50</sub> LOELR <sub>(growth)</sub> NOELR <sub>(growth)</sub>	2.7 mg/L 3.0 1.2	EMBSI, 2004a
			<b>Endpoint Value (µM/mL PDMS)</b>	
		28-d LC <sub>50</sub> LOEC <sub>(growth)</sub> NOEC <sub>(growth)</sub>	24.4 26.4 13.7	

In this study, reduced survival and growth rate were seen at the highest loading rate WAF used in the test (3.0 mg/L). Based on the WAF loading rates used in the test, a 28-d LL<sub>50</sub> for survival was 2.7 mg/L, with corresponding LOELR and NOELR values of 3.0 and 1.2 mg/L, respectively. Analysis of the exposure solutions involved extraction of the bioavailable petroleum

hydrocarbons (BPH) onto solid phase micro-extraction fibers (SPME) that were coated with polydimethylsiloxane (PDMS). Analytical detection of the extracted BPH was by GC/FID. Reporting of the total BPH was in units of  $\mu\text{M}$  of hydrocarbons (as 2,3-dimethylnaphthalene)/mL of PDMS.

**Conclusion:** The no-observed-effect loading rate for chronic toxicity of blended middle distillate fuels to fish is expected to be approximately 1.2 mg/L.

### 5.1.2.2 Chronic Toxicity to Aquatic Invertebrates

The chronic toxicity of a fuel oil No. 2 to *Daphnia magna* was measured following the OECD 211 guideline (OECD, 1998). Survival and reproduction of daphnids were measured during a 21-day exposure to WAF preparations of the test substance. The results of this test are shown in the following table.

**Table 9. Chronic Toxicity of Gas Oils to Aquatic Invertebrates.**

Test Substance	Test Species and Type (WAF or OWD)	Toxicity Endpoint	Endpoint Value (loading rate)	Reference
CAS No. 68476-30-2, No. 2 fuel oil	<i>D. magna</i> WAF	21-d $\text{EL}_{50}$ LOELR <sub>(reproduction)</sub> NOELR <sub>(reproduction)</sub>	>0.5 mg/L 0.5 0.15	EMBSI, 2004b
			<b>Endpoint Value (<math>\mu\text{M}/\text{mL}</math> PDMS)</b>	
		21-d $\text{EC}_{50}$ LOELR <sub>(reproduction)</sub> NOELR <sub>(reproduction)</sub>	>7.24 7.24 3.09	

In this study, reduced reproduction was seen at the highest loading rate WAF used in the test (0.5 mg/L). Based on the WAF loading rates used in the test, a 21-d  $\text{LL}_{50}$  for survival was >0.5 mg/L, with corresponding LOELR and NOELR values of 0.5 and 0.15 mg/L, respectively. Analysis of the exposure solutions involved extraction of the bioavailable petroleum hydrocarbons (BPH) onto solid phase micro-extraction fibers (SPME) that were coated with polydimethylsiloxane (PDMS). Analytical detection of the extracted BPH was by GC/FID. Reporting of the total BPH were in units of  $\mu\text{M}$  of hydrocarbons (as 2,3-dimethylnaphthalene)/mL of PDMS.

**Conclusion:** The no-observed-effect loading rate for chronic toxicity of blended middle distillate fuels to aquatic invertebrates is expected to be approximately 0.15 mg/L.

## 5.2 Assessment Summary for Environmental Effects

Multiple ecotoxicological studies on heating and transportation fuels (e.g., No. 2 fuel oil and diesel fuel) have been conducted. In general, these commercial distillate fuels show moderate

toxicity to aquatic life. LL<sub>50</sub> values for fish ranged from 3.2 to 65 mg/L (Shell, 1995a,b; EBSI, 1998a-c; 1999), while EL<sub>50</sub> values for invertebrates ranged from 2.0 to 210 mg/L (Shell, 1994, 1995a,b; Clark, et al., 2003; EBSI, 2001; Fraunhofer, 2000). All studies cited here and used to establish read-across ranges for untested category members used water accommodated fractions of the gas oils. EL<sub>50</sub> values for inhibition of algal growth rate and biomass ranged from 1.9 to 78 mg/L. (Shell, 1995 a,b; Clark et al., 2003; EBSI, 1998d,e). While there were no obvious differences in the acute toxicity between fish and daphnids to the substances that were tested, daphnids appeared to show a greater sensitivity compared to fish for chronic toxicity. While the data was limited to one test substance and one test per species, the NOELR for fish (1.2 mg/L) compared to daphnids (0.15 mg/L) suggests a sizeable difference in the chronic toxicity to gas oils for these two species.

## 6.0 HUMAN HEALTH ENDPOINTS

Reviews of this category of fuels have been published by several organizations (ATSDR, 1995, CONCAWE, 1991, 1996, 2001; IARC, 1988; IPCS, 1996). Because fuel oils and transportation fuels of the same grade (e.g. No. 2 home heating oil and No. 2 diesel fuel) are virtually indistinguishable on the basis of their gross physical and chemical properties (IARC, 1988), data generated on either material can be used to characterize the toxicity of both materials. In preparing this 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.

This Interim Category Assessment document addresses the health effects endpoints by:

- Evaluating the toxicology database for the gas oil related refinery streams and products,
- Using read-across information whenever possible among category members, and other API HPV categories

In the final CAD, modeling data based on PAC profile for repeat dose, developmental toxicity, and *in vitro* genetic toxicity endpoints will be employed to predict toxicity of untested streams. .

## 6.1 Human Health Effects

### 6.1.1 Acute Toxicity

#### 6.1.1.1 Oral

**Table 10. Acute Oral Toxicity**

CAS RN/ Composition	LD <sub>50</sub> value	Species	Observations	Reference
64741-59-9 Light Catalytic Cracked Distillate				
API 83-07 72.4% aromatics 24.3% saturates 3.7% Olefins	4.7g/kg males 3.2g/kg females	Rat	Hypoactivity, diarrhea, yellow-stained urogenital/abdominal area, hairloss on anal region/abdomen/hind legs, ataxia, red-stained nose and mouth, prostration, lacrimation, catalepsy, dyspnea, possible respiratory congestion,	API 1982a
API 83-08 60.8% aromatics 31.4% saturates	7.2g/kg/males 6.8g/kg females	Rat		API 1985d

7.8% Olefins			hypothermic to touch, inflamed anal region and death.	
64741-44-2 Straight run Middle Distillate				
API 83-11 21.2% aromatics 78.8% saturates	>5.0g/kg	Rat	Hypoactivity, ataxia, diarrhea, lacrimation, oily coat, yellow- or urine-stained abdomen and hair loss on or around the anus, abdomen & hind legs. Animals gained weight in the study.	API 1985e
64742-80-9 Hydrodesulfurized Middle Distillate				
API 81-09 20.6% aromatics 79.4% saturates	>5.0g/kg	Rat	Hypoactivity, ptosis, diarrhea, urine stained abdomen, oily fur	API 1982b
API 81-10 34.3% aromatics 65.6% saturates	>5.0g/kg	Rat		API 1982c
68476-34-6 Commercial Diesel fuel				
API 79-6 72.6% saturates	9.0ml/kg [95% CI 5.6-14.5]	Rat	No robust summary but clinical signs likely similar to API 83-11 above	API 1980d
68476-30-2 No. 2 fuel oil [Home heating oil] <sup>a</sup>				
API 78-02 [83-02] Medium Catalytic cracked stock 30% 22.1% aromatics 73.4% saturates 22.1% Olefins	19ml/kg [95% CI 16.8 – 21.5]	Rat	No robust summary but clinical signs likely similar to AP 83-11 above.	API 1980a
API 78-03 [83-01] Low Catalytic cracked stock 10% 17.9% aromatics 79.2% saturates 2.9% Olefins	14.5ml/kg [95% CI 12.3 – 17.0]	Rat	No robust summary but clinical signs likely similar to API 83-11 above.	API 1980b
API 78-04 [83-03] High Catalytic cracked stock 50% 26.1% aromatics 67.8% saturates 6.1% Olefins	21.2ml/kg [95% CI 18.7 – 24.9]	Rat	No robust summary but clinical signs likely similar to API 83-11 above.	API 1980c

a- Combination of Straight run Middle Distillate, CAS RN 64741-44-2 and Light Catalytic Cracked Distillate CAS RN 64741-59-9

### 6.1.1.2 Dermal

**Table 11. Acute Dermal Toxicity**

CAS RN /Composition <sup>a</sup>	LD <sub>50</sub> value	Species	Observations	Reference
64741-59-9 Light Catalytic Cracked Distillate				
API 83-07	>2.0g/kg	Rabbit		API 1982a
API 83-08	>2.0g/kg	Rabbit	Irritation from slight to severe for erythema, and edema, slight to moderate atonia, desquamation, coriaceousness, slight to marked for fissuring. Some subcutaneous	API 1985d

			hemorrhage and blanching	
64741-44-2 Straight run Middle Distillate				
API 83-11	>2.0g/kg	Rabbit	Irritation slight to moderate for erythema, edema and atonia, desquamation and fissuring. Slight coriaceousness	API 1985e
64742-80-9 Hydrodesulfurized Middle Distillate				
API 81-09	>2.0g/kg	Rabbit		API 1982b
API 81-10	>2.0g/kg	Rabbit		API 1982c
68476-34-6 Commercial Diesel Fuel				
API 79-6	>5.0ml/kg	Rabbit		API 1980d
68476-30-2 No. 2 fuel oil [Home heating oil <sup>b</sup>				
API 78-02 [83-02] Medium Catalytic cracked stock 30%	>5.0ml/kg	Rabbit		API 1980a
API 78-03 [83-01] Low Catalytic cracked stock 10%	>5.0ml/kg	Rabbit		API 1980b
API 78-04 [83-03] High Catalytic cracked stock 50%	>5.0ml/kg	Rabbit		API 1980c

a- Composition provided in Acute Oral Table 10

b- Combination of Straight run Middle Distillate, CAS RN 64741-44-2 and Light Catalytic Cracked Distillate CAS RN 64741-59-9

### 6.1.1.3 Inhalation

**Table 12. Acute Inhalation**

CAS RN /Composition <sup>a</sup>	LC <sub>50</sub> value	Species	Observations	Reference
64741-59-9 Light Catalytic Cracked Distillate				
API 83-07	5.4mg/L Combined sexes	Rat	Effects similar to API 83-08	API 1986a
API 83-08	4.7mg/L Combined sexes	Rat	Hair coat and some skin abnormalities in exposed animals, at higher exposure levels crust seen around the nose 2 to 4 days post exposure. Some, decreased activity/mobility . Dark red lungs in animals that died. Lung changes in surviving animals were mild and chronic included interstitial inflammation, focal alveolar histiocytosis and localized emphysema.	API 1986b
64741-44-2 Straight run Middle Distillate				
API 83-11	1.78mg/L combined sexes [95%CL 1.44 – 2.2]	Rat	Decreased activity, wet inguinal area, eyes partially closed, wet coat and oily coat. In the seven days following exposure there were signs of poor condition and respiratory distress. In the	API 1987a

			second week survivors were considered to be normal . Dark red lungs were observed in all animals that died within a day or two of exposure.	
64742-80-9 Hydrodesulfurized Middle Distillate				
API 81-09	4.60 Combined sexes	Rat	-	API, 1983a
API 81-10	7.64 Combined sexes	Rat	-	API, 1983b

a- Composition provided in Acute Oral Table 10

#### 6.1.1.4 Skin Irritation

**Table 13. Skin Irritation: 24 hrs occluded**

CAS RN/ Composition <sup>a</sup>	Irritation Index PII	Species	Observations	Reference
64741-59-9 Light Catalytic Cracked Distillate				
API 83-07	5.6	Rabbit		API 1982a
API 83-08	6.9	Rabbit	Moderate to severe irritation Blanching in 2 rats at 24 hours, in six rats.at 72 hours. At 96 hours subcutaneous hemorrhaging within the test sites seen in all animals. No differences between abraded, intact skin.	API 1985d
CONCAWE MD-7 69.1% aromatics	-	Rabbit	Moderate to severe erythema in 2/3 rabbits at 60 min. Semi-occluded	Exxon 1996b
64741-44-2 Straight run Middle Distillate				
API 83-11	3.2	Rabbit	Slight to moderate irritation, no differences between abraded, intact skin	API 1985e
CONCAWE MD-6 73.7% saturates	-		Minimal transient irritation Semi-occluded	Exxon 1996b
64742-80-9 Hydrodesulfurized Middle Distillate				
API 81-09	4.3	Rabbit	Blanching, subcutaneous hemorrhage	API 1982b
API 81-10	5.9	Rabbit	Blanching, subcutaneous hemorrhage, severe fissuring, desquamation	API 1982b
68476-34-6 Commercial Diesel Fuel				
API 79-6	-	Rabbit	Extremely irritating	API 1980d
68476-30-2 No. 2 fuel oil [Home heating oil <sup>b</sup>				
API 78-02 [83-02] Medium Catalytic cracked stock 30%	3.37	Rabbit	Moderate irritation	API 1980a
API 78-03 [83-01] Low Catalytic cracked stock 10%	3.98	Rabbit	Moderate irritation	API 1980b
API 78-04 [83-03] High Catalytic cracked	3.83	Rabbit	Moderate irritation	API 1980c

stock 50%				
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a- Composition provided in Acute Oral Table 10

b- Combination of Straight run Middle Distillate, CAS RN 64741-44-2 and Light Catalytic Cracked Distillate CAS RN 64741-59-9

### 6.1.1.5 Eye Irritation

**Table 14. Eye Irritation: 24 hrs**

CAS RN/ Composition	Irritation Indices 24 hr	Species	Observations	Reference
64741-59-9 Light Catalytic Cracked Distillate				
API 83-07	1.7 unwashed; 2.0 washed	Rabbit		API 1982a
API 83-08	3.2 unwashed; 0.0 washed	Rabbit	No corneal irritation	API, 1985d
64741-44-2 Straight run Middle Distillate				
API 83-11	1.0 unwashed; 0.0 washed	Rabbit	No corneal or irridial irritation	API 1985e
64742-80-9 Hydrodesulfurized Middle Distillate				
API 81-09	2.0 unwashed; 0.0 washed	Rabbit		API 1982b
API 81-10	1.0 unwashed; 0.0 washed	Rabbit	Minimal irritation	API 1982c
68476-34-6 Commercial Diesel Fuel				
API 79-6	-	Rabbit	Non-irritating	API 1980d
68476-30-2 No. 2 fuel oil [Home heating oil] <sup>b</sup>				
API 78-02 [83-02] Medium Catalytic cracked stock 30%	0.7 unwashed; 0.7 washed	Rabbit	Minimal irritation	API 1980a
API 78-03 [83-01] Low Catalytic cracked stock 10%	1.3 unwashed; 0.0 washed	Rabbit	Minimal irritation	API 1980b
API 78-04 [83-03] Hlgh Catalytic cracked stock 50%	0.33 unwashed; 0.0 washed	Rabbit	Non irritation	API 1980c

a- Composition provided in Acute Oral Table 10

b- Combination of Straight run Middle Distillate, CAS RN 64741-44-2 and Light Catalytic Cracked Distillate CAS RN 64741-59-9

### 6.1.1.5 Sensitization

**Table 15. Sensitization**

CAS RN/ Composition	Challenge Response	Species	Observations	Reference
64741-59-9 Light Catalytic Cracked Distillate				
API 83-07	-	Guinea Pig	Non-Sensitizing	API 1982a
API 83-08	0/10	Guinea Pig	Non-Sensitizing	API 1985d
64741-44-2 Straight run Middle Distillate				
API 83-11	0/10	Guinea Pig	Non-Sensitizing	AP! 1985d
64742-80-9 Hydrodesulfurized Middle Distillate				

API 81-09	0/10	Guinea Pig	Non-Sensitizing	API 1984b
API 81-10	-	Guinea Pig	Non-Sensitizing	API 1984c
68476-34-6 Commercial Diesel Fuel				
API 79-6		Guinea Pig	Non-Sensitizing	API 1980d
68476-30-2 No. 2 fuel oil [Home heating oil] <sup>b</sup>				
API 78-02 [83-02] Medium Catalytic cracked stock 30%		Guinea Pig	Non-Sensitizing	API 1980a
API 78-03 [83-01] Low Catalytic cracked stock 10%		Guinea Pig	Non-Sensitizing	API 1980b
API 78-04 [83-03] High Catalytic cracked stock 50%		Guinea Pig	Non-Sensitizing	API 1980c

a- Composition provided in Acute Oral Table 10

b- Combination of Straight run Middle Distillate, CAS RN 64741-44-2 and Light Catalytic Cracked Distillate CAS RN 64741-59-9

## Conclusions

Gas Oil streams and fuels induce minimal acute toxicity by the oral, dermal and inhalation routes. Although skin irritation tended to be moderate to severe, these responses may be exaggerated since the 24 hour exposure period in these studies was significantly longer than the OECD 404 protocol recommended exposure period of 4 hours used for classification purposes. It is suggested that mild to moderate skin irritation is a more realistic assessment. No dermal sensitization was reported. Eye irritation was minimal to slight in unwashed eyes and minimal to unapparent in washed eyes. Existing data are sufficient to characterize acute toxicity for this category.

### 6.1.2 Repeat dose and Developmental Toxicity Statistical Modeling

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 Mobil Method-2, [PAC-2 method]. The PAC-2 analyses provided the weight percent of each aromatic ring class that served as a basis for the models (the ARC in Table 16). 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 (Sect. 6.1.6.1) and repeated-dose toxicity (Sect 6.1.3) discussed in the relevant section. The test material samples 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  $\geq 650$  °F [ $\geq 343$ °C] and for which toxicity is related to polycyclic aromatic carbon content.

