

**ROBUST SUMMARY
OF INFORMATION ON**

Substance Group

**LUBRICATING OIL
BASESTOCKS**

Summary prepared by

American Petroleum Institute (API) Petroleum HPV
Testing Group. Consortium No. 1100997

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298

NB. Reliability of data included in this summary has been assessed using the approach described by Klimisch et al.

Klimisch, H. J., Andreae, M. and Tillman, U, (1997)

A systematic approach for evaluating the quality of experimental toxicological and ecotoxicological data.

Regulatory Toxicology and Pharmacology 25, 1-5.

1. General Information

Id Lubricating oil
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1.1.1 GENERAL SUBSTANCE INFORMATION

Substance type : Petroleum product
Physical status : Liquid

Remark : The group of base oils consists of products that are derived from both distillates and residues of the vacuum distillation process in petroleum refining.
Base oils consist predominantly of hydrocarbons but may also contain small quantities of sulfur and nitrogen compounds with traces of a number of metals. The oils contain complex hydrocarbons with variable mixtures of paraffins, naphthenes and aromatics with carbon numbers in the range 15 to 50. Hydrocarbon constituents derived from vacuum distillates boil generally in the range 300 to 600 °C, whereas those derived from residual oils may boil up to 800 °C.
Unrefined vacuum distillates contain polycyclic aromatic compounds (PACs) which are removed during any subsequent refining process. The more severe the refining, the lower the PAC content will be of the refined base oil.
Physical chemical data for a range of base oils have been summarized by CONCAWE and these are tabulated in the attached document.
For most of the mammalian toxicology endpoints, information has been used that was derived by the American Petroleum Institute on a wide range of base oils. For simplicity, this robust summary contains detailed information on an API sample of an unrefined distillate (high PAC) and an API sample of a highly refined distillate (low PAC). If data was available on other samples, it has either been summarized in tabular form in the relevant sections of this summary or discussed in detail when appropriate. The API sample of highly refined base oil for which data have been selected is one with a low average molecular weight since this is likely to represent the worst case from a toxicological perspective.

The physico-chemical characteristics of the two samples are as follows:

	Method	Unrefined oil	Highly refined oil
API sample No.		84-01	83-12
CAS No.		64741-50-0	64742-53-6
API Gravity @60°	D287	31.9	25.9
Density @15°C	D287	0.8651	0.8981
Molecular wt. (gm/mol)	D2224	300	260
Refractive index (RI units @20 °C)		1.4815	1.4910
Total Sulfur (wt. %)	D3120	0.38	0.04
Total Nitrogen (ppm/wt)	Chemil	210	38
Total oxygen (wt.%)	NAA	0.038	0.077
Total Chloride (ppm/wt)	coulom	11	2
Viscosity (cSt @ 40°C)	D445	14.07	0.44
Viscosity (cSt @ 100°C)	D445	2.79	2.14
Pour point (°F)	D93	+60	<-20
Carbon residue (wt. %)	D524	0.15	0.14
Distillation	D1160		
	IBP (°F)	595	450
	FBP (°F)	810	785
Hydrocarbon type analysis			
Nonaromatics (wt. %)	D2549	79.1	67.3
Aromatics (wt. %)	D2549	20.9	31.9

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TOTAL 100 100

Some oils are destined for food use or pharmaceutical applications and for these the refining process that they undergo is particularly severe to ensure that aromatic materials have been removed and that the resulting oil is colorless. Such oils are known as white oils. Unlike the other base oils in which oral intake is unintentional, the white oils are intended for uses in which an oral intake is likely. For these materials, oral studies are available and, where appropriate, are included in this Robust Summary.

Several individual companies have generated data on environmental effects and ecotoxicity. The relevant CAS descriptions of the materials that have been tested are included in the relevant sections of this robust summary.