**Table 16. PAC Analytical Profile of Gas Oils**

CAS RN/ Sample No.	DMSO wt % <sup>1</sup>	ARC 1 <sup>2</sup> (%)	ARC 2 (%)	ARC 3 (%)	ARC 4 (%)	ARC 5 (%)	ARC 6 (%)	≥ARC 7 (%)
<b>68476-34-6 Ultralow sulfur diesel (ULSD) samples from USA in 2009</b>								
080801	4.9	1.0	3.4	0.5	0.0	0.0	0.0	0.0
080802	4.1	0.4	2.9	0.4	0.0	0.0	0.0	0.0
080803	2.5	0.2	1.7	0.5	0.0	0.0	0.0	0.0
080804	2.7	0.2	1.6	0.8	0.0	0.0	0.0	0.0
080805	2.5	0.2	2.0	0.5	0.0	0.0	0.0	0.0
080806	3.1	0.3	2.2	0.3	0.0	0.0	0.0	0.0
080807	4.7	0.9	3.3	0.5	0.0	0.0	0.0	0.0
080808	4.9	1.0	3.4	0.5	0.0	0.0	0.0	0.0
080809	2.4	0.2	1.7	0.5	0.0	0.0	0.0	0.0
080810	2.5	0.2	2.0	0.3	0.0	0.0	0.0	0.0
080811	4.3	0.4	2.6	1.3	0.1	0.0	0.0	0.0
080812	4.2	0.4	2.5	1.3	0.1	0.0	0.0	0.0
080813	4.0	0.3	3.2	0.4	0.0	0.0	0.0	0.0
080814	2.6	0.3	1.8	0.5	0.0	0.0	0.0	0.0
080815	4.1	0.4	2.5	0.8	0.0	0.0	0.0	0.0
080816	2.2	0.2	1.5	0.4	0.0	0.0	0.0	0.0
080817	2.9	0.3	2.3	0.3	0.0	0.0	0.0	0.0
080818	3.3	0.3	2.3	0.3	0.0	0.0	0.0	0.0
080819	2.4	0.2	1.9	0.2	0.0	0.0	0.0	0.0
080820	2.8	0.2	1.7	0.8	0.0	0.0	0.0	0.0
080821	4.4	0.2	2.7	1.3	0.0	0.0	0.0	0.0
080822	4.8	0.4	2.9	1.4	0.0	0.0	0.0	0.0
080823	4.2	0.4	2.9	0.8	0.0	0.0	0.0	0.0
080824	3.9	0.3	2.7	0.8	0.0	0.0	0.0	0.0
080825	3.2	0.3	2.2	0.6	0.0	0.0	0.0	0.0
080826	3.0	0.3	2.1	0.6	0.0	0.0	0.0	0.0
080827	6.4	0.5	3.8	1.9	0.1	0.0	0.0	0.0
080828	4.1	0.4	3.3	0.4	0.0	0.0	0.0	0.0
080829	5.2	0.5	3.6	1.0	0.0	0.0	0.0	0.0
080830	7.1	0.6	5.0	1.4	0.0	0.0	0.0	0.0
080831	5.2	0.4	3.6	1.6	0.0	0.0	0.0	0.0
080832	5.3	0.5	3.2	1.6	0.0	0.0	0.0	0.0
080833	4.4	0.4	3.1	0.9	0.0	0.0	0.0	0.0
080834	4.3	0.4	3.0	0.9	0.0	0.0	0.0	0.0
080835	3.5	0.3	2.4	0.7	0.0	0.0	0.0	0.0
080836	4.0	0.3	2.8	0.8	0.0	0.0	0.0	0.0
080837	1.3	0.1	1.1	0.3	0.0	0.0	0.0	0.0
080838	2.5	0.2	1.7	0.5	0.0	0.0	0.0	0.0
080839	3.7	0.3	2.2	1.1	0.0	0.0	0.0	0.0
080840	4.3	0.4	3.0	0.9	0.0	0.0	0.0	0.0
120801	2.8	0.1	2.2	0.6	0.0	0.0	0.0	0.0
<b>68334-30-5</b>								
060812	1.3	0.1	1.0	0.1	0.0	0.0	0.0	0.0
081001	3.4	0.2	2.7	0.3	0.0	0.0	0.0	0.0
081003	2.5	0.2	1.8	0.5	0.0	0.0	0.0	0.0
091648		0.1	3.0	4.0	0.1	0.1	0.1	0.0
094523	2.4	0.0	0.7	1.2	0.5	0.0	0.1	0.0
085202	6.8	0.7	4.1	2.0	0.3	0.0	0.0	0.0
085203	7.0	0.7	4.2	2.1	0.1	0.0	0.0	0.0
<b>68476-30-2 Middle distillates</b>								
089164	1.8	0.0	1.1	0.7	0.1	0.0	0.0	0.0

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CAS RN/ Sample No.	DMSO wt % <sup>1</sup>	ARC 1 <sup>2</sup> (%)	ARC 2 (%)	ARC 3 (%)	ARC 4 (%)	ARC 5 (%)	ARC 6 (%)	≥ARC 7 (%)
089165	2.8	0.1	1.4	1.1	0.1	0.0	0.0	0.0
089166	4.0	0.0	3.2	0.8	0.0	0.0	0.0	0.0
089167	1.4	0.1	0.8	0.6	0.1	0.0	0.0	0.0
089169	4.2	0.0	1.7	2.1	0.1	0.0	0.0	0.0
089170	3.2	0.2	1.6	1.3	0.2	0.0	0.0	0.0
089175	11.3	0.1	4.5	5.7	1.1	0.0	0.0	0.0
089180	4.0	0.4	1.6	2.0	0.1	0.0	0.0	0.0
089181	2.5	0.3	1.3	0.8	0.0	0.0	0.0	0.0
089182	4.0	0.4	1.6	1.6	0.2	0.0	0.0	0.0
089183	8.3	0.8	2.5	4.2	1.7	0.1	0.0	0.0
091022	3.4	0.3	2.4	0.6	0.0	0.0	0.0	0.0
091023	3.6	0.1	2.9	0.6	0.0	0.0	0.0	0.0
091024	4.0	0.2	3.2	0.6	0.0	0.0	0.0	0.0
091025	3.6	0.3	2.9	0.5	0.0	0.0	0.0	0.0
091026	3.8	0.2	3.0	0.6	0.0	0.0	0.0	0.0
091027	3.6	0.2	2.9	0.5	0.0	0.0	0.0	0.0
091675	15.2	0.3	6.1	4.6	1.5	0.8	1.5	0.9
089172	5.4	0.2	1.6	2.7	0.5	0.0	0.0	0.0
<b>DGMK Middle Distillate Samples (no CAS number)</b>								
091673 <sup>b</sup>	16.0	0.3	9.6	4.8	0.0	0.2	0.5	1.0
089168 <sup>b</sup>	3.7	0.0	1.5	1.9	0.4	0.0	0.0	0.0
089171 <sup>b</sup>	4.7	0.2	3.3	0.9	0.1	0.0	0.0	0.0
089173 <sup>b</sup>	5.3	0.4	2.1	2.1	0.5	0.0	0.0	0.0
089174 <sup>b</sup>	2.7	0.3	1.6	0.8	0.1	0.0	0.0	0.0
089176 <sup>b</sup>	6.0	0.4	2.4	2.4	0.6	0.0	0.0	0.0
089177 <sup>b</sup>	2.4	0.5	1.4	0.5	0.0	0.0	0.0	0.0
089178 <sup>b</sup>	4.4	0.4	2.6	1.3	0.2	0.0	0.0	0.0
089179 <sup>b</sup>	2.7	0.5	1.9	0.5	0.0	0.0	0.0	0.0
089184 <sup>b</sup>	3.8	0.4	1.5	1.5	0.2	0.0	0.0	0.0
089185 <sup>b</sup>	1.0	0.1	0.7	0.1	0.0	0.0	0.0	0.0
089186 <sup>b</sup>	2.0	0.6	1.2	0.2	0.0	0.0	0.0	0.0
089187 <sup>b</sup>	2.1	0.4	0.8	0.6	0.2	0.0	0.0	0.0
<b>64741-43-1</b>								
085288	8.8	0.0	2.6	5.3	0.2	0.3	0.4	0.3
091646		0.0	2.0	4.0	2.0	0.7	2.0	0.0
090901	5.1	0.1	2.1	2.6	0.2	0.0	0.0	0.0
090903	4.8	0.1	2.4	1.9	0.1	0.0	0.0	0.0
090904	7.1	0.0	0.6	6.4	0.2	0.0	0.0	0.0
<b>64741-58-8</b>								
030917	4.6	0.0	0.1	4.4	0.1	0.0	0.0	0.0
<b>64741-60-2</b>								
060948	41.0	0.4	28.7	12.3	0.0	0.0	0.0	0.0
060939	48.0	0.0	0.5	33.6	14.4	1.0	0.0	0.0
<b>64741-77-1</b>								
030922	4.8	1.4	3.4	0.0	0.0	0.0	0.0	0.0
030923	2.1	0.6	1.5	0.0	0.0	0.0	0.0	0.0
087525	3.4	1.4	2.0	0.1	0.0	0.0	0.0	0.0
<b>64741-82-8</b>								
010919	9.8	0.5	7.9	1.0	0.0	0.0	0.0	0.0
060928	12.0	0.1	6.0	6.0	0.0	0.0	0.0	0.0
060931	8.6	0.2	5.2	3.4	0.3	0.0	0.0	0.0
060942	9.8	0.9	6.9	2.0	0.0	0.0	0.0	0.0
087213	10.5	0.1	4.2	6.3	0.3	0.0	0.0	0.0
091652		0.1	4.0	10.0	0.0	0.0	0.0	0.0
091037	10.4	0.6	5.7	3.8	0.3	0.0	0.0	0.0
091038	10.3	0.5	5.7	3.9	0.3	0.0	0.0	0.0
091039	10.2	0.6	6.2	3.3	0.2	0.0	0.0	0.0
<b>64742-80-9</b>								
010908	3.4	0.0	2.4	1.0	0.0	0.0	0.0	0.0
010916	2.5	0.2	2.0	0.5	0.0	0.0	0.0	0.0

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CAS RN/ Sample No.	DMSO wt % <sup>1</sup>	ARC 1 <sup>2</sup> (%)	ARC 2 (%)	ARC 3 (%)	ARC 4 (%)	ARC 5 (%)	ARC 6 (%)	≥ARC 7 (%)
010917	7.4	0.2	3.7	3.7	0.0	0.0	0.0	0.0
086413	3.3	0.0	3.0	0.3	0.0	0.0	0.0	0.0
086414	10.5	0.8	6.3	3.2	0.0	0.0	0.0	0.0
<b>64742-38-7</b> 060950	3.6	0.7	2.9	0.0	0.0	0.0	0.0	0.0
<b>68333-25-5</b>								
030925	9.4	0.5	6.6	2.8	0.0	0.0	0.0	0.0
030926	2.1	0.0	1.5	0.4	0.0	0.0	0.0	0.0
<b>68333-88-0</b>								
010921	12.0	3.6	4.8	3.6	0.0	0.0	0.0	0.0
080903	31.0	9.3	18.6	0.6	0.0	0.0	0.0	0.0
080904	8.8	4.4	3.5	0.3	0.0	0.0	0.0	0.0
094628		7.0	4.0	0.0	0.0	0.0	0.0	0.0
<b>68477-31-6</b>								
080906	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
080907	1.4	1.3	0.1	0.0	0.0	0.0	0.0	0.0
<b>68915-96-8</b>								
060911	5.7	0.0	0.5	2.3	2.9	0.2	0.0	0.0
060924	5.4	0.2	1.6	2.2	1.1	0.5	0.1	0.0
060929	4.7	0.0	0.9	1.9	0.9	0.5	0.2	0.0
060941	5.0	0.1	1.0	2.0	1.0	0.5	0.1	0.0
<b>64741-44-2</b>								
087523	4.2	0.4	2.5	1.3	0.0	0.0	0.0	0.0
088773	0.9	0.0	0.7	0.2	0.0	0.0	0.0	0.0
<b>64741-49-7</b>								
085242	6.0	0.2	1.8	2.4	0.6	0.4	0.1	0.1
086175	6.7	0.0	2.0	3.4	1.3	0.4	0.1	0.1
086178	8.0	0.0	0.8	4.0	1.6	0.8	0.3	0.2
086186	8.9	0.1	2.7	6.2	0.3	0.1	0.1	0.3
086270	8.8	0.9	2.6	3.5	0.9	0.4	0.0	0.4
081005	7.7	0.0	4.6	3.1	0.0	0.0	0.0	0.0
086279	8.0	0.8	4.8	1.6	0.1	0.0	0.0	0.0
<b>64741-59-9</b>								
008281	49.1	2.0	29.5	14.7	0.0	0.5	0.5	0.0
010912	39.8	0.4	27.9	8.0	0.0	0.0	0.0	0.0
010915	31.5	0.0	22.1	9.5	0.0	0.0	0.0	0.0
086182	29.0	0.0	17.4	11.6	0.0	0.0	0.0	0.0
086191	22.0	0.0	13.2	8.8	0.0	0.0	0.0	0.0
086195	36.2	0.4	25.3	10.9	0.0	0.0	0.0	0.0
086280	30.1	0.3	18.1	9.0	0.0	0.0	0.3	0.0
087524	28.0	2.0	16.8	8.4	0.0	0.0	0.0	0.0
087527	4.0	0.8	2.0	0.8	0.1	0.0	0.0	0.0
091679		0.4	20.0	20.0	0.4	0.0	0.0	0.0
010903	32.5	3.3	19.5	9.8	0.0	0.0	0.0	0.0
010913	23.9	2.4	16.7	4.8	0.0	0.0	0.0	0.0
010914	38.2	0.0	34.4	3.8	0.0	0.0	0.0	0.0
086273	18.1	0.4	10.9	5.4	0.2	0.0	0.2	0.0
089295	42.2	0.4	42.2	0.0	0.0	0.0	0.0	0.0
097526	16.0	1.1	9.6	6.4	0.2	0.0	0.0	0.0
<b>64741-86-2</b>								
087088	2.7	0.0	2.4	0.3	0.0	0.0	0.0	0.0
094629		3.0	0.0	2.3	0.6	0.0	0.0	0.0
087467	2.9	0.0	2.3	0.6	0.0	0.0	0.0	0.0
<b>64742-46-7</b>								
060809	4.3	0.3	3.0	1.3	0.0	0.0	0.0	0.0
060811	3.2	0.3	2.6	0.3	0.0	0.0	0.0	0.0
081004	0.3	0.0	0.2	0.1	0.0	0.0	0.0	0.0
<b>64742-87-6</b> 081008	9.5	0.0	3.8	4.8	0.3	0.0	0.0	0.0
<b>68814-87-9</b>								
081002	4.3	0.1	2.6	1.7	0.1	0.0	0.0	0.0

CAS RN/ Sample No.	DMSO wt % <sup>1</sup>	ARC 1 <sup>2</sup> (%)	ARC 2 (%)	ARC 3 (%)	ARC 4 (%)	ARC 5 (%)	ARC 6 (%)	≥ARC 7 (%)
081006	9.6	0.5	5.8	2.9	0.1	0.0	0.0	0.0
081007	14.0	0.7	9.8	4.2	0.0	0.0	0.0	0.0
<b>68915-97-9</b>								
086174	5.8	0.0	0.3	4.6	0.6	0.1	0.1	0.1
086183	6.2	0.0	0.4	4.3	1.2	0.2	0.1	0.1
086190	5.2	0.3	3.6	1.0	0.1	0.2	0.0	0.0
086271	10.5	0.1	0.8	5.3	3.2	0.4	0.2	0.1
<b>Gas Oil Stream Blends No CAS RN</b>								
060806	3.8	0.3	3.0	0.4	0.0	0.0	0.0	0.0
060807	3.6	0.2	2.9	0.7	0.0	0.0	0.0	0.0
060808	2.1	0.4	1.5	0.2	0.0	0.0	0.0	0.0
060810	4.4	0.4	3.1	0.9	0.0	0.0	0.0	0.0
<b>10% 64741-59-9 and 90% 64741-44-2</b> 088415	5.1	0.3	4.1	1.0	0.0	0.0	0.0	0.0
<b>30% 64741-59-9 and 70% 64741-44-2</b> 088416	7.4	0.7	5.2	1.5	0.0	0.0	0.0	0.0
<b>50% 64741-59-9 and 50% 64741-44-2</b> 088416	8.7	0.9	5.2	2.6	0.0	0.0	0.0	0.0

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 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.

### 6.1.3 Repeated Dose Toxicity

Four dermal studies in rats of 13 week, four dermal studies of 4 week duration and two 4 week inhalation studies have been performed with samples in the Gas Oil category and are described below by CAS number [CAS RN]. Table 17 summarizes the results of rat dermal repeated dose toxicity studies. Dermal irritation occurred in all studies to varying degrees and was not used in establishing LOAEL/NOAEL. Treatment at very high doses was sometimes terminated due to severe dermal irritation. Repeat dose dermal studies in New Zealand white rabbits are provided for supplemental information.