Attached document : Attachment 1: Physico-chemical data (81)

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

Type of limit : TLV (US)
Limit value : 5 mg/m³
Short term exposure limit value
Limit value : 10 mg/m³

Remark : A TWA TLV of 0.005 mg/m³ is proposed for the sum total of 15 polynuclear aromatic hydrocarbons (PAHs) listed as carcinogens by the U.S. National Toxicology Program (NTP). (1)

1.13 REVIEWS

Memo : IARC reviewed the carcinogenicity information on lubricating base oils and the outcome of their review was published in a Monograph (IARC 1984). (101)

Memo : Bingham reviewed the literature for information on the carcinogenic potential of petroleum hydrocarbons. This review contained information on base oils. (23)

Memo : CONCAWE demonstrated that it was possible to distinguish between carcinogenic and non-carcinogenic base oils on the basis of the level of DMSO extractables.

Remark : The DMSO method was adopted subsequently in the EU to distinguish between carcinogenic and non-carcinogenic oils for classification and labeling purposes. (80) (86)

Memo : The EU Scientific Committee for Food (SCF) and the WHO Joint Expert Committee on Food Additives (JECFA) have reviewed the available data on the toxicology of mineral hydrocarbons for food uses. (102) (112)

Memo : The WHO published an Environmental Health Criteria document which included summarized information on lubricating base oil stocks (127)

2. Physico-Chemical Data

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2.1 MELTING POINT

- Sublimation** :
Method : ASTM D97
GLP : No data
Test substance : Lubricating Base Oils; distillate oils, residual oils, and white oils
- Remark** : By definition, melting point is the temperature at which a solid becomes a liquid at normal atmospheric pressure. For complex mixtures like petroleum products, melting point may be characterized by a range of temperatures reflecting the melting points of the individual components. To better describe 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 2002). In addition, the pour point methodology defines a "no-flow" point, defined as the temperature of the test specimen at which a wax crystal structure or viscosity increase, or both, impedes movement of the surface of the test specimen under the conditions of the test (ASTM 2002). Because not all petroleum products contain wax in their composition, the pour point determination encompasses either change in physical state (i.e., crystal formation) and/or viscosity property.
- Result** : See following Table and Remarks Section

<u>Oil type</u>	<u>Pour Point, °C</u>
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Distillate Oils

Highly/Severely Refined

Solvent de-waxed, light paraffinic (CAS No. 64742-56-9)	-18
Solvent de-waxed, heavy paraffinic (CAS No. 64742-65-0)	-12
Hydrotreated, light paraffinic (CAS No. 64742-55-8)	-18
Hydrotreated, heavy paraffinic (CAS No. 64742-54-7)	-9
Hydrotreated, light naphthenic (CAS No. 64742-53-6)	-60
Hydrotreated, heavy naphthenic (CAS No. 64742-52-5)	-24
White mineral oil (CAS No. 8042-47-5)	-15

Residual Oils

Solvent de-waxed (CAS No. 64742-62-7)	-6
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- Reliability** : (2) valid with restrictions
Results of standard method testing were reported in a reliable review dossier.

(18) (19) (81)

2. Physico-Chemical Data

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Category Chemical :	Lubricating Oil Basestocks		
Test Substance :	Distillates (petroleum), hydrotreated heavy naphthenic (CAS RN 64742-52-5)		
Test Substance Purity/Composition and Other Test Substance Comments:	API Gravity @ 60°C	19.4	ASTM D287
	Density @ 15°C	0.9368	ASTM D287
	Viscosity @ 40°C	880.0	ASTM D445
	Viscosity @ 100°C	26.94	ASTM D445
	Hydrocarbon Type (ASTM D2549):		
	Nonaromatics, wt %	53.1	
	Aromatics, wt %	46.9	
Category Chemical Result Type :	Measured		
Test Substance Result Type :	Measured		
RESULTS			
Melting Indicator :			
Melting Point Input type :	Value		
Melting Point Value: Temperature:	4.4 °C		
Results Remarks :	Petroleum substances such as lubricating oil basestocks do not have well defined melting points, but gradually become viscous at temperature falls. To better describe the flow characteristics of petroleum substances the pour point is routinely used.		
STUDY/METHOD			
Key Study Sponsor Indicator :	Key		
Year Study Performed :	1985 – 1987		
Method/Guideline Followed :	ASTM D97		
Method/Guideline and Test Condition Remarks:	The pour point was measured according to ASTM D97 utilizing a graduated refrigerated bath. The interpretation of the pour point was made manually.		
GLP :			
Study Reference :	API. 1987. Comprehensive Analytical Analysis of API Generic Refinery Streams. American Petroleum Institute, Washington, DC. April, 1987.		
RELIABILITY/DATA QUALITY			
Reliability :	2		
Reliability Remarks :	Reliable with restrictions.		

2. Physico-Chemical Data

Id Lubricating oil
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Category Chemical :	Lubricating Oil Basestocks		
Test Substance :	Distillates (petroleum), hydrotreated light naphthenic (CAS RN 64742-53-6)		
Test Substance Purity/Composition and Other Test Substance Comments:	API Gravity @ 60°C	25.9	ASTM D287
	Density @ 15°C	0.8981	ASTM D287
	Viscosity @ 40°C	8.44	ASTM D445
	Viscosity @ 100°C	2.14	ASTM D445
	Hydrocarbon Type (ASTM D2549):		
	Nonaromatics, wt %	67.3	
	Aromatics, wt %	31.9	
Category Chemical Result Type :	Measured		
Test Substance Result Type :	Measured		
RESULTS			
Melting Indicator :			
Melting Point Input type :	Value		
Melting Point Value: Temperature:	-29 °C		
Results Remarks :	Petroleum substances such as lubricating oil basestocks do not have well defined melting points, but gradually become viscous at temperature falls. To better describe the flow characteristics of petroleum substances the pour point is routinely used.		
STUDY/METHOD			
Key Study Sponsor Indicator :	Key		
Year Study Performed :	1985 – 1987		
Method/Guideline Followed :	ASTM D97		
Method/Guideline and Test Condition Remarks:	The pour point was measured according to ASTM D97 utilizing a graduated refrigerated bath. The interpretation of the pour point was made manually.		
GLP :			
Study Reference :	API. 1987. Comprehensive Analytical Analysis of API Generic Refinery Streams. American Petroleum Institute, Washington, DC. April, 1987.		
RELIABILITY/DATA QUALITY			
Reliability :	2		
Reliability Remarks :	Reliable with restrictions.		

2. Physico-Chemical Data

Id Lubricating oil
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Category Chemical :	Lubricating Oil Basestocks		
Test Substance :	Distillates (petroleum), light paraffinic (CAS RN 64741-50-0)		
Test Substance Purity/Composition and Other Test Substance Comments:	API Gravity @ 60°C	31.9	ASTM D287
	Density @ 15°C	0.8651	ASTM D287
	Viscosity @ 40°C	14.07	ASTM D445
	Viscosity @ 100°C	2.79	ASTM D445
	Hydrocarbon Type (ASTM D2549):		
	Nonaromatics, wt %	79.1	
	Aromatics, wt %	20.9	
Category Chemical Result Type :	Measured		
Test Substance Result Type :	Measured		
RESULTS			
Melting Indicator :			
Melting Point Input type :	Value		
Melting Point Value: Temperature:	15.5 °C		
Results Remarks :	Petroleum substances such as lubricating oil basestocks do not have well defined melting points, but gradually become viscous at temperature falls. To better describe the flow characteristics of petroleum substances the pour point is routinely used.		
STUDY/METHOD			
Key Study Sponsor Indicator :	Key		
Year Study Performed :	1985 - 1987		
Method/Guideline Followed :	ASTM D97		
Method/Guideline and Test Condition Remarks:	The pour point was measured according to ASTM D97 utilizing a graduated refrigerated bath. The interpretation of the pour point was made manually.		
GLP :			
Study Reference :	API. 1987. Comprehensive Analytical Analysis of API Generic Refinery Streams. American Petroleum Institute, Washington, DC. April, 1987.		
RELIABILITY/DATA QUALITY			
Reliability :	2		
Reliability Remarks :	Reliable with restrictions.		