#### 13 week Rat Dermal Studies

##### CAS RN 64741-41-7

Vacuum Tower Overheads was applied undiluted to the shaved backs of Sprague-Dawley rats once daily, five days per week for 13 weeks, at doses of 0, 30, 125 or 500mg/kg/day (Mobil 1989a, Study #62326). Slight decreases in body weight gain [11%] were seen in males at 500mg/kg/day. Small decreases in haematology, and changes in serum chemistry were seen in both sexes at 500 and 125mg/kg day. Liver weight (relative and/or absolute) increased in both sexes at 500 and 125mg/kg. Thymus weight decreased and a mild reduction in thymocytes was observed at 500mg/kg in both sexes. No other effects were seen histologically. Reproductive organs, spermatozoa and spermatids counts and morphology were comparable to untreated controls. Skin irritation was not reported. LOAEL = 125mg/kg/day; NOAEL = 30mg/kg day.

### **CAS RN 64741-59-9**

Light cycle oil (79.8% aromatic hydrocarbons) was applied undiluted to the shaved backs of Sprague Dawley rats once daily, five days per week for 13 weeks, at doses of 0, 8, 25, 125, 500, or 1250mg/kg/day (Mobil 1985, Study #20535). After 2 weeks of exposure rats dosed at 1250mg/kg/day were terminated due to poor growth and appearance. At 500mg/kg male rats showed marked reduction in body weight and thymus size and weight accompanied by decreased lymphocytes in thymus, and slight decreases at 125mg/kg. Liver weights were increased in both sexes at 500mg/kg. In females, kidney, adrenal, ovary and liver weights (relative and/or absolute) were increased at 500mg/kg. Dose related marked persistent skin irritation was seen including severe erythema and edema but was not used to define LOAEL/NOAEL values. LOAELs were 125mg/kg for males and 500mg/kg for females. NOAEL males = 25mg/kg and NOAEL females = 125mg/kg.

### **CAS RN 64741-82-8**

Coker light gas oil (56.9% saturated hydrocarbons) was applied undiluted to the shaved backs of Sprague Dawley rats once daily, five days per week for 13 weeks, at doses of 0, 30, 125, 500 or 2000mg/kg/day (Mobil 1991a, Study #61996). Animals in the 500 and 2000mg/kg/day were sacrificed in moribund conditions at week 9 and 2 respectively. Perineal staining and dose related skin irritation (generally severe) were seen in all dose groups. Body weights were decreased and changes in hematology and serum chemistry parameters were seen at 125mg/kg and above. Increases in lymphocytes were seen at 125 mg/kg in both sexes and at 30mg/kg in females. Differences in organ weights (absolute and/or relative) were observed at 125mg/kg and above and male thymus weight was decreased at 30mg/kg. Histologically skin irritation and slight effects on kidneys and bone marrow were reported. Bone marrow effects included severe reduction in erythropoietic cells and megakaryocytes at 2000mg/kg and structural changes in megakaryocytes at 2000, 500 and 125mg/kg. LOAEL = 30mg/kg based on decreased thymus weight in males and increased lymphocytes in females. NOAEL was not determined, <30mg/kg.

### **CAS RN 68915-97-9**

Heavy atmospheric gas oil was applied undiluted to the shaved backs of Sprague Dawley rats once daily, five days per week for 13 weeks, at doses of 0, 30, 125, 500 or 2000mg/kg/day (Mobil 1992, Study #63456). 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*. 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. Organ weight (absolute and relative) differences were seen in the 125 and 500 mg/kg/day groups. Histologically, treatment related changes in the 500mg/kg group 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.

#### **4 week Rat Dermal Studies**

##### **CAS RN 64741-43-1**

F-130, a gas oil intermediate was applied to the shaved backs of Sprague-Dawley rats once daily, five days per week for four weeks, at a dose of 0, 0.01, 0.10 or 0.50 ml/kg/day (9.2, 92, 460 mg/kg/day) (ARCO, 1992b ATX-90-0050). Slight skin irritation was observed at 460mg/kg/day and was very slight at 92mg/kg/day. No adverse effects were observed in terminal body weights, hematology or serum chemistry parameters or organ weights. Histological evaluation indicated treated animals were comparable to controls and reproductive organs were normal. The NOAEL for both sexes excluding slight skin irritation was 460mg/kg the highest dose tested. LOAEL >460mg/kg

##### **CAS RN 64741-77-1**

F-188, a light hydrocracked distillate was applied to the shaved backs of Sprague-Dawley rats once daily, five days per week for four weeks, at a dose of 0, 0.05, 0.25 or 1.0 ml/kg/day (41, 205, 820 mg/kg/day) (ARCO, 1992a ATX-91-0094). No adverse effects seen on terminal body weight, organ weights or hematology parameters. Slight changes in globulin level at highest dose in males and A/G ratio in both sexes were not compound related or biologically relevant by study investigators. No abnormal histopathology was seen; reproductive organs were comparable to untreated controls. Skin irritation [very slight to moderate] was observed in all treated animals in a dose related manner but was not used in setting LOAEL/NOAEL; NOAEL for both sexes = 820mg/kg LOAEL > 820mg/kg [highest dose tested]

##### **CAS RN 64741-86-2**

F-233 a sweetened middle distillate [DHDS Stove Oil] was applied to the shaved backs of Sprague-Dawley rats once daily, five days per week for four weeks, at a dose of 0, 0.05, 0.5 or 1.0 ml/kg/day (41, 410, 820 mg/kg/day) (ARCO, 1993a ATX-91-0233). Effects seen at 820mg/kg in both sexes included decreased terminal body weight (9%), increased adrenal weight relative to brain weight and decreased kidney weight relative to brain weight and varying changes in serum chemistry. Absolute liver weight and weight relative to brain weight was decreased in males. Absolute ovary weight and weight relative to brain weight was decreased at 820mg/kg but no abnormalities were seen in ovaries or testes histologically. Skin irritation was slight to moderate increasing in a dose-related manner and was not used in setting LOAEL/NOAEL. Histologically the only changes were hyperplasia of the axillary lymph nodes in both sexes at 820mg/kg/day considered secondary to dermal irritation and inflammation. LOAEL = 820mg/kg/day and NOAEL = 410mg/kg/day.

#### **4-week Rat Inhalation Studies**

Two samples of a hydrosulfurized middle distillate (CAS RN 64742-80-9, API 81-09 79.4% saturated hydrocarbons) and API 81-10, 65.6% saturated hydrocarbons) were administered at nominal concentration of 25mg/m<sup>3</sup>, 6 hours/day, 5 days a week for 4 weeks (API, 1986f). No systemic effects were observed except for increased leukocyte counts in rats exposed to API 81-10 and subacute inflammation of the respiratory mucosa lining in animals exposed to API 81-09.

Supplemental data: Repeat dose dermal studies in New Zealand White rabbits.

A light catalytic cracked distillate (CAS RN 64741-59-9, API 83-07, 72.4% aromatic hydrocarbons) was applied undiluted to the shaved skin of rabbits (5/sex/group), at concentrations of 0, 250, 500 or 1000mg/kg, 3 times/week for 4 weeks (API, 1982a). No systemic effects were observed. Treatment related skin irritation ranging up to severe was seen and histologic examination of tissue from high dose animals identified moderate to severe proliferation and inflammatory changes in skin associated with increased granulopoiesis of bone marrow attributed to stress of severe skin irritation.

A diesel fuel was applied to the skin of New Zealand white rabbits 5 days/week for 3 weeks at dose levels of 0.2, 0.67 and 2.0 g/kg/day (IITRI, 1984). Severe skin irritation was seen in all the dosed groups. One of ten males and two of the ten females in the highest dose group died prematurely. A variety of compound-related effects were seen.

One, 3 & 10 ml/kg/day of a No. 2 home heating oil (67.8% saturated hydrocarbons) was applied undiluted to the skin of male and female New Zealand white rabbits (API, 1980c). The test material was applied daily for 5 days, the animals were given a two day dose-free rest and then the test material was applied daily for an additional 5 days. Severe skin irritation was seen at all dose levels. Two of eight and 7/8 animals died prematurely in the 3 and 10 ml/kg/day groups, respectively. The only significant histological findings were those associated with the severe skin lesions.

Two additional samples of No. 2 home heating oils (containing 79.2% and 73.4% saturated hydrocarbons) have been tested for repeat-dose toxicity (API, 1980a, b). In these studies, material was applied to the skin of rabbits for two weeks. Doses in the first study were 2.5, 4 and 10 ml/kg/day, while those in the second study 1, 2.5 and 10 ml/kg/day. Both materials produced severe skin irritation at all dose levels. In the first study, 8/8 animals receiving 10/kg/day died prematurely. In the second study, 1/8 and 6/8 animals died prematurely in the 2.5 and 10 ml/kg/day groups, respectively.

The market-place sample of diesel fuel that was summarized in the acute toxicity section was also tested in a two week repeat-dose study (API, 1980d). Applied to the skin of rabbits for two weeks at dose levels of 4 and 8 ml/kg/day, the material produced a 67% mortality rate in the 8 ml/kg/day group.

## **Conclusions**

The 13-week rat dermal studies on gas oil streams indicate LOAEL values for both sexes of 125mg/kg and NOAEL of 25-30mg/kg with the exception of a light coker gas oil (CAS RN 64741-82-8 sample 87213) with a LOAEL of 30mg/kg, the lowest dose tested, effects likely exacerbated by severe skin irritation at all dose levels. Skin irritation in the other studies generally ranged from slight to moderate. Effects in all studies when present were seen primarily on liver and thymus weights and hematologic endpoints. Only light cycle oil (CAS RN 64741-59-9) had a PAC analytical profile with a relatively higher percentage of C2 and C3 aromatic rings than the other streams tested although the LOAEL and NOAEL were similar. The 4 week duration rat dermal studies showed slight to moderate skin irritation and minimal systemic toxicity. No significant adverse effects were seen in reproductive organs in any rat dermal study.

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The two 4 week inhalation studies with samples of hydrodesulfurized distillates at a single dose of 25mg/m<sup>3</sup> resulted in minimal systemic effects and some inflammation of respiratory tissue. Supplemental studies of rabbit dermal exposure focused on irritation and mortality and are provided for general information.

**Table 17. Gas Oils Dermal Repeat Dose Studies in Rats [28 day and 13 week exposures]**

CAS RN	Study: Species/ Route/Duration	Dose/ Frequency	Results	References
<b>64741-43-1 Gas Oil Intermediate (C11-25) straight run</b>				
<b>Gas Oil Intermediate F-130</b> [64741-43-1]	Rats (10/sex/group) dermal, 4 weeks	0, 9.2, 92, 460mg/kg/d (0, 0.01, 0.10, 0.50ml/kg/d) 5 days/week; 6 hr/day occluded	NOAEL = 460 mg/kg [highest dose] LOAEL > 460mg/kg No systemic effects. No adverse effects on reproductive organs Slight skin irritation at highest dose	ARCO, 1992b ATX-90-0050
<b>64741-49-7 Vacuum Tower Condensate (C11-25)</b>				
<b>Vacuum Tower Overheads</b> Sample # 86270 [64741-47-7]	Rats (10/sex/group) dermal, 13 weeks	0, 30, 125, 500mg/kg/d, 5 days/week Elizabethan collars, weekly wipe off	LOAEL=125mg/kg Based on decreased hematology, changes in serum chemistry parameters, liver weight increases, thymus weight decreases and reduced thymocytes at 500mg/kg. No adverse effects on reproductive organs or spermatozoa, spermatids. NOAEL = 30 mg/kg	Mobil 1989a Study 62326 Used in PAC model <sup>a</sup>
<b>64741-59-9 Catalytic cracked Distillate Light (C9-C25)</b>				
<b>Light cycle oil</b> Sample #8281 [64741-59-9]	Rats (10/sex/group) dermal, 13 weeks	0, 8, 25, 125, 500, 1250mg/kg/d 1250mg/kg terminated after 2 weeks 5 days/week Elizabethan collars, weekly wipe off	LOAEL male = 125mg/kg; NOAEL =25mg/kg Based on reduced body weight, thymus, testes, adrenal weights, decreased thymocytes, increased liver weights LOAEL females = 500mg/kg based on increased organ weights – ovary, liver, adrenal, kidney. NOAEL = 125mg/kg. No adverse histologic effects on reproductive organs. Dose related skin irritation	Mobil 1985 Study 20535 Used in PAC model <sup>a</sup>
<b>64741-77-1 Hydrocracked Distillate light (C10-C18)</b>				
<b>Light Hydrocracked Distillate F-188</b> [64741-77-1]	Rats (10/sex/group) dermal, 4 weeks	0, 41, 205,820mg/kg/d (0, 0.05, 0.25, 1.0ml/kg/d) 5 days/week;	NOAEL = 820mg/kg [highest dose] LOAEL >820mg/kg No systemic effects. No adverse effects on reproductive organs Slight –moderate dose related skin irritation	ARCO 1992a <sup>a</sup> ATX-91-0094

CAS RN	Study: Species/ Route/Duration	Dose/ Frequency	Results	References
		6 hr/day occluded		
<b>64741-82-8 Thermocracked Distillate, Light (C10-18)</b>				
<b>Coker Light Gas Oil</b> Sample #87213 [64741-82-8]	Rats (10/sex/group) dermal, 13 weeks	0, 30, 125, 500, 2000mg/kg/d 500, 2000mg/kg terminated at wk 9 and 2, respectively 5 days/week Elizabethan collars, weekly wipe off	LOAEL = 30mg/kg Based on decreased body wt (males), changes in serum chemistry, hematology, organ weights, increased lymphocytes in females and decreased thymus wt in males at 30mg/kg, Severe skin irritation, bone marrow effects. NOAEL undetermined, <30mg/kg	Mobil 1991a Study 61996 Used in PAC model <sup>a</sup>
<b>64741-86-2 Sweetened Distillate (C9-20)</b>				
<b>DHIS Stove Oil F-233</b> [64741-86-2]	Rats (10/sex/group) dermal, 4 weeks	0, 41, 410, 820mg/kg/d (0, 0.05, 0.5, 1.0ml/kg/d) 5 days/week; 6 hr/day occluded	LOAEL = 820mg/kg Based on decreased terminal body weight, changes in serum chemistry values, changes in liver, adrenal, kidney and ovary weight not reflected histologically. Dose related slight to moderate skin irritation NOAEL = 410mg/kg	ARCO 1993a ATX-91-0233
<b>68915-97-9 Gas Oil Heavy</b>				
<b>Heavy Atmospheric Gas Oil</b> 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, 1992 Study #63456 Used in PAC Model <sup>a</sup>

a – Gas 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 will be presented in Tables 18 and 19 in a subsequent version

Repeated dose toxicity will also be characterized using predictive models based on PAC profiles (Appendix C). Values to be shown in Table 18 are the PDR<sub>10</sub>s and where appropriate BMD<sub>10</sub>s based on the method of Crump, 1984 employing data from actual studies. The PDR<sub>10</sub> 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 for each sample constitutes the overall sample PDR<sub>10</sub> (highlighted in Table 18). The study BMD<sub>10</sub> is also the lowest of the original BMD<sub>10</sub> endpoint values. The BMD<sub>10</sub> calculations from 13 week dermal rat studies that meet the criteria for the modeling domain give similar values to the PDR<sub>10</sub>s.

Table 19 will show how modeling of endpoints based on analytical distribution of 1-7 ring PAC provides estimates of effects for Gas Oil streams. Given the complex composition of gas oils even when identified by the same CAS RN, individual streams will vary in aromatic ring distribution which may alter the values expressed as PDR<sub>10</sub>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<sub>10</sub>s and BMD<sub>10</sub>s are also useful when animal studies are available but the dose ranges are widely spaced.

**Table 18. Repeated-dose PDR<sub>10</sub> and BMD<sub>10</sub> of Gas Oils by Endpoint**

CAS RN/ Sample No.	PDR <sub>10</sub> or BMD <sub>10</sub> mg/kg/day								Sample PDR <sub>10</sub> mg/kg/day [Endpoint]	Sample BMD <sub>10</sub> mg/kg/day
	Thymus weight		Platelet Count		Hemoglobin Count		Relative Liver Wt.			
	Male	Female	Male	Female	Male	Female	Male	Female		
Example	>2000	>2000	300	300	>2000	>2000	>2000	>2000	300 [platelets]	260-
Example	220	190			1000	1000	320	310	190 [♀ thymus]	110
This is an interim Category Assessment Document without modeled data included. The modeled PDR <sub>10</sub> and BMD <sub>10</sub> values will be available in a subsequent version.										

**Table 19. Modeled Repeat Dose PDR10 Values of Gas Oils from Most to Least Severe**

CAS RN	Sample No.	Repeat Dose PDR10 mg/kg	ARC 1 (%)	ARC 2 (%)	ARC 3 (%)	ARC 4 (%)	ARC 5 (%)	ARC 6 (%)	≥ARC 7 (%)
ABCD-EF-G	123456	200	0.2	1.7	0.5	6.3	2.1	1.3	0.2
This is an interim Category Assessment Document without modeled data included. The modeled PDR <sub>10</sub> values will be available in a subsequent version.									