2.4 VAPOUR PRESSURE

- Method** : Directive 84/449/EEC, A.4 "Vapour pressure"
Year : 1991
GLP : Yes
Test substance : CAS No. 64742-65-0, Distillates (petroleum), solvent-dewaxed, paraffinic
- Result** : Three runs on the sample were conducted. There was initially substantial reduction (equivalent to 3°C temperature change) of estimated VP on prolonged pumping after Run 1 but this was reduced to the equivalent of 0.65°C change between Runs 2 and 3. The latter runs provided values at room temperature of 1.882 and 1.563×10^{-4} Pascals, yielding a mean value of $V_p(298.15K) = 1.723 \times 10^{-4}$ Pascals. The condensation rates onto the pan observed in Run 3 increased with temperature more rapidly than the mass difference indicating an increasing efficiency of condensation and thus precluding the use of the condensation data to produce a satisfactory VP relation. The final values of rate of condensation were however equivalent in pressure regime to the mass differences assuming a rough equality between the numerical magnitudes of temperature and molar mass.
- Test condition** : The vapor pressure (VP) was determined using a VP balance based on a CI Electronics micro-balance with a sensitivity of approximately 0.1 mg. Sample temperature was controlled electronically ($\pm 1^\circ\text{C}$) over the range from ambient to 250°C.
Mass readings and temperature were recorded directly onto a 2-channel chart recorder. The VP balance was designed such that on opening the slide across the orifice in the temperature controlled evaporation furnace, the escaping vapor jet was directed at the scale pan. VP was determined directly from the pressure on the scale pan by measuring the difference of mass readings when the slide across the orifice was open and closed. When condensation occurred onto the pan the VP can be calculated from the condensation rate if the molar mass is known. VP of the sample was measured at several temperatures to yield VP curves for subsequent extrapolation to give 298.15K values. Slope and intercept of VP curve were estimated by an unweighted least squares statistical treatment of the data and errors are \pm standard deviation of the respective quantity. Maximum and minimum values of VP at 298.15K were calculated directly from the VP relationship using the ranges of errors in slope and intercept respectively. The quoted errors in VP at 298.15K were then calculated directly by extrapolation from these values.
- Reliability** : (2) valid with restrictions
The reported measurement was an extrapolation below the method limit of sensitivity.

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Category Chemical:	Lubricating Oil Basestocks
Test Substance:	Various
Test Substance Purity/Composition and Other Test Substance Comments:	
Category Chemical Result Type:	Estimated
Test Substance Result Type:	Estimated
RESULTS	
Vapor Pressure Input type:	Value or Range?
<u>Vapor Pressure Value</u> : @ <u>Temperature</u>: 25°C	
The following vapor pressure values for individual hydrocarbons were either estimated by MPBPWIN, V1.40 or were cited as empirical values in the EPI-Suite experimental database.	
<u>Modeled Compound</u>	<u>VP, Pa</u>
C15 Hydrocarbon	
Pentadecane	0.457*
Nonylcyclohexane	0.331*
4-isopropyl-1,6-dimethylnaphthalene	0.149
C20 Hydrocarbon	
Icosane	6×10^{-4} *
2-hexyl-6-butyl[4.4.0]bicyclodecane	3×10^{-2}
3-hexylphenanthrene	1×10^{-4}
C50 Hydrocarbon	
n-pentacontane	2×10^{-7}
2-tetracontyl[4.4.0]bicyclodecane	2×10^{-13}
<u>2-tetracontylpyrene</u>	1×10^{-16}
* These values were cited in the EPI-Suite experimental database.	
Results Remarks:	Members of the lubricating oil basestocks contain hydrocarbons having the principal ranges of either C15 – C50 or C20 – C50 depending on the category member. As molecular weight increases, vapor pressure decreases. Eventually, the vapor pressures of the constituent hydrocarbons fall below the capabilities of standard measurement techniques. Vapor pressure estimates or measurements, if provided by MPBPWIN v1.40, were provided for individual isomeric structures representative of those constituents. Since the total vapor pressure of mixtures is a function of the sum of the individual vapor pressures times their mole fraction in the mixture (Raoult's Law), complex mixtures such as lubricating oil basestocks would be expected to have exceedingly low total vapor pressure.
STUDY/METHOD	