#### 6.1.4 Genetic Toxicity *In Vitro*

**Table 20. Summary of *In Vitro* Genetic Toxicity Studies**

CAS RN/Sample	Assay	Results	Reference
<b>64741-59-9 Catalytic cracked Distillate, light</b>			
API 83-07 [72.4% aromatic HC]	Mouse Lymphoma	Positive with activation	API, 1985i
	Sister Chromatid Exchange [CHO cells]	Equivocal with and without activation	API, 1988b
API 83-08 [60.8% aromatic HC]	Mouse Lymphoma	Positive with and without activation	API, 1985f
<b>64741-49-7 Vacuum Tower Overheads</b>			
Vacuum Tower Overheads	Chinese Hamster Ovary cells [CHO]	Not clastogenic	Mobil Study 52242
<b>64742-80-9 Hydrodesulfurized Middle distillate</b>			
API 81-09 [79.4% saturated HC]	Mouse Lymphoma	Positive without activation Equivocal with activation	API, 1985h
API 81-10 [65.6% saturated HC]	Mouse Lymphoma 3 trials	Positive with and without activation	API, 1984a, 1986d, 1987e
API 81-10 aromatic fraction	Mouse Lymphoma	Negative	API, 1987b
API 81-10 saturate fraction	Mouse Lymphoma	Negative	API, 1987c
API 81-10	Sister Chromatid Exchange [CHO cells]	Negative without activation Equivocal with activation	API, 1988c
<b>DGMK Middle Distillate Samples</b>			
3 samples [52.4 to 59.8% aromatic HC]	Optimized Ames <sup>a</sup>	Positive with activation MI 7.6 – 9.3	DMGK, 1991
11 samples [52.7 to 79.0% saturated HC]	Optimized Ames <sup>a</sup>	Inactive to positive with activation MI 0.7 – 4.0	DMGK, 1991
Diesel Fuel - 3 samples [59.4 to 76.6% saturated HC]	Optimized Ames <sup>a</sup>	Positive with activation MI 1.7 – 3.9	DMGK, 1991
<b>Distillate Fuels</b>			
68476-34-6 Diesel Fuel No. 2-D [76.1% saturated HC]	Standard Ames	Negative with and without activation	API, 1978
	Mouse Lymphoma	Negative with and without activation	API, 1978
68476-30-2 Home heating oil API 78-4 [67.8% saturated HC]	Mouse Lymphoma	Positive with and without activation	API, 1979a

HC = hydrocarbons

<sup>a</sup> -Optimized Ames test (previously Modified Ames test) was developed to increase the sensitivity of the Ames *Salmonella* bacteria assay for PAC-rich petroleum streams.

In vitro genetic toxicity studies demonstrate that representative gas oil streams and distillate fuels generally induce gene mutation in bacterial and 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 D]. Table 21 summarizes the results of Optimized Ames tests on 53 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

189 samples of other high PAC petroleum streams with final boiling point  $\geq 650$  °F [ $\geq 343$ °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 D, McKee et al., 2011).

**Table 21. Gas 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 %	Optimized Ames MI	Modeled MI
<b>64741-44-2 Gas Oil, light</b>										
64741-44-2	87523	0.4	2.5	1.3	0.0	0.0	0.0	0.0	1.0	GE 1
<b>64741-49-7 Vacuum Tower Condensate</b>										
64741-49-7	85242	0.2	1.8	2.4	0.6	0.4	0.1	0.1	5.2	GE 1
64741-49-7	86175	0.0	2.0	3.4	1.3	0.4	0.1	0.1	6.8	GE 1
64741-49-7	86178	0.0	0.8	4.0	1.6	0.8	0.3	0.2	10.6	GE 1
64741-49-7	86186	0.1	2.7	6.2	0.3	0.1	0.1	0.3	6.7	GE 1
64741-49-7	86270	0.9	2.6	3.5	0.9	0.4	0.0	0.4	6.7	GE 1
64741-49-7	86279	0.8	4.8	1.6	0.1	0.0	0.0	0.0	4.6	GE 1
<b>64741-59-9 Catalytic Cracked Distillate, light</b>										
64741-59-9	8281	2.0	29.5	14.7	0.0	0.5	0.5	0.0	28.3	GE 1
64741-59-9	86182	0.0	17.4	11.6	0.0	0.0	0.0	0.0	57.9	GE 1
64741-59-9	86191	0.0	13.2	8.8	0.0	0.0	0.0	0.0	25.1	GE 1
64741-59-9	86195	0.4	25.3	10.9	0.0	0.0	0.0	0.0	34.6	GE 1
64741-59-9	86273	0.4	10.9	5.4	0.2	0.0	0.2	0.0	19.8	GE 1
64741-59-9	86280	0.3	18.1	9.0	0.0	0.0	0.3	0.0	20.1	GE 1
64741-59-9	87524	2.0	16.8	8.4	0.0	0.0	0.0	0.0	13.8	GE 1
64741-59-9	87526	1.1	9.6	6.4	0.2	0.0	0.0	0.0	7.9	GE 1
64741-59-9	87527	0.8	2.0	0.8	0.1	0.0	0.0	0.0	1.2	GE 1
64741-59-9	89295	0.4	42.2	0.0	0.0	0.0	0.0	0.0	0.0	LT 1
64741-59-9	89296	0.0	0.5	0.5	1.0	0.2	0.0	0.0	0.0	LT 1
64741-59-9	89297	0.2	15.2	0.0	0.0	0.0	0.0	0.0	0.0	LT 1
<b>64741-82-8 Thermocracked Distillate, light</b>										
64741-82-8	87213	0.1	4.2	6.3	0.3	0.0	0.0	0.0	13.3	GE 1
<b>64741-86-2 Sweetened Distillate</b>										
64741-86-2	87088	0.0	2.4	0.3	0.0	0.0	0.0	0.0	1.1	LT 1
64741-86-2	87467	0.0	2.3	0.6	0.0	0.0	0.0	0.0	0.0	LT 1
<b>68334-30-5 Diesel Oil and DMGK Middle Distillates</b>										
68334-30-5	85202	0.7	4.1	2.0	0.3	0.0	0.0	0.0	3.8	GE 1
68334-30-5	85203	0.7	4.2	2.1	0.1	0.0	0.0	0.0	3.9	GE 1
68476-30-2	89165	0.1	1.4	1.1	0.1	0.0	0.0	0.0	1.0	GE 1

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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 %	Optimized Ames MI	Modeled MI
68476-30-2	89166	0.0	3.2	0.8	0.0	0.0	0.0	0.0	1.2	GE 1
68476-30-2	89167	0.1	0.8	0.6	0.1	0.0	0.0	0.0	0.7	LT 1
68476-30-2	89169	0.0	1.7	2.1	0.1	0.0	0.0	0.0	4.1	GE 1
68476-30-2	89170	0.2	1.6	1.3	0.2	0.0	0.0	0.0	3.8	GE 1
68476-30-2	89175	0.1	4.5	5.7	1.1	0.0	0.0	0.0	9.0	GE 1
68476-30-2	89180	0.4	1.6	2.0	0.1	0.0	0.0	0.0	2.1	GE 1
68476-30-2	89181	0.3	1.3	0.8	0.0	0.0	0.0	0.0	2.8	GE 1
68476-30-2	89182	0.4	1.6	1.6	0.2	0.0	0.0	0.0	4.0	GE 1
68476-30-2	91673	0.3	9.6	4.8	0.0	0.2	0.5	1.0	12.6	GE 1
68476-30-2	92200	0.0	5.5	5.5	0.0	0.0	0.0	0.0	8.2	GE 1
DMGK	89164	0.0	1.1	0.7	0.1	0.0	0.0	0.0	0.8	LT 1
DMGK	89168	0.0	1.5	1.9	0.4	0.0	0.0	0.0	3.1	GE 1
DMGK	89171	0.2	3.3	0.9	0.0	0.0	0.0	0.0	1.4	GE 1
DMGK	89172	0.2	1.6	2.7	0.5	0.0	0.0	0.0	7.6	GE 1
DMGK	89173	0.4	2.1	2.1	0.5	0.0	0.0	0.0	8.4	GE 1
DMGK	89174	0.3	1.6	0.8	0.1	0.0	0.0	0.0	2.0	GE 1
DMGK	89176	0.4	2.4	2.4	0.6	0.0	0.0	0.0	6.5	GE 1
DMGK	89177	0.5	1.4	0.5	0.0	0.0	0.0	0.0	2.3	LT 1
DMGK	89178	0.4	2.6	1.3	0.2	0.0	0.0	0.0	2.7	GE 1
DMGK	89179	0.5	1.9	0.5	0.0	0.0	0.0	0.0	0.0	LT 1
DMGK	89183	0.8	2.5	4.2	1.7	0.1	0.0	0.0	9.3	GE 1
DMGK	89184	0.4	1.5	1.5	0.2	0.0	0.0	0.0	4.0	GE 1
DMGK	89185	0.1	0.7	0.1	0.0	0.0	0.0	0.0	0.7	LT 1
DMGK	89187	0.4	0.8	0.6	0.2	0.0	0.0	0.0	4.2	LT 1
<b>68915-97-9 Gas Oil, heavy</b>										
68915-97-9	86271	0.1	0.8	5.3	3.2	0.4	0.2	0.1	18.3	GE 1
68915-97-9	86190	0.3	3.6	1.0	0.1	0.2	0.0	0.0	2.0	GE 1

GE 1 = modeled MI greater than or equal to 1; predicts that the sample is mutagenic  
 LT 1 = modeled MI less than 1; predicts that the sample is not mutagenic  
 DMGK designation identifies distillate fuel oil samples tested in Germany for which CAS RNs are not available.

The results of the Optimized Ames assay confirm the likelihood that most Gas Oils can cause bacterial mutagenicity [MI ≥ 1.0]. The modeled MI determinations were generally in agreement with the test results. CAS RN 64741-59-9 catalytic cracked distillate samples which generally contain higher content of C1-C7 aromatic rings induced higher mutagenicity indices than other CAS RNs. A few samples under a given CAS RN may have very low MIs or be inactive as the result of different crude oil sources and the type and severity of processing.

#### 7.1.4 Genetic Toxicity *In Vivo*

**Table 22. Summary of In Vivo Genetic Toxicity Assays**

CAS RN	Assay/Species	Route/Dose	Results	Reference
<b>64741-59-9 Catalytic Cracked Distillate, light</b>				
API 83-07 [72.4% aromatic HC]	Chromosome Aberrations Rat [M.F.]	Intraperitoneal, single dose. 0, 0.3, 1.0, 3.0g/kg	Negative	API, 1986e
	Sister Chromatid Exchange Mice [M, F]	Intraperitoneal. 0, 340, 1700, 3400mg/kg	Positive at 1700, 3400mg/kg	API, 1985b
API 83-08 [60.8%aromatic HC]	Chromosome Aberrations Rat [M.F.]	Intraperitoneal, single dose. 0, 0.3, 1.0, 3.0g/kg	Negative	API, 1985b
<b>64742-46-7 Diesel No. 2</b>				
API 79-06 [76.1% saturated HC]	Chromosome Aberrations Rat [M.F]	Intraperitoneal, single dose. 0, 2400, 8000, 24000mg/kg	Positive at 8000, 24000mg/kg ma	API, 1978
	Dominant Lethal Mice [M.F]	Inhalation, 100, 400ppm 8 weeks to males, mated with untreated females at end of exposure	Negative	API, 1980e
Diesel No. 2	Micronucleus Mice [M, F]	Oral gavage, 1-3 days 0, 1.0, 2.5, 5.0g/kg	Negative	McKee et al., 1994
<b>68476-30-2</b> Home Heating Oil	Micronucleus Mice [M, F]	Oral gavage, 1-3 days 0, 1.0, 2.5, 5.0g/kg	Negative	McKee et al., 1994
<b>64741-82-8</b> Coker Light Gas Oil	Micronucleus Rat [M,F]	Dermal, 13 weeks, 0, 30, 125, 500, 2000mg/kg	Negative	Mobil, 1988c Study 61997
<b>68915-97-9</b> Heavy Atmospheric Gas Oil	Micronucleus Rat [M,F]	Dermal, 13 weeks, 0, 30, 125, 500mg/kg	Stat. significant at 125, 500 in females only	Mobil, 1990 Study 63457
<b>64741-49-7 Vacuum Tower Overheads</b>				
Vacuum Tower Overhead -T	Micronucleus Rat [M,F]	Dermal, 13 weeks, 0, 30, 125, 500mg/kg	Negative	Mobil, 1988a Study 62327

HC = hydrocarbons

In vivo studies evaluating cytogenetic damage of a selection of gas oils indicate that most of these substances do not induce chromosome damage or statistically significant increases in micronucleus formation in bone marrow of treated animals when administered orally, dermally or by inhalation, the most realistic routes of human exposure. Heavy atmospheric gas oil (CAS RN 68915-97-9) applied dermally for 13 weeks did cause increases in percent of micronucleated polychromatic erythrocytes in female rats based statistically on the total number polychromatic erythrocytes counted in all animals of each sex/group rather than using the animal [5/sex/group] as the investigative unit. The ANOVA results were negative. This occurrence in one sex only and the varying statistical outcomes raise questions about the biological relevance of this finding. Intraperitoneal administration, a severe route of exposure, of diesel Oil No. 2 (CAS RN 64742-46-7) resulted in chromosome damage but inhalation exposure of male mice in a dominant lethal study throughout the spermatogenic cycle did not cause adverse mutational effects on reproductive [failure to impregnate] and developmental activity [i.e. decreased number of fetuses] when males were mated to untreated females. The sister chromatid exchanges were induced by intraperitoneal treatment with a catalytic cracked distillate (CAS RN 64741-59-9; API 83-07), an indication of DNA perturbation. Most likely any

DNA lesions were repaired as no chromosome damage was reported at similar doses by the same route.

## **Conclusions**

Overall, the weight of evidence from studies for chromosome damage or micronucleus formation indicates that gas oils are generally not clastogenic in animals. This conclusion is further supported by extensive testing of other PAC category petroleum-derived streams (aromatic extracts, asphalt, crude oils and heavy fuel 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).

### **6.1.6. Developmental/Reproductive Toxicity**

#### **6.1.6.1, Developmental Toxicity**

Developmental toxicity studies are summarized below and listed in Table 23 where studies used in developing the PAC model are identified. Dermal irritation occurred in all studies to varying degrees and was not used in establishing LOAEL/NOAEL. Treatment at very high doses was sometimes terminated due to severe dermal irritation.

#### **CAS RN 64741-43-1 Gas Oil, Intermediate**

An intermediate gas oil, F-193 (CAS RN 64741-43-1, ATX 92-0011, ARCO, 1993b) was applied to the shaved backs of presumed pregnant rats at concentrations of 0, 50, 250 and 500mg/kg day from GD 0-19. Animals were sacrificed on GD20. Dose-related increases in skin irritation were observed. Decreased maternal body weights, weight gain and absolute and relative food consumption were seen at 250 and 500mg/kg groups. Average litter size, number of live fetuses and reduced fetal body weight were seen at 250 and 500mg/kg. At 500mg/kg statistically significant increased resorptions and increased number of dams with resorptions were observed with an increasing trend in resorptions seen in the 250mg/kg group. Other developmental parameters were unaffected by treatment. Fetal aberrations seen at 250 and 500mg/kg included eye malformations, non-dose related cleft palate, increased incidence of hydronephrosis and bifid thoracic vertebral centra. Umbilical hernia and delayed sternal ossification were seen at 500mg/kg. Delayed ossification was also reported at these doses. LOAEL maternal and developmental = 250mg/kg; NOAEL = 50mg/kg.

#### **64741-49-7 Vacuum Tower Condensates**

A Vacuum Tower Overheads sample [VTO, CAS RN 64741-49-7, #086270] was applied to the shaved backs of presumed pregnant rats at dose levels of 0, 30, 125, 500 and 1000mg/kg/day from GD0 – 19 and at a dose of 1000mg/kg/day from GD 10-12 to identify any effects obscured by fetal mortality from longer term exposure and for bioavailability determinations. (Mobil 1989b. study 62328). Animals were sacrificed on GD20. Postnatal groups treated with 0 or 500mg/kg day from GD0-15 were allowed to deliver and litters maintained LD0-4. This group was originally scheduled to be treated from GD 0-19. However treatment was discontinued after day 15 because of a high incidence of resorption noted, and an attempt to increase the in utero survival of offspring. GD 15 is also the last day of treatment in a standard EPA/FDA teratology

studies. Dose related skin irritation was seen at all doses. Vaginal bleeding, decreased body weight and food consumption, decreased thymus weight were seen at 500 and 1000mg/kg. Histologically thymus size was decreased at 125mg/kg and above. Differences in clinical chemistry parameters were seen at 500 and 1000mg/kg dams treated for GD0-19. For the GD 0-19 groups, treatment at 500 mg/kg/day and higher adversely affected the number and percent of dams with resorptions, the number of resorptions, and litter size. With the exception of litter size, no treatment related differences were noted in other parameters measured including number of pregnant females, duration of gestation, implantation sites, and number of litters with live born. None of the parameters evaluated at GD 10-12 at 1000mg/kg appeared to be adversely affected. Decreased fetal body weight and crown rump length at 500 and 1000mg/kg GD0-19 and increased incidence of soft tissue anomalies including lower spleen weight were observed. Increased urinary anomalies were seen in pups from dams exposed to 125mg/kg GD0-19. For the offspring of the postnatal group, no treatment-related differences were observed between the control and the VTO exposed groups for pup survival, pup body weight or male to female ratio. Maternal LOAEL = 500mg/kg [decreased thymus weights], NOAEL = 125mg/kg. Developmental LOAEL = 125mg/kg [based on urinary anomalies] NOAEL = 30mg/kg.

In the accompanying bioavailability study 5 rats were treated with 1000mg/kg VTO radiolabeled with <sup>14</sup>C-carbazole and <sup>3</sup>H-benzo(a)pyrene, applied within a protective chamber from GD10-12. 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, 51.2%% of <sup>14</sup>C-carbazole and 12.9% <sup>3</sup>H-benzo(a)pyrene was measured 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.

### **CAS RN 64741-59-9 Catalytic Cracked Distillate, Light**

A light cycle oil [LCO, CAS RN 64741-59-9, 79.8% aromatic hydrocarbons, sample # 08281] was applied to the shaved backs of presumed pregnant rats at dose levels of 0, 25, 50, 125, 250 and 500 mg/kg/day from GD0 – 19 (Mobil, 1988b, Study # 50511). At 1000mg/kg day, animals were treated either from GD0-6 or GD6-15 due to severe irritation observed at the onset of treatment. Gestation day 15 was chosen because it is the last day of treatment in a standard EPA/FDA teratology studies. All animals were sacrificed on GD20. In the dams, erythema and flaking of the skin were observed in all gas oil exposed groups. Skin effects were observed in all but the 25 mg/kg group. At doses greater than 25 mg/kg there was a decrease in maternal body weight and body weight gain compared to the controls, with an accompanying reduction in food consumption. There were no treatment-related findings at necropsy. Blood levels of triglycerides were increased in a dose-related manner in the 250, 500 and 1000 mg/kg groups. Fetal body weights were reduced in the 500 and 1000 mg/kg groups, with only the reduction in the 1000 mg/kg group being statistical significant. Resorptions were also increased in the 1000mg/kg GD6-15 group. There were no significant increases in resorptions at 500mg/kg or lower doses and soft tissue variations and malformations, and skeletal malformations in any of the dose groups. As identified by the investigators, maternal LOAEL = 50mg/kg based on decreased body weight, although statistical significance only occurred at the 250 mg/kg/day level and greater; NOAEL = 25mg/kg. Developmental LOAEL = 500mg/kg; NOAEL = 250mg/kg.

A different light cycle oil, F-213 [FCCU light cycle oil, CAS RN 64741-59-9] was applied to the shaved backs of presumed pregnant rats at dose levels of 0, 50, 333, and 1000mg/kg/day from GD0-20 (ARCO 1994a; ATX 91-0262). Litters were maintained to lactation day (LD) 4. One female died at GD20 in the 333mg/kg group. Dose related dermal irritation was observed in all groups. Treatment related decreased body weight and food consumption, vaginal discharge and increased gestation length was observed at 333 and 1000mg/kg groups. Animals delivering pups were 5/9 pregnant in 333mg/kg and 6/9 in 1000mg/kg compared to 11/11 and 15/15 in 50mg/kg groups and control group respectively. Lower total and live pups were seen at Lactation day 0 in the 333 and 1000mg/kg groups. Fewer pups survived to LD4 in the 333mg/kg group and decreased pup body weights were observed. In the 1000mg/kg group pup weights were higher at LD0 and 4 likely due to longer gestation and smaller litter sizes. LOAEL maternal and developmental = 333mg/kg; NOAEL = 50mg/kg

### **CAS RN 64741-82-8 Thermocracked Distillates, Light**

A light coker gas oil, light thermal cracked distillate sample [LCGO, CAS RN 64741-82-8, #087213] was applied to the shaved backs of presumed pregnant rats at dose levels of 0, 15, 60, from GD0 – 19, at 250mg/kg day from GD0-15 due to severe irritation [last treatment day in standard EPA/FDA teratology studies] and at a dose of 500mg/kg/day from GD 10-12 to identify any effects obscured by fetal mortality from longer term exposure, and for bioavailability determinations. (Mobil 1989c, study 61998). Animals were sacrificed on GD20. Postnatal groups treated with 0 or 60mg/kg day from GD0-15 were allowed to deliver and litters were maintained LD0-4. Moderate to severe skin irritation increased with increasing doses. Dams treated with 250 or 500mg/kg/day LCGO gained significantly less weight than controls and food consumption was lower during gestation. No reproductive parameters were adversely affected in GD0-19 groups or postnatal litters. Mean fetal body weight, crown rump length and pup growth were comparable to controls. No treatment related malformations, soft tissue or skeletal anomalies were observed. Maternal LOAEL = 250mg/kg; NOAEL = 60mg/kg. Developmental LOAEL >250mg/kg; NOAEL = 250mg/kg.

In the accompanying bioavailability study 5 rats were treated with 60mg/kg LCGO radiolabeled with <sup>14</sup>C-carbazole and <sup>3</sup>H-benzo(a)pyrene, applied within a protective chamber from GD10-12. Over 72 hours of exposure, dermal penetration of <sup>14</sup>C-carbazole occurred more extensively and rapidly than <sup>3</sup>H-benzo(a)pyrene in the dam and the amount of radiolabeled material was less than 0.01% in fetal tissue demonstrating 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.

Another light coker gas oil, F-199 [CAS RN 64741-82-8] was applied to the shaved backs of presumed pregnant rats at dose levels of 0, 50, and 100mg/kg/day from GD0-19 and at 250mg/kg/day from GD6-11 (ARCO 1993c; ATX 92-0013). Animals were sacrificed on GD20. Skin irritation to varying degrees occurred at all dose levels. Statistically significant incidences of vocalization were observed in animals in the 100 and 250mg/kg groups and in the previous pilot study as well. No significant decreases in body weights were seen but some decreases in weight gain occurred at various times throughout gestation at 100 and 250mg/kg. No adverse effects occurred on pregnancy incidence, duration of gestation or any reproductive parameters (corpora lutea incidence, implantation, litter size, resorptions, live fetuses, fetal body weight or sex ratio. No significant gross external, soft tissue or skeletal effects were seen. Maternal LOAEL = 100mg/kg; NOAEL = 50mg/kg. Developmental NOAEL > 100mg/kg for GD0-19 treatment and 250mg/kg for GD6-11 treatment LOAEL was not determined.

### **CAS RN 64741-86-2 Sweetened Distillate**

DHHS Stove oil, F-233 [CAS RN 64741-86-2] was applied to the shaved backs of presumed pregnant rats at dose levels of 0, 100, and 500mg/kg/day from GD0-20 and at 1000mg/kg/day from GD0-5 (ARCO 1994f; ATX 91-0133). Litters were maintained to lactation day (LD) 4. Dosage at 1000mg/kg was discontinued at GD 5 due to severe dermal irritation and vocalization of the rats and animals retained untreated on study through LD4. Dose related dermal irritation was seen at 100mg/kg and above. Absolute maternal body weight and/or body weight gains and food consumption were significantly lower at doses of 100mg/kg and above at different time intervals throughout the study. No treatment related adverse developmental effects were seen at any dose group. Maternal LOAEL = 100mg/kg; NOAEL not determined, <100mg/kg. Developmental NOAEL = 500mg/kg, highest dose group treated from GD0-20.

### **CAS RN 68334-30-5 Diesel Oils, C9-20**

A straight run diesel oil, F-195 [SRDO, CAS RN 68334-30-5] was applied to the shaved backs of presumed pregnant rats at dose levels of 0, 50, 150, and 300mg/kg/day from GD0-19 (ARCO 1993d; ATX 92-0156). Animals were sacrificed on GD20. Dose related dermal irritation was seen at all doses and vocalization occurred in rats of 150 and 300mg/kg groups. Maternal body weight gains were reduced at 150 and 300mg/kg various times intervals throughout gestation although absolute body weights were not significantly different from controls in any dose group. Food consumption was decreased at 300mg/kg/day. No significant treatment-related adverse effects or soft tissue or skeletal malformation/anomalies were observed in this study. Maternal LOAEL = 150mg/kg; NOAEL = 50mg/kg. Developmental NOAEL = 300mg/kg, highest dose tested

In another study, F-195 [SRDO, CAS RN 68334-30-5] was applied to the shaved backs of presumed pregnant rats at dose levels of 0, 125, and 250mg/kg day from GD0-20 and at 1000mg/kg/day from GD6-11 (ARCO 1994c; ATX 91-0129). Litters were maintained to lactation day (LD) 4. Dosing adjustment at 1000mg/kg was based on a previous study [data not shown] indicating severe irritation and poor mating performance. Despite short duration of treatment, litters from the 1000mg/kg group were maintained to LD 4. Dose related skin irritation was observed at all dose levels. Decreased maternal body weight, body weight gains and food consumption was seen at 250 and 1000mg/kg. For all dose groups, there were no significant differences in gestation length, number of implantation sites, external pup alterations, proportion of pups dead on lactation day 0, proportion of pups surviving to lactation day 4, or the proportion of males on lactation day 0. Pup body weights were significantly lower ( $p < 0.01$ ) at a dose of 250 mg/kg/day on lactation Days 0 and 4. There were no effects on pup body weights at doses of 125 and 1000 mg/kg/day. LOAEL maternal and developmental = 250mg/kg; NOAEL = 125mg/kg.

Results of these two studies indicate that maintenance of pregnancy, delivery and survival of fetuses/pups were comparable but that growth of offspring to lactation day 4 appeared somewhat affected by *in utero* exposure to SRDO.

### **CAS RN 68915-97-9 Gas Oil, Heavy**

Heavy atmospheric gas oil [CAS RN 68915-97-9, Sample #086271] was applied daily to the shaved backs of presumed-pregnant rats at concentrations of 0, 8, 30, 125 and 500 mg/kg/day from GD 0-19 (Mobil, 1991b, Study # 64146). Animals were sacrificed on GD20. Signs of maternal toxicity included decreased body weights, body weight gain, food consumption, thymus weights (absolute & relative), increased liver weights (relative), and changes in 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 discharge in high dose rats was considered compound related. The significance of 2 rats with vaginal discharge in 125mg/k group is questionable as similar incidence is seen in untreated control rats in this laboratory. Evaluation of reproductive parameters in the 8 and 30 mg/kg found no compound-related effects. Statistically non-significant 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 pups 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, sternbrae, 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. LOEL maternal and developmental = 125mg/kg; NOAEL = 30mg/kg.

#### **Supplemental data: Inhalation study**

##### **CAS RN 68476-34-6 Diesel Fuel, Market place sample**

A developmental toxicity study has been reported on a diesel fuel consisting of 76.1% saturated hydrocarbons (API, 1979b). Groups of presumed-pregnant Sprague-Dawley rats were exposed to nominal atmospheric concentrations of 100 and 400 ppm for 6 hours each day from GD6-15. On day 20 all the animals were sacrificed. One third of the fetuses were fixed for soft tissue examination. The remaining fetuses were examined for skeletal abnormalities. There were no deaths during the study and all animals were normal in appearance throughout. The 400 ppm maternal group had a reduced food intake during days 7-15 of gestation. No treatment-related differences were found in a variety of parameters, including sex ratios of the fetuses, number of implantation sites, resorptions, and live fetuses. With the exception of subcutaneous hematomas that occurred at a higher rate in the test article exposure groups, there were no test article-related abnormalities found in either the soft tissues or skeletons of the fetuses. Developmental NOAEL = 400ppm.

#### **Conclusions**

The substances tested in the Gas Oil Category for which treatment began with the onset of presumed pregnancy (Gestation day 0) had developmental LOELs ranging from 125 – 500mg/kg and NOAELs from 30 – 500mg/kg, attributed primarily to fewer live fetuses or pup per litter at delivery and lower fetal or pup body weight at delivery or Lactation days 0-4. Fetal malformations were reported for CAS RN 64741-43-1 [F-192] and CAS RN 64741-49-7 [Vacuum Tower Overheads]. Developmental toxicity was seen only at doses that were maternally toxic [except for VTO urinary anomalies] expressed as decreased body weights and weight gain, and decreased food consumption, making it difficult to determine whether effects were directly induced by the test material or resulted from maternal stress. Some gas oils showed no developmental toxicity at the highest doses tested even in the presence of maternal

toxicity [two coker gas oils, a sweetened distillate and a straight run diesel oil (treated GD0-19)]. These results contribute to the wide range of of NOAELs in this data set.

There are three studies in which females were treated from 7 days pre-mating through mating and gestation, with litters maintained untreated until LD4 [CAS RN 64741-43-1, F-193; CAS RN 64741-82-8, F-199, F-277] that are discussed in Section 7.1.6.2 Reproductive toxicity. Two of the materials F-199 and F-193 showed developmental and maternal toxicity at 250-259mg/kg, NOAEL = 1.0mg/kg respectively while F-277 had a NOAEL = 50mg/kg, a maternally toxic dose. Only F-277 had an intermediate dose between 250 and 1.0mg/kg making the dose range from the other studies too wide to use in setting the category developmental NOAEL. [see Table 21]

**Table 23. Developmental Toxicity Studies of Gas Oils in Sprague Dawley Rats by the Dermal Route of Exposure**

CAS RN	Sex /Duration	Dose mg/kg/day	Results	References
<b>64741-43-1 Gas Oil, Intermediate</b>				
<b>F-193</b> [sample # 091646]	Presumed pregnant, (25/group) Treated GD0-19, Sacrificed GD20	0, 50, 250, 500	Decreased maternal body weight, weight gain, food consumption. Decreased fetal body weight, embryo/fetal viability, soft tissue, skeletal alterations LOAEL maternal/developmental = 250mg/kg NOAEL maternal/developmental = 50mg/kg	ARCO, 1993b ATX 92-0011 Used in PAC Model <sup>a</sup>
<b>F-193</b> [sample # 091646] See Section 7.1.6.2 Reproductive toxicity	Females (15/group treated; 20 controls) Treated 7 days pre mating, mating, GD0-20. Litters maintained LD0-4	0, 1.0, 259, 1036	Decreased maternal body weights, weight gains, food consumption. No adverse effects on mating, pregnancy, delivery of implantation. At 1036mg/kg, 2/9 delivered and total and live pups decreased at LD0. Pup body weights decreased in 259mg/kg and 1036groups at LD0 and LD4. LOAEL maternal and developmental = 259mg/kg; NOAEL maternal and developmental = 1.0mg/kg	ARCO 1994b, ATX 91-0127
<b>64741-49-7 Vacuum Tower Condensates</b>				
<b>Vacuum Tower Overheads</b> [sample # 86270]	Presumed pregnant, (10/group) Treated GD0-19, Sacrificed GD20	0, 30, 125, 500, 1000 for GD0-19; 1000mg/kg GD10-12 0, 500mg/kg GD0-15, litters maintained LD0-4	Decreased maternal body weight, food consumption, vaginal bleeding , decreased thymus weight and Clinical chemistry and Hematology changes at 500, 1000mg/kg Decreased thymus size at greater than 125mg/kg. At 500mg/kg and above, increased number and % of dams with resorptions, number of resorptions, decreased litter size, fetal body weight and length, increased soft tissue anomalies. Increased urinary anomalies at 125mg/kg. Maternal LOAEL = 500mg/kg; NOAEL = 125mg/kg Developmental LOAEL = 125mg/kg; NOAEL = 30mg/kg	Mobil , 1989b Study # 62328 Used in PAC Model <sup>a</sup>
<b>64741-59-9 Catalytic Cracked Distillate, Light</b>				
<b>Light Cycle Oil</b> [sample #08281]	Presumed pregnant, (10/goup) Treated GD0-19, Sacrificed GD20	0, 25, 50, 125, 250, 500 1000mg/kg GD0-6 or GD6-15 (5/subgroup) due to dermal irritation	Decreased maternal body weight, weight gain and food consumption at 50mg/kg and above. Triglycerides increased at 250 and above. Fetal body weight decreased at 500, 1000; resorptions at 1000mg/kg GD6-15; No other adverse developmental effects. LOAEL maternal = 50mg/kg; NOAEL = 25mg/kg LOAEL developmental = 500mg/kg; NOAEL = 250mg/kg	Mobil 1988b Study # 50511 Used in PAC Model <sup>a</sup>

CAS RN	Sex /Duration	Dose mg/kg/day	Results	References
<b>F-213 [FCCU light cycle oil]</b> [sample # 091679]	Presumed pregnant, (12/treated group, 15 controls) Treated GD0-20 Litters maintained to LD 4	0, 50, 333, 1000	Increased gestation length, vaginal discharge, decreased maternal body weight, weight gain and food consumption. Decreased total and live pups/litter, number of litters with live pups, decreased pup body weight on LD0, 4 and decreased pup survival at LD4 LOAEL maternal/developmental = 333mg/kg NOAEL maternal/developmental = 50mg/kg	ARCO, 1994a ATX 91-0262
<b>64741-82-8 Thermocracked Distillates, Light</b>				
<b>Light coker gas oil</b> [sample # 087213]	Presumed pregnant, (10/group) Treated GD0-19, Sacrificed GD20	0, 15, 60, GD0-19; 250mg/kg GD0-15; 500mg/kg GD10-12 0, 60mg/kg GD0-15 litters maintained to LD4	Decreased maternal body weight, weight gain, food consumption. No adverse developmental effects at any dose. Maternal LOAEL = 250mg/kg; NOAEL = 60mg/kg Developmental NOAEL = 250mg/kg	Mobil 1989c Study # 61998 Used in PAC Model <sup>a</sup>
<b>F-199</b> [sample # 091652]	Presumed pregnant (25/group) Treated GD0-19, Sacrificed GD20	0, 50, 100 GD0-19; 250mg/kg GD6-11	Decreased maternal body weight gain, increased vocalization at 100mg/kg and above. No adverse developmental effects. Maternal LOAEL = 100mg/kg; NOAEL =50mg/kg Developmental NOAEL > 100mg/kg [GD0-19] Developmental NOAEL = 250mg/kg [GD6-11]	ARCO 1993c ATX 92-0013 Used in PAC Model <sup>a</sup>
<b>F-199</b> [sample # 091652] See Section 7.1.6.2 Reproductive toxicity	Females (15/ treated group, 20 controls) Treated 7 days pre mating, mating, GD0-20 Litters maintained LD0-4	0, 1.0 pre mating to GD20; 250mg/kg pre mating to GD8-11, 1000mg/kg pre mating days -7 to mating day 4, sacrificed day 5 due to dermal irritation	Decreased maternal body weight, weight gain, food consumption at 250 and 1000mg/kg. Decreased number of implantation sites and decrease in total and live pup numbers on day 0; pup survival and weight comparable at LD4. [dosing at 250mg/kg ended at GD8-11] LOAEL maternal/developmental = 250mg/kg NOAEL maternal/developmental = 1.0mg/kg	ARCO 1994d ATX 91-0133
<b>F-277</b> [sample # 094628] See Section 7.1.6.2 Reproductive toxicity	Females (15/ treated group, 12 controls) Treated 7 days pre mating, mating, GD0-20 Litters maintained LD0-4	0, 1.0, 50, 250	Changes in maternal body weight and weight gain at 250mg/kg and food consumption at 50 and 250mg/kg. Decreased pup body weight on LD0 and 4 at 250mg/kg. Maternal LOAEL = 50mg/kg; NOAEL =1.0mg/kg Developmental LOAEL = 250mg/kg; NOAEL = 50mg/kg	ARCO 1994e ATX 93-0075
<b>64741-86-2 Sweetened Distillate</b>				
<b>F-233 DHHS Stove Oil</b>	Presumed pregnant,	0, 100, 500	Decreased maternal body weight, weight gain, food	ARCO 1994f

CAS RN	Sex /Duration	Dose mg/kg/day	Results	References
[sample # 094629]	(12/treated group, 15 controls) Treated GD0-20 Litters maintained to LD 4	1000mg/kg GD0-5 due to vocalization, severe irritation	consumption at 100mg/kg and above. No developmental effects seen up to 500mg/kg. 1000mg/kg group not considered since dosing ended at GD5 although maintained to LD4 Maternal LOAEL = 100mg/kg; NOAEL not determined, <100mg/kg Developmental NOAEL = 500mg/kg [highest dose to GD20]	ATX 91-0133
<b>68334-30-5 Diesel Oils</b>				
<b>F-195 straight run diesel oil</b> [sample # 091648]	Presumed pregnant (25/group) Treated GD0-19, Sacrificed GD20	0, 50, 150, 300	Decreased maternal body weight gains, vocalization at 150 and 300mg/kg. Decreased food consumption at 300mg/kg. No adverse developmental effects Maternal LOAEL = 150mg/kg; NOAEL = 50mg/kg Developmental NOAEL = 300mg/kg [highest dose tested]	ARCO, 1993d ATX 92-0156 Used in PAC Model <sup>a</sup>
<b>F-195 straight run diesel oil</b> [sample # 091648]	Presumed pregnant, (14-15/treated group, 19 controls) Treated GD0-20 Litters maintained to LD 4	0, 125, 250 1000mg/kg GD 5-9	Decreased maternal body weight, weight gain and food consumption at 250, 1000mg/kg. No adverse developmental effects except decreased pup body weight on LD0 and 4 at 250mg/kg. LOAEL maternal/developmental = 250mg/kg NOAEL maternal/developmental = 125mg/kg	ARCO 1994c ATX 91-0129
<b>68915-97-9 Gas Oil, Heavy</b>				
<b>Heavy Atmospheric Gas oil</b> [sample # 086271]	Presumed pregnant, (12/group) 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. LOAEL maternal/developmental = 125mg/kg NOAEL maternal/developmental = 30mg/kg	Mobil, 1991b Study 64146 Used in PAC Model <sup>a</sup>

a- Only developmental studies with treatment for GD0-19 and sacrifice at GD20 were used for PAC modeling activities [see Appendix D].

Statistical models will be 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 is being developed using only animal studies with treatment for GD0-19 days and sacrifice at GD20. Sensitive endpoints for developmental toxicity are fetal body weight, number of live fetuses per litter and resorptions per implantations. Maternal thymus weight was included as a biomarker of exposure but has not been used in identifying the sample PDR<sub>10</sub>. For most gas oil samples the most sensitive endpoints were fetal body weight and live fetuses per litter. Results of modeling will be presented in Table 24.

Table 25 will presents CAS RN samples in order of average developmental PDR<sub>10</sub> values organized by severity of effects from lowest PDR<sub>10</sub> to highest.

**Table 24. Developmental Toxicity PDR<sub>10</sub> and BMD<sub>10</sub> for Gas Oils by Endpoint**

CAS RN/ Sample No.	PDR <sub>10</sub> or BMD <sub>10</sub> mg/kg/day				Sample PDR <sub>10</sub> mg/kg/day [Endpoint]	Sample BMD <sub>10</sub> mg/kg/day [Endpoint]
	Maternal Thymus Wt PDR <sub>10</sub> <sup>a</sup>	Fetal body weight PDR <sub>10</sub>	Live fetus per litter PDR <sub>10</sub>	Resorption s/Implants PDR <sub>10</sub>		
Example	56	250	65	110	65 [live fetuses]	75
This is an interim Category Assessment Document without modeled data included. The modeled PDR <sub>10</sub> and BMD <sub>10</sub> values will be available in a subsequent version.						

**Table 25. Modeled Developmental Toxicity PDR<sub>10</sub> Values from Most to Least Severe**

CAS RN	Sample No.	Develop PDR <sub>10</sub> mg/kg	ARC 1 <sup>2</sup> (%)	ARC 2 (%)	ARC 3 (%)	ARC 4 (%)	ARC 5 (%)	ARC 6 (%)	≥ARC 7 (%)
1234-56-7	Example	45	0.0	0.7	10.0	30.0	20.0	6.0	0.0
This is an interim Category Assessment Document without modeled data included. The modeled PDR <sub>10</sub> values will be available in a subsequent version.									

### 6.1.6.2 Reproductive Toxicity

Information on the reproductive effects of gas oils is provided from studies in which female rats were treated dermally for 7 days pre-mating, through mating and gestation to gestation day 20 [GD20] conducted on a sample of CAS RN 64741-43-1 Straight run gas oil [F-193] and 2 samples of CAS RN 64741-82-8 light cycle oil [F-199, F-277] also listed in Table 23.

#### **CAS RN 64741-43-1 Straight Run Gas Oils**

Test article F-193, (CAS RN 64741-43-1, ATX 91-0127 ARCO, 1994b) 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, 1.0 259 and 1036 mg/kg/day. Females were mated to untreated males. Litters were maintained to lactation day (LD) 4. One death occurred at 1036mg/kg on

LD 1. Dose-related vaginal discharge, decreased maternal body weight and weight gain and food consumption and some skin irritation were reported in 259 and 1036mg/kg groups. At 1036mg/kg only 2/9 pregnant females delivered, total and live pups were decreased at delivery; surviving pup body weights were decreased at LD0 and LD4. No adverse effects were seen on mating capability, gestation length, delivery or number of implantation sites. At 259mg/kg pup body weights were decreased on LD1 and LD4. No adverse effects were seen on proportion of surviving pups at LD4 or male/female pup ratio. LOAEL maternal and developmental = 259mg/kg; NOAEL maternal and developmental = 1.0mg/kg.

### **CAS RN 64741-82-8 Light Cycle Oils**

Test article F-199, Light thermal cracked distillate (CAS RN 64741-82-8, ATX 91-0133 ARCO, 1994d) 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, 1.0 mg/kg/day, from pre-mating day 7 through GD 8-11 at 250mg/kg/day and from pre-mating day 7 to mating day 4 at 1000mg/kg/day. Females were mated to untreated males. Surviving litters were maintained to lactation day (LD) 4. One female in the 1000mg/kg group died after 1 night of mating and all other females in this group were killed on mating day 5 due to severe skin irritation. Slight to severe skin irritation was observed in the 250mg/kg group resulting in termination of treatment at GD 8 -11 and maintenance of the untreated animals and litters to LD4. Decreased body weight, weight gain and changes in food consumption were observed in the 250 and 1000mg/kg groups. No adverse effects were seen on mating capability, initiation of pregnancy, pup survival to LD4, ratio of male to female pups or appearance of gross malformations were seen at 1.0 or 250mg/kg. Despite termination of test material administration at GD8-11 females in the 250mg/kg group had fewer mean implantation sites and fewer total pups or live pups/litter on LD0. LOAEL maternal and developmental = 250mg/kg; NOAEL maternal and developmental = 1.0mg/kg.

Test article F-277, Light coker gas oil (CAS RN 64741-82-8, ATX 93-0075 ARCO, 1994e) 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, 1.0, 50 and 250mg/kg/day. Females were mated to untreated males. Litters were maintained to lactation day (LD) 4. Dose related increases in skin irritation were observed. Maternal body weights were lower at 250mg/kg from the last day of pre-mating through LD 4 and body weight gain was lower pre-mating to GD 4, comparable through the remainder of gestation and higher than controls at LD0-4. Changes in relative food consumption at 50 and 250mg/kg were considered treatment related and used to establish the maternal LOAEL. No treatment related effects were seen on reproductive parameters, number of litters, total number of pups or live pups/litter on LD0, ratio of male pups or malformations. Average pup body weight was lower than controls at LD0 and 4 in the 250mg/kg group. Maternal LOAEL = 50mg/kg; NOAEL = 1.0mg/kg. Developmental LOAEL = 250mg/kg; NOAEL = 50mg/kg.

The reproductive toxicity potential of gas 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 as outlined in the EPA HPV guidance document.

### **Conclusions**

Reproductive parameters in developmental toxicity studies addressing fertility, successful insemination and implantation demonstrate that in general these endpoints are not adversely

affected by treatment with gas 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 at doses ranging up to 500-820mg/kg/day.

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 several gas oils did not adversely affect mating and establishment of pregnancy but did affect successful completion of pregnancy and pup viability to varying degrees at maternally toxic doses of 250mg/kg and above. Only F-277 had an intermediate dose level between 250 and 1.0mg/kg allowing a NOAEL determination of 50mg/kg for that substance, falling within the range of developmental NOAELs. 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

## **6.2 Health Effects - Other**

### **6.2.1 Carcinogenicity**

In addition to the studies discussed above, a number of dermal carcinogenicity studies have been performed on gas oils and distillate fuels. Although carcinogenicity is not a required endpoint of the HPV program, these results are provided to complete the profile of gas oil toxicity. These studies have been fully summarized and reviewed elsewhere (ATSDR, 1995; CONCAWE, 1996; IARC, 1988). The general conclusions that can be drawn from the animal carcinogenicity studies are:

- Gas oils and distillate fuels are potential skin carcinogens after repeated skin application.
- When applied repeatedly to the skin, carcinogenic gas oils and distillate fuels are associated only with skin tumors and not with an increase in non-metastatic systemic tumors (Freeman and McKee, 1993).
- The skin carcinogenicity of the petroleum streams with high boiling ranges and PAC content correlates with 3-7 ring PAC distribution.
- Skin tumors produced by materials containing low or no PAC is likely due to a non-genotoxic promotion effect and only observed in the presence of sustained severe skin irritation (Nessel et al., 1998).

### **Gas Oils Streams**

- **Streams Composed Predominantly of Aromatic Hydrocarbons**

A cracked gas oil, CAS RN 64741-59-9 (69.7% aromatic hydrocarbons) was applied to the skins of male C3H mice 2, 4 or 7 days/week for 104 weeks (Exxon, 1996a, Nessel et al., 1988). The test material was applied either undiluted or at 50% or 28.5% dilutions in mineral oil. The concentration and dosing frequencies were adjusted to ensure that each animal received the same total weekly dose of test material irrespective of dosing frequency. Thus, the 100% animals were dosed 2x/week, while the 50% and 28.5% groups were dosed 4x/week and 7x/week respectively. Survival was less in the treated groups compared to the negative controls; at the lower two concentrations (28.5 and 50 %) the difference was statistically significant. Dermal irritation occurred in the groups exposed to the gas oil, scores ranging from 0.0 to 4.0. There were no other treatment-related clinical findings. Treatment related findings at

post mortem were limited to dermal irritation. A variety of skin tumors developed in the positive control and gas oil treated groups. Tumor types found included squamous cell carcinomas, fibrosarcomas, melanoma (only 1 treated animal) and papillomas.

Two samples of gas oils with a high aromatic content (48.3% & 55.1% aromatic hydrocarbons) have been tested in an initiation-promotion assay in male CD-1 mice (DGMK, 1993; Jungen et al., 1995). Animal survival was not affected by exposure to the gas oil samples. During both the initiation and promotion phases, the gas oil samples caused slight to moderate skin irritation which was found to be reversible. There were no other treatment-related clinical findings. Of the two samples, both appeared to have weak initiating potentials, while only one showed a weak promoting effect.

- **Streams Composed Predominantly of Saturated Hydrocarbons**

A straight run, hydrotreated gas oil CAS RN 64742-54-7 (73.8% saturated hydrocarbons) was applied to the skins of male C3H mice 2, 4 or 7 days/week for 104 weeks (Exxon, 1996a). The test material was applied either undiluted or at 50% or 28.5% dilutions in mineral oil. The concentration and dosing frequencies were adjusted to ensure that each animal received the same total weekly dose of test material irrespective of dosing frequency. Thus, the 100% animals were dosed 2x /week, while the 50% and 28.5% groups were dosed 4x/week and 7x/week respectively. Survival figures of the gas oil treated groups were comparable to that seen in the negative control group. Dermal irritation scores in the gas oil groups ranged from 0.0 to 4.0. There were no other treatment-related clinical findings. Dermal irritation was the only treatment-related finding at post mortem. A variety of skin tumors developed in the positive control and the 100% and 28.5% gas oil groups. The tumor incidence was highest in the group in which skin irritation was greatest. The incidence of the tumors in the gas oil groups was much lower than that seen in the study of a cracked gas oil described above.

Three gas oils with high saturated hydrocarbon contents (57.5% - 76.4%) have been tested in an initiation-promotion assay in male CD-1 mice (DGMK, 1993). Animal survival was not affected by exposure to the gas oil samples. During both the initiation and promotion phases, two of the three gas oil samples caused reversible, slight to moderate skin irritation. There were no other treatment-related clinical findings. Of the three samples, two appeared to have weak, if any initiating potentials and one had a very weak, if any promoting potential.

### ***Distillate Fuels***

A dermal carcinogenicity study of a diesel fuel (saturate content unknown) in C3H mice has been reported by IITRI (IITRI, 1985). Over the lifetime of the animals, 50µl of undiluted test material was applied 2x /week to the shaved backs of male mice. There was a significant increase in the incidence of malignant skin tumors (squamous cell carcinoma or fibrosarcoma) in the treated mice compared to the controls. Other lesions of the treated skin included sloughing of the skin and lesions resembling infection, both of which were seen more frequently in the treated animals.

A sample of a diesel fuel (76.6% saturated hydrocarbons) has been tested in an initiation-promotion assay in male CD-1 mice (DGMK, 1993). Animal survival was not affected by exposure to the diesel fuel. The study's authors concluded that the diesel fuel sample might be a promoter.

### 6.3 Assessment Summary for Human Health Effects

Gas Oil streams and distillate fuels demonstrated minimal acute toxicity by the oral dermal and inhalation routes, minimal eye irritation, moderate to severe skin irritation with 24 hours exposure, and no dermal sensitization.

*In vitro* genetic toxicity studies demonstrate that representative gas oil streams and distillate fuels generally induce gene mutation in bacterial and some streams are also active in mouse lymphoma tests. In addition to the standard Ames Test (Ames et al, 1975), the Optimized Ames test (previously the Modified Ames test) confirms that most Gas Oils cause bacterial mutagenicity. Results of *in vivo* studies evaluating chromosome damage or micronucleus formation in bone marrow cells indicate that gas oils are generally not clastogenic in laboratory animals.

The 13-week rat dermal studies on gas oil streams indicate LOAEL of 125mg/kg and NOAEL of 25-30mg/kg with the exception of a light coker gas oil with a LOAEL of 30mg/kg, the lowest dose tested, effects likely exacerbated by severe skin irritation at all dose levels. Skin irritation in the other studies generally ranged from slight to moderate. Effects in all studies when present were seen primarily on liver, thymus weights and hematologic endpoints. The 4 week duration rat dermal studies showed slight to moderate skin irritation and minimal systemic toxicity with NOAEL = 400-800mg/kg. No significant adverse effects were seen in reproductive organs in any rat dermal study.

Substances tested in the Gas Oil Category had developmental LOAEL ranging from 125 – 500mg/kg and NOAELs from 30 – 500mg/kg attributed primarily to fewer live fetuses or pups per litter at delivery and lower fetal or pup body weight at delivery or Lactation days 0-4, respectively seen only at doses that were maternally toxic. Fetal malformations were reported for 2 members of the category, CAS RN 64741-43-1 [F-192, intermediate gas oil] and CAS RN 64741-49-7 [Vacuum Tower Overheads]. Some gas oils showed no developmental toxicity at the highest doses tested even in the presence of maternal toxicity. These results contribute to the wide range of of NOAELs in this data set.

Reproductive parameters in developmental toxicity studies addressing fertility, successful insemination and implantation demonstrate that in general these endpoints are not adversely affected by treatment with gas oil streams. Evaluation of reproductive organs and sperm morphology and motility in repeated dose studies consistently demonstrated no adverse effects on ovary or testes weights or abnormal histopathology or effects on sperm at doses ranging up to 500-820mg/kg/day. In three studies in which females were treated for a week prior to mating through mating and gestation to GD20, exposure to maternally toxic concentrations of 250mg/kg did not adversely affect mating and establishment of pregnancy but did adversely affect successful completion of pregnancy and pup viability. Only one sample, F-277 had an intermediate dose level between 250 and 1.0mg/kg allowing a NOAEL determination of 50mg/kg based on average pup weight, falling within the range of developmental NOAELs. 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.

Dermal carcinogenicity studies indicate that Gas oils and distillate fuels are potential skin carcinogens after repeated skin application but are not associated with the induction of systemic

tumors. The skin carcinogenicity of the petroleum streams with high boiling ranges has been demonstrated to correlate with 3-7 ring PAC content. Skin tumors produced by substances in this category containing low or no PAC are likely due to a non-genotoxic promotion effect and only observed in the presence of sustained severe skin irritation.

## **7. HUMAN EXPOSURE SUMMARY**

Because the No. 2 distillate fuels have widespread use in transportation and industrial and residential heating applications, both occupational and consumer exposures are possible. Exposure to children is not anticipated. The other substances in the Gas Oil Category are only used in industrial applications.

Very limited information on human exposure to substances in the Gas Oil Category is available in the literature. Dermal exposure is the principle route of exposure because of the low vapor pressure of these substances. A significant effort to develop human exposure data was conducted and published by the European trade association, CONCAWE (CONCAWE, 2006).

Information on levels of human exposure resulting from the manufacturing, distribution and use of gas oils and blending components was developed for the CONCAWE report. Technical guidance for the collection of exposure information to support EU risk assessment was followed, including direct measurement of exposure levels and indirect, modelling approaches. Exposure estimates were developed for workers and for consumers, but not for the general public. Inhalation exposure data were retrieved and collated from member companies and open literature, and supplemented with new measurements from a dedicated monitoring campaign. Dermal exposure levels were estimated using a simple modelling approach. The collection and collation of exposure information for gas oils vapour from CONCAWE member companies confirmed that worker exposure by inhalation is generally well below the exposure limit of 100 mg/m<sup>3</sup> recommended by the American Conference of Governmental Industrial Hygienists (ACGIH); that a wide range of control measures are in place; and that occurrences of elevated exposure appear to be infrequent. Exposures are often simultaneous with other petroleum products, in particular gasoline, making it difficult to characterise those originating from gas oils alone. Inhalation and dermal exposures were estimated to be of the same order of magnitude.

CONCAWE reported conservative estimates of consumer exposure resulting from car refuelling with automotive diesel were 1 milligram per day via inhalation and 21 milligram per day as dermal exposure per refuelling event. The inhalation estimate was based on measured data, whereas the dermal estimate was derived through modelling. Consumer exposure estimates were considerably lower than worker exposure estimates.

For worker exposures, 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 US laws and regulations are in place to limit occupational exposure and environmental release of Gas Oil substances and distillate fuel 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

## 8. CATEGORY ANALYSIS CONCLUSIONS

The Gas Oil Category includes 28 members comprised of 4 finished products (distillate fuels) and 24 refinery streams with similar carbon ranges. The category members are complex substances, containing variable amounts of alkanes, cycloalkanes, olefins, and aromatics. The saturated and aromatic hydrocarbon content of the category members form a continuum from high saturate content to high aromatic content. In comparison to gas oil refinery streams and fuel oil No. 4 which do not have product specification and can contain a range of 1-7 ring polyaromatic compounds (PAC), Fuel Oil No. 2 and the ultralow sulfur diesel (ULSD) fuels must meet stringent ASTM and EPA standards for commercialization. The boiling point specifications for these fuels essentially limit the aromatics to 1, 2, 3-ring compounds with minimal if any 4-ring PACs. Key parameters when analyzing this category for environmental hazards are the distribution of aromatic and saturated hydrocarbons, and for some mammalian endpoints (repeated-dose, developmental, and mutagenic) the content and distribution of 1-7 ring PAC are significant.

**Physical-Chemical Properties:** Gas oils are variable and complex substances of hydrocarbons, predominantly having carbon chains from C<sub>9</sub> to C<sub>30</sub>, and boiling over the

temperature range of 150°C to 450°C. Vapor pressures are within a measurable range, with values of 0.4 kPa and 2 kPa being reported. Partition coefficients of constituent hydrocarbons range from 3.3 to >6. Water solubility values for these substances have been reported from 2.0 mg/L to 8.7 mg/L for dissolved hydrocarbons

**Environmental Fate:** If gas oils are released to the environment, individual components will disperse and partition according to their individual physical-chemical properties. Their final dispositions are shaped by both abiotic and biotic processes. Based on modeling individual structures encompassing the different types and molecular weights of hydrocarbons, volatilization to the atmosphere is an important process for the low molecular weight fractions. Residence times in the atmosphere are relatively short due to indirect photodegradation reactions. In water, hydrolysis is not likely to occur, as the chemical linkages of hydrocarbons do not allow for these reactions. Components in gas oils will biodegrade, and moderate to rapid rates of biodegradation were measured in standard tests. Gas oils are considered to be inherently biodegradable, and for some individual gas oil samples, biodegradation rates may be high enough to achieve ready biodegradability classification.

**Environmental Effects:** This area includes acute and chronic toxicity to fish and aquatic invertebrates (i.e. daphnids) and toxicity to aquatic plants (i.e. algae) expressed as growth inhibition. Testing of commercial distillate fuels used for heating and transportation (e.g., No. 2 fuel oil and diesel fuel) using water accommodated fractions of the gas oils show moderate toxicity to aquatic life. LL<sub>50</sub> values for fish ranged from 3.2 to 65 mg/L and EL<sub>50</sub> values for invertebrates ranged from 2.0 to 210 mg/L. EL<sub>50</sub> values for inhibition of algal growth rate and biomass ranged from 1.9 to 78 mg/L. While there were no obvious differences in the acute toxicity between fish and daphnids to the substances that were tested, daphnids appeared to show a greater sensitivity compared to fish for chronic toxicity. While the data was limited to one test substance and one test per species, the NOELR for fish (1.2 mg/L) compared to daphnids (0.15 mg/L) suggests a sizeable difference in the chronic toxicity to gas oils for these two species.

**Human Health Effects:** .

Gas Oil streams and fuels induce minimal acute toxicity by the oral, dermal and inhalation routes. Moderate to severe skin irritation has been reported with 24 hour exposure which is likely to be mild to moderate under 4 hour exposure conditions recommended for classification purposes. No dermal sensitization has been reported. Eye irritation was minimal to slight.

Representative gas oil streams and distillate fuels generally induce gene mutation in bacterial and mammalian cells as demonstrated in both standard *in vitro* assays and the Optimized Ames Test. Overall, the weight of evidence from studies for chromosome aberrations or micronucleus formation indicate that gas oils generally do not cause cytogenetic damage in animals

Repeated dose 13-week rat dermal studies on gas oil streams indicate LOAEL values of 125mg/kg and NOAEL of 25-30mg/kg with the exception of a light coker gas oil (CAS RN 64741-82-8 sample 87213) with a LOAEL of 30mg/kg, the lowest dose tested, effects likely exacerbated by severe skin irritation at all dose levels. Skin irritation in the other studies generally ranged from slight to moderate. In all studies effects were seen primarily on liver and thymus weights and hematologic endpoints. The 4 week duration rat dermal studies showed slight to moderate skin irritation and minimal systemic toxicity. No significant adverse effects were seen in reproductive organs in any rat dermal study. Supplemental studies of rabbit dermal exposure focused on irritation and mortality and are provided for general information.

For developmental toxicity the substances tested in the Gas Oil Category for which dermal treatment began with the onset of presumed pregnancy (Gestation day 0) had developmental LOELs ranging from 125 – 500mg/kg and NOAELs from 30 – 500mg/kg, attributed primarily to fewer live offspring at delivery and lower fetal or pup body weight at delivery or Lactation days 0-4. Fetal malformations were reported only for CAS RN 64741-43-1 [an intermediate gas oil] and CAS RN 64741-49-7 [Vacuum Tower Overheads]. Developmental toxicity was seen primarily at doses that were maternally toxic. Some gas oils showed no developmental toxicity at the highest doses tested even in the presence of maternal toxicity.

Reproductive parameters in developmental toxicity studies addressing fertility, successful insemination and implantation demonstrate that in general these endpoints are not adversely affected by treatment with gas oil streams. Three studies in which females were treated dermally for a week prior to mating through mating and gestation demonstrated that exposure to high concentrations of several gas oils did not adversely affect mating and establishment of pregnancy but did affect successful completion of pregnancy and pup viability at maternally toxic doses of 250mg/kg and above. 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, no abnormal histopathology or no effects on sperm at doses ranging up to 500-820mg/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 expected to be effects on fetal survival and growth resulting from *in utero* exposure.

Inhalation Studies: Two 4 week repeat dose inhalation studies with samples of hydrodesulfurized distillates and one developmental toxicity study with a marketplace sample of diesel fuel [CAS RN 68476-34-6] did not show any significant substance induced effects. In the inhalation studies with hydrodesulfurized distillates at a single dose of 25mg/m<sup>3</sup>, minimal systemic effects and some inflammation of respiratory tissue were seen. In the developmental study presumed-pregnant rats were exposed to nominal atmospheric concentrations of diesel fuel at 100 and 400 ppm for 6 hours each day from GD6-15. No adverse effects were seen on reproductive or developmental parameters or in soft tissue or skeletons of the fetuses.

Dermal carcinogenesis studies indicate that gas oils and distillate fuels are potential skin carcinogens after repeated skin application but dermal application is not associated with the induction of non-metastatic systemic tumors. The skin carcinogenicity of the petroleum streams with high boiling ranges has been demonstrated to correlate with 3-7 ring PAC content. Skin tumors produced by substances in this category containing low or no PAC are likely due to a non-genotoxic promotion effect and only observed in the presence of sustained severe skin irritation.

### **Human Exposure**

Because the No. 2 distillate fuels have widespread use in transportation and industrial and residential heating applications, both occupational and consumer exposures are possible. Exposure to children is not anticipated. The other substances in the Gas Oil Category are only used in industrial applications.

In conclusion, the information provided in this Gas Oils Category Assessment Document is sufficient to characterize the SIDS endpoints for physiochemical properties, environmental fate, ecotoxicity, and human health hazards of gas oil refinery streams and distillate fuels.

## 9.0 MATRICES OF GAS OIL CATEGORY DATA

### 9.1 Data Matrix for Gas Oils: Physical Chemical Properties, Environmental Fate and Environmental Effects

Endpoint	Measured Results	Predicted Results
<b>Physical Chemical Properties</b>		
Melting Point (°C)	No sharply defined melting points	
Pour Point (°C)	approximate range of -50°C to 0°C.	
Freezing Point (°C)	NA	NA
Boiling Point (°C)	approximately within the range 150°C to 450°C (302° F to 842° F).	Gas oils do not have a single numerical value for boiling point, but rather a boiling or distillation range that reflects the individual components in the complex hydrocarbon substance. CONCAWE (1996) provided a boiling range of 150°C to 450°C (302° F to 842° F) as a general distribution for this category. Ranges for specific streams or products vary depending on the refinery processes used and sources of the feedstocks.
Vapor Pressure	approximate the range of 0.4 kPa to 2 kPa when measured at approximately 40°C.	
Partition Coefficient Log Kow	The partition coefficients of individual constituent hydrocarbons found in gas oils can be expected to cover the range of 3.3 to >6.	
Water Solubility <sup>1</sup> (mg/L)	Individual water solubility may range from essentially insoluble (e.g., <0.001 mg/L) to 52 mg/L, depending on the molecular structure.	Precise measurements of water solubility for complex substances such as gas oils are complicated by factors such as the sensitivity of the analytical method and the water-to-oil ratio. When the ratio is optimized to achieve maximum hydrocarbon concentrations, measurements have ranged from 2.05 mg/L to 8.7 mg/L. Solubility values of individual constituents in gas oils vary widely due to the wide range of molecular weights.
<b>Environmental Fate</b>		

Endpoint	Measured Results	Predicted Results
Photodegradation, OH <sup>-</sup> reaction T <sub>1/2</sub> (d)	0.1 – 1.5	Direct photodegradation is not likely to be an important fate process for gas oils due to their relatively low concentrations of photosensitive constituents. Indirect photodegradation will be an important degradation pathway for constituents that volatilize to the atmosphere
Stability in Water	stable	Substances in this category will be stable and not react with water. Constituent compounds do not contain chemical moieties that undergo hydrolysis.
Transport between Environmental Compartments		The low molecular weight constituents in gas oils will tend to partition to the air. As molecular weight increases, partitioning shifts to the soil compartment.
Biodegradation classification		Although gas oils may not pass criteria for ready biodegradability, current data show that biodegradation rates may be high, and these substances are considered inherently biodegradable. Depending on the sample tested, some gas oils may pass the criterion for ready biodegradability..
<b>Environmental Effects</b>		
Acute Fish LL50 (mg/L WAF loading rate)	3.2 – 65 mg/L	The acute toxicity (LL <sub>50</sub> ) to fish is expected to fall within the range 3.2 to 65 mg/L based on WAF studies and expressed as the loading rate.
Acute Daphnia EL50 (mg/L WAF loading rate)	2.0 – 210 mg/L	The acute toxicity (EL <sub>50</sub> ) to invertebrates is expected to fall within the range 2.0 to 210 mg/L based on WAF studies and expressed as the loading rate.
Algae EL50 (mg/L WAF loading rate) Raphidocelis subcapitata	1.9 – 25 mg/L (biomass) 2.2 – 78	The toxicity (EL <sub>50</sub> ) to algae, when based on algal biomass, is expected to fall within the approximate range of 1.9 - 25mg/L when expressed as loading rate. When based on algal growth rate, E <sub>r</sub> L50 values are anticipated to fall within the range 2.2 to 78 mg/L.
Chronic Fish LL50 (mg/L WAF loading rate)	CAS No. 68476-30-2, No. 2 fuel oil <i>O. mykiss</i> WAF Endpoint value Loading rate 28d LL <sub>50</sub> = 2.7mg/L LOELR <sub>(growth)</sub> = 3.0 mg/L NOELR <sub>(growth)</sub> = 1.2mg/L	The no-observed-effect loading rate for chronic toxicity of blended middle distillate fuels to fish is expected to be approximately 1.2 mg/L.

Endpoint	Measured Results	Predicted Results
	Endpoint value (uM/mL PDMS) 28d LC50 = 24.4 LOEC <sub>(growth)</sub> = 26.4 NOEC <sub>(growth)</sub> = 13.7	
Chronic Daphnia EL50 (mg/L WAF loading rate)	CAS No. 68476-30-2, No. 2 fuel oil <i>D. magna</i> WAF Endpoint value Loading rate 21d EL <sub>50</sub> > 0.5mg/L LOELR <sub>(reproduction)</sub> = 0.5 mg/L NOELR <sub>(reproduction)</sub> = 0.15mg/L  Endpoint value (uM/mL PDMS) 21d EC50 > 7.24 LOELR <sub>(reproduction)</sub> = 7.24 NOELR <sub>(reproduction)</sub> = 3.09	The no-observed-effect loading rate for chronic toxicity of blended middle distillate fuels to aquatic invertebrates is expected to be approximately 0.15 mg/L.

WAF = Water Accommodated fraction

## 9.2 Data Matrix for Gas Oils: Human Health Effects

CAS RN	Acute Oral Rat (mg/kg)	Acute Dermal Rabbit (mg/kg)	Acute Inhalation Rat (mg/L)	Repeated Dose LOAEL/NOAEL (mg/kg) Rats	Genetic Toxicity <i>In vitro</i>	Genetic Toxicity- <i>In vivo</i>	Developmental Toxicity Dermal LOAEL/NOAEL (mg/kg) <sup>1</sup>	Reproductive toxicity <sup>2</sup>
Read Across Values for Untested Substances	LD <sub>50</sub> ≥ 5000 LD <sub>50</sub> ≥ 9.0ml/kg	LD <sub>50</sub> > 2000 LD <sub>50</sub> > 5.0ml/kg	LC <sub>50</sub> = 1.8 to 7.6	<u>13 week studies</u> LOAEL = 30 to 125 NOAEL ≤ 30	All CAS RN are considered positive with metabolic activation unless testing of individual samples in Salmonella gives negative results.	All CAS RN are considered for negative for cytogenetic effects.	LOAEL = 125 to 500 NOAEL = 30 to 500	Developmental toxicity values can be read across
64741-59-9	[2 samples] LD <sub>50</sub> ♂ = 4700 to 7200 LD <sub>50</sub> ♀ = 3200 to 6800	[2 samples] LD <sub>50</sub> > 2000	[2 samples] 4.4 to 5.4	<u>13 week study</u> LOAEL ♂ = 125 NOAEL ♂ = 25 LOAEL ♀ = 500 NOAEL ♀ = 125			[2 samples] LOAEL = 333 to 500 NOAEL = 50 to 250	
64741-43-1				4 week study LOAEL > 460 NOAEL = 460 [highest dose tested]			LOAEL = 250 NOAEL = 50	
64741-44-2	LD <sub>50</sub> > 5000	LD <sub>50</sub> > 2000	1.78					
64741-49-7				<u>13 week study</u> LOAEL = 125 NOAEL = 30			LOAEL = 125 NOAEL = 30	
64741-77-1				4 week study LOAEL > 820 NOAEL = 820 [highest dose tested]				
64741-82-8				<u>13 week study</u> LOAEL = 30 NOAEL < 30 [lowest dose tested]			[2 samples] LOAEL ≥ 250 NOAEL > 100 to 250	

CAS RN	Acute Oral Rat (mg/kg)	Acute Dermal Rabbit (mg/kg)	Acute Inhalation Rat (mg/L)	Repeated Dose LOAEL/NOAEL (mg/kg) Rats	Genetic Toxicity <i>In vitro</i>	Genetic Toxicity- <i>In vivo</i>	Developmental Toxicity Dermal LOAEL/NOAEL (mg/kg) <sup>1</sup>	Reproductive toxicity <sup>2</sup>
64741-86-2				4 week study LOAEL = 820 NOAEL = 410			LOAEL > 500 NOAEL = 500 [highest dose tested]	
64742-80-9	[2 samples] LD <sub>50</sub> >5000	[2 samples] LD <sub>50</sub> >2000	[2 samples] 4.60 – 7.64					
68334-30-5							[2 samples] LOAEL = 250 to > 300 NOAEL = 125 to 300	
68476-34-6	LD <sub>50</sub> = 9.0ml/kg	LD <sub>50</sub> >5.0ml/kg		4 week study LOAEL = 0.5ml/kg NOAEL < 0.5ml/kg				
68576-30-2	[3 samples] LD <sub>50</sub> = 14.5 to 21.2ml/kg	[3 samples] LD <sub>50</sub> >5.0ml/kg						
68915-97-9				13 week study LOAEL = 125 NOAEL = 30			LOAEL = 125 NOAEL = 30	

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

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## 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  
°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<sub>50</sub> – effective loading rate lethal to 50% of the test population  
E<sub>bL50</sub> – effective loading rate that causes 50% reduction in algal cell biomass  
E<sub>rL50</sub> – effective loading rate that causes 50% reduction in algal growth rate  
EPA/US EPA – United States Environmental Protection Agency  
g/cm<sup>3</sup> – 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  
°K – degrees Kelvin  
kPa - kilopascal  
LC<sub>50</sub> – lethal concentration for 50% of the test population  
LC<sub>50</sub> – lethal dose level for 50% of the test population  
LL<sub>50</sub> – 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<sup>3</sup> – 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

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< 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 a 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<sub>50</sub>, 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 studied 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 studied 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<sub>10</sub>:** 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 gas oils and distillate fuels, 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.

The Petroleum HPV Testing Group has included in its listing of CAS numbers an indication of the corresponding category adopted by the European Union (EU) in their legislation (Official Journal of the European Communities, L84 Volume 36, 5 April 1993, *Council Regulation (EEC) No 793/93 of 23 March 1993 on the evaluation and control of risks of existing substances*) and updated by CONCAWE [*Classification and labeling of petroleum substances according to EU dangerous substances directive (CONCAWE recommendations – July 2005)*, Report No. 6/05]. The EU category information is being included in this test plan to facilitate the international harmonization of classification and the coordination of efforts to summarize existing data and develop new hazard data that will be appropriate for hazard and risk characterization worldwide. In doing so, it will help avoid unnecessary duplication of testing.

### Distillate Fuels

68334-30-5

Diesel Oil ..C9-20 325F-675F

Petroleum products, diesel oil

A complex combination of hydrocarbons produced by the distillation of crude oil. It consists of hydrocarbons having carbon numbers predominantly in the range of C9 through C20 and boiling in the range of approximately 163 degrees C to 357 degrees C (325 degrees F to 675 degrees F).

[EU Category: Other Gas Oils - Distillate Fuel Oils]

CONCAWE Vacuum Gas Oil, hydrocracked gas oils and distillate fuels

68476-30-2

Fuel Oil No. 2 ..32.6 To 37.9 SSU

A distillate oil having a minimum viscosity of 32.6 SUS at 37.7 degrees C (100 degrees F) to a maximum of 37.9 SUS at 37.7 degrees C (100 degrees F).

[EU Category: Other Gas Oils - Distillate Fuel Oils]

CONCAWE Vacuum Gas Oil, hydrocracked gas oils and distillate fuels

68476-31-3

Fuel Oil No. 4 ..45 To 125 SSU

A distillate oil having a minimum viscosity of 45 SUS at 37.7 degrees C (100 degrees F) to a maximum of 125 SUS at 37.7 degrees C (100 degrees F).

[EU Category: Other Gas Oils - Distillate Fuel Oils]

CONCAWE Vacuum Gas Oil, hydrocracked gas oils and distillate fuels

68476-34-6

Diesel Fuel No. 2 ..32.6 To 40.1 SSU

Fuels diesel, no. 2

The distillate oil having a minimum viscosity of 32.6 SUS at 37.7 degrees C (100 degrees F) to a maximum of 40.1 SUS at 37.7 degrees C (100 degrees F).

[EU Category: Other Gas Oils - Distillate Fuel Oils]

CONCAWE Vacuum Gas Oil, hydrocracked gas oils and distillate fuels

### Refinery Streams

64741-43-1

Gas Oil, Intermediate ..C11-25 401F-752F

*Gas oils (petroleum), straight-run*

A complex combination of hydrocarbons produced by the distillation of crude oil. It consists of hydrocarbons having carbon numbers predominantly in the range of C11 through C25 and boiling in the range of approximately 205 degrees C to 400 degrees C (401 degrees F to 752 degrees F).

[EU Category: Straight Run Gas Oils]

CONCAWE Straight run gas oils

64741-44-2

Gas Oil, Light ..C11-20 401F-653F

*Distillates (petroleum), straight- run middle*

A complex combination of hydrocarbons produced by the distillation of crude oil. It consists of hydrocarbons having carbon numbers predominantly in the range of C11 through C20 and boiling in the range of 205 degrees C to 345 degrees C (401 degrees F to 653 degrees F).

[EU Category: Straight Run Gas Oils]

CONCAWE Straight run gas oils

64741-49-7

Vacuum Tower Condensate ..C11-25 401F-752F

Condensates (petroleum), vacuum tower

A complex combination of hydrocarbons produced as the lowest boiling stream in 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 C25 and boiling in the range of approximately 205 degrees C to 400 degrees C (401 degrees F to 752 degrees F).

[EU Category: Vacuum Gas Oils]

CONCAWE Vacuum Gas Oil, hydrocracked gas oils and distillate fuels

64741-58-8

Vacuum Distillate, Light Paraffin ..C13-30 446F-842F

Gas Oils (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 C13 through C30 and boiling in the range of approximately 230 degrees C to 450 degrees C (446 degrees F to 842 degrees F).

[EU Category: Vacuum Gas Oils]  
CONCAWE Vacuum Gas Oil, hydrocracked gas oils and distillate fuels

64741-59-9

Cat Cracked Distillate, Light ..C9-25 302F-752F

*Distillates (petroleum), light 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 C9 through C25 and boiling in the range of approximately 150 degrees C to 400 degrees C (302 degrees F to 752 degrees F). It contains a relatively large proportion of bicyclic aromatic hydrocarbons.

[EU Category: Cracked Gas Oils [excluding hydrocracked gas oils]]  
CONCAWE Cracked gas oils

64741-60-2

Cat Cracked Distillate, Intermediate ..C11-30 401F-842F

*Distillates (petroleum), intermediate 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 C11 through C 30 and boiling in the range of approximately 205 degrees C to 450 degrees C (401degrees F to 842 degrees F). It contains a relatively large proportion of tricyclic aromatic hydrocarbons.

[EU Category: Cracked Gas Oils [excluding hydrocracked gas oils]]  
CONCAWE Cracked gas oils

64741-77-1

Hydrocracked Distillate, Light ..C10-18 320F-608F

*Light Hydrocracked Distillate (Petroleum)*

A complex combination of hydrocarbons from distillation of the products from a hydrocracking process. It consists predominantly of saturated hydrocarbons having carbon numbers predominantly in the range of C10 through C18, and boiling in the range of approximately 160 degrees C to 320 degrees C (320 degrees F to 608 degrees F).

[EU Category: Hydrocracked Gas Oils]  
CONCAWE Vacuum Gas Oil, hydrocracked gas oils and distillate fuels

64741-82-8<sup>1</sup>

Thermocracked Distillate, Light ..C10-18 320F-698F

*Distillates (petroleum), light 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 C10 through C22 and boiling in the range of approximately 160 degrees C to 370 degrees C (320 degrees F to 698 degrees F).

[EU Category: Cracked Gas Oils [excluding hydrocracked gas oils]]  
CONCAWE Cracked gas oils

64741-86-2

Sweetened Distillate ..C9-20 302F-653F

*Distillates (petroleum), sweetened middle*

A complex combination of hydrocarbons obtained by subjecting a petroleum distillate to a sweetening process to convert mercaptans or to remove acidic impurities. It consists of hydrocarbons having carbon numbers predominantly in the range of C9 through C20 and

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<sup>1</sup> Overlaps with ICCA C10 - C12 Aromatic Hydrocarbon Solvents and OECD C10+ Aromatics Hydrocarbon Solvents

boiling in the range of approximately 150 degrees C to 345 degrees C (302 degrees F to 653 degrees F).

[EU Category: Other Gas Oils]

CONCAWE Other gas oils

64741-90-8

Solvent Refined Gas Oils..C11-25 401F-752F

Gas oils (petroleum), solvent refined

A complex combination of hydrocarbons obtained as the raffinate from a solvent extraction process. It consists predominantly of aliphatic hydrocarbons having carbon numbers predominantly in the range of C11 through C25 and boiling in the range of approximately 205 degrees C to 400 degrees C (401 degrees F to 752 degrees F).

[EU Category: Other Gas Oils]

CONCAWE Other gas oils

64741-91-9<sup>2</sup>

Solvent Refined Distillate, Middle..C9-20 302F-653F

Distillates (petroleum), solvent-refined middle

A complex combination of hydrocarbons obtained as the raffinate from a solvent extraction process. It consists predominantly of aliphatic hydrocarbons having carbon numbers predominantly in the range of C9 through C20 and boiling in the range of approximately 150 degrees C to 345 degrees C (302 degrees F to 653 degrees F).

[EU Category: Other Gas Oils]

CONCAWE Other gas oils

64742-29-6

Neutralized Gas Oils..C13-25 446F-752F

Gas oils (petroleum), chemically neutralized

A complex combination of hydrocarbons produced by a treating process to remove acidic materials. It consists of hydrocarbons having carbon numbers predominantly in the range of C13 through C25 and boiling in the range of approximately 230 degrees C to 400 degrees C (446 degrees F to 752 degrees F).

[EU Category: Other Gas Oils]

CONCAWE Other gas oils

64742-30-9

Neutralized Distillate, Middle ..C11-20 401F-653F

Distillates (petroleum) chemically neutralized middle

A complex combination of hydrocarbons produced by a treating process to remove acidic materials. It consists of hydrocarbons having carbon numbers predominantly in the range of C11 through C20 and boiling in the range of approximately 205 degrees C to 345 degree C (401 degrees F to 653 degrees F).

[EU Category: Other Gas Oils]

CONCAWE Other gas oils

64742-38-7

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<sup>2</sup> Overlaps with ICCA C14 - C20 Aliphatics (2% aromatics or less) and OECD C14+ Aliphatic Hydrocarbons Solvents (<2% aromatics)

Clay Treated Distillate ..C9-20 302F-653F

Distillates (petroleum), clay-treated

A complex combination of hydrocarbons resulting from treatment of a petroleum fraction with natural or modified clay, usually in a percolation process to remove the trace amounts of polar compounds and impurities present. It consists of hydrocarbons having carbon numbers predominantly in the range of C9 through C20 and boiling in the range of approximately 150 degrees C to 345 degrees C (302 degrees F to 653 degrees F).

[EU Category: Other Gas Oils]

CONCAWE Other gas oils

64742-46-7<sup>3</sup>

Hydrotreated Distillate, Middle ..C11-25 401F-752F

*Distillates (petroleum), hydrotreated middle*

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 C11 through C25 and boiling in the range of approximately 205 degrees C to 400 degrees C (401 degrees F to 752 degrees F).

[EU Category: Other Gas Oils]

CONCAWE Other gas oils

64742-79-6

Hydrodesulfurized Gas Oil ..C13-25 446F-752F

Gas oils (petroleum), hydrodesulfurized

A complex combination of hydrocarbons obtained from a petroleum stock by treating with hydrogen to convert organic sulfur to hydrogen sulfide which is removed. It consists predominantly of hydrocarbons having carbon numbers predominantly in the range of C13 through C25 and boiling in the range of approximately 230 degrees C to 400 degrees C (446 degrees F to 752 degrees F).

[EU Category: Other Gas Oils]

CONCAWE Other gas oils

64742-80-9<sup>4</sup>

Hydrodesulfurized Distillate, Middle ..C11-25 401F-752F

Distillates (petroleum), hydrodesulfurized middle

A complex combination of hydrocarbons obtained from a petroleum stock by treating 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 C25 and boiling in the range of approximately 205 degrees C to 400 degrees C (401 degrees F to 752 degrees F).

[EU Category: Other Gas Oils]

CONCAWE Other gas oils

64742-87-6

Hydrodesulfurized Gas Oil, Light Vacuum ..C13-30 446F-842F

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<sup>3</sup> Overlaps with ICCA C14 - C20 Aliphatics (2% aromatics or less) and OECD C14+ Aliphatic Hydrocarbons Solvents (<2% aromatics)

<sup>4</sup> Overlaps with ICCA C14 - C20 Aliphatics (2-35% aromatics)

Gas oils (petroleum), hydrodesulfurized light vacuum

A complex combination of hydrocarbons obtained from a catalytic hydrodesulfurization process. It consists of hydrocarbons having carbon numbers predominantly in the range of C13 through C30 and boiling in the range of approximately 230 degrees C to 450 degrees C (446 degrees F to 842 degrees F).

[EU Category: Vacuum Gas Oils]

CONCAWE Vacuum Gas Oil, hydrocracked gas oils and distillate fuels

68333-25-5

Hydrodesulfurized Distillate, Light Cat Cracked ..C9-25 302F-752F

Distillates (petroleum), hydrodesulfurized light catalytic cracked

A complex combination of hydrocarbons obtained by treating light 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 C9 through C25 and boiling in the range of approximately 150 degrees C to 400 degrees C (302 degrees F to 752 degrees F). It contains a relatively large proportion of bicyclic aromatic hydrocarbons.

[EU Category: Cracked Gas Oils (excluding hydrocracked gas oils)]

CONCAWE Cracked gas oils

68333-88-0<sup>5</sup>

Aromatic Hydrocarbons, C9-17

No description

[EU Category: none] CONCAWE none

68477-31-6

Reformate Still Bottoms, Light ..To 550F

Distillates (petroleum), catalytic, reformer fractionator residue, low-boiling

The complex combination of hydrocarbons from the distillation of catalytic reformer fractionator residue. It boils approximately below 288 degrees C (550 degrees F).

[EU Category: Other Gas Oils]

CONCAWE Other gas oils

68814-87-9

Gas Oil, Intermediate ..C9-25 320F-752F

Distillates (petroleum), full-range straight-run middle

A complex combination of hydrocarbons produced by the distillation of crude oil. It consists of hydrocarbons having carbon numbers predominantly in the range of C9 through C25 and boiling in the range of approximately 150 degrees C to 400 degrees C (302 degrees F to 752 degrees F).

[EU Category: Straight Run Gas Oils]

CONCAWE Straight run gas oils

68915-96-8

Gas Oil Heavy ..550F-880F

*Distillates (petroleum), straight-run, b. 557-880 degrees F.*

[EU Category: Straight Run Gas Oils]

CONCAWE Straight run gas oils

68915-97-9

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<sup>5</sup> Overlaps with ACC Low Benzene Naphthas

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Gas Oil, Heavy ..540F-660F

Gas oils (petroleum), straight-run, high-boiling

A complex combination of hydrocarbons produced by the atmospheric distillation of crude oil. It boils in the range of approximately 282 degrees C to 349 degrees C (540 degrees F to 660 degrees F).

[EU Category: Straight Run Gas Oils]

CONCAWE Straight run gas oils

## **APPENDIX B. Links to Additional Resources**

### **Refining Processes: General Descriptions**

[http://www.chevron.com/about/learning\\_center/refinery](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.osha-slc.gov/dts/osta/otm/otm_toc.html)  
[http://www.shellglobalsolutions.com/base\\_oils/library/library.htm](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.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](http://www.mts.net/~dbrad1/base_oil.htm)

### **Petroleum Related Glossaries**

[http://www.caltex.com.au/products\\_glo.asp](http://www.caltex.com.au/products_glo.asp)  
<http://www.citgo.com/CommunityInvolvement/Classroom/Glossary.jsp>  
<http://www.eplp.com/gloss.html>  
[http://www.prod.exxon.com/exxon\\_productdata/lube\\_encyclopedia/](http://www.prod.exxon.com/exxon_productdata/lube_encyclopedia/)  
[http://www.hellenic-petroleum.gr/english/glossary/gl\\_main.htm](http://www.hellenic-petroleum.gr/english/glossary/gl_main.htm)  
[http://www.prod.exxon.com/exxon\\_productdata/lube\\_encyclopedia/](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.shellglobalsolutions.com/base_oils/glossary/a_g.htm)  
[http://www.ursa-texaco.com/English/glossary\\_a.html](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](http://www.eia.doe.gov/pub/oil_gas/petroleum/data_publications/petroleum_marketing_annual/current/pdf/glossary.pdf)

## **APPENDIX C. 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<sup>6</sup> 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  $\geq 650^{\circ}\text{F}$  [ $>343^{\circ}\text{C}$ ] (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<sub>50</sub> values for high-boiling petroleum substances are generally greater than the

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<sup>6</sup> 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).

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.

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 (Gephart et al, 2001).
- The  $PDR_{10}$  can be applied to untested materials for which there are compositional data (ie, PAC profiles) but no response data, whereas the BMD cannot be used for untested materials.

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- 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).

## **Appendix D. 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  $\geq 650^{\circ}\text{F}$   $\geq 343^{\circ}\text{C}$  (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). 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  $\geq 1$ .

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.