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Key Study Sponsor Indicator:	
Year Study Performed:	
Method/Guideline Followed:	EPI-Suite estimation program MPBPWIN, V1.40
Method/Guideline and Test Condition Remarks:	
GLP:	
Study Reference:	US EPA. 2010. Estimation Programs Interface for Windows (EPI-Suite). United States Environmental Protection Agency, Washington, DC.
RELIABILITY/DATA QUALITY	
Reliability:	2
Reliability Remarks:	Reliable with restrictions. The vapor pressure values of these individual hydrocarbons were either estimated by a validated structure-activity computer model or were cited in the model's experimental database.

2.5 PARTITION COEFFICIENT

Category Chemical:	Lubricating Oil Basestocks
Test Substance:	Various
Test Substance Purity/Composition and Other Test Substance Comments:	
Category Chemical Result Type:	Estimated
Test Substance Result Type:	Estimated
RESULTS	
Partition Coefficient Input type:	Value or Range?
Partition Coefficient Range: Log K_{ow} : @ Temperature: 25°C	
The following Log Kow values for individual hydrocarbons were either estimated by KOWWIN, V1.67 or were cited as empirical values in the EPI-Suite experimental database.	
Modeled Compound	Log Kow
C15 Hydrocarbon	
Pentadecane	7.7
Nonylcyclohexane	7.5

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4-isopropyl-1,6-dimethylnaphthalene	5.7
C20 Hydrocarbon	
Icosane	10
2-hexyl-6-butyl[4.4.0]bicyclodecane	9.0
3-hexylphenanthrene	7.4
C50 Hydrocarbon	
n-pentacontane	25
2-tetracontyl[4.4.0]bicyclodecane	24
<u>2-tetratriacontylpyrene</u>	<u>22</u>
Note: Kow values greater than approximately 8 are outside the model limits.	
Results Remarks:	Estimated partition coefficient values for representative C15, C20, and C50 hydrocarbon constituents in lubricating oil basestocks were ≥ 5.7 .
STUDY/METHOD	
Key Study Sponsor Indicator:	
Year Study Performed:	
Method/Guideline Followed:	EPI-Suite estimation program KOWWIN, V1.67
Method/Guideline and Test Condition Remarks:	
GLP:	
Study Reference:	US EPA. 2010. Estimation Programs Interface for Windows (EPI-Suite). United States Environmental Protection Agency, Washington, DC.
RELIABILITY/DATA QUALITY	
Reliability:	2
Reliability Remarks:	Reliable with restrictions. The partition coefficient values of these individual hydrocarbons were estimated by a validated structure-activity computer model.

Test Substance*:	CAS No. 64742-62-7, Residual oils (petroleum) solvent-dewaxed
Method/Guideline:	EC L383A Test A8
Year (guideline):	1992
Type (test type):	Indirect estimation by reverse phase thin layer chromatography
GLP:	Yes
Year (study performed):	1998
Test Conditions (FT-TC):	Duplicate TLC plates (Merck KC18F, 10 cm x 20 cm) were preconditioned before use. Plates were heated at 120 deg C for 15 minutes, allowed to cool to ambient, then fully eluted with methanol/water, and left to dry. Solutions of the reference and test substances in methanol (10 μ l) were applied to the plates using a
<ul style="list-style-type: none"> Note: Concentration prep., vessel type, replication, test conditions. 	

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	10 µl syringe, and allowed to dry. The amount of reference substances applied ranged from 61 to 95 µg; 76 µg of test substance was applied. The TLC plate was run for approximately 90 minutes in methanol/water (90/10 v/v), allowed to dry, and the spots located under UV light (254 nm, fluorescence quenching). The log P _{ow} of the test substance was obtained by comparison of the R _f values of the test and reference substances.																								
Results (FT-RS): Units/Value: <ul style="list-style-type: none"> Note: Deviations from protocol or guideline, analytical method. 	<table border="1"> <thead> <tr> <th><u>Reference substance</u></th> <th><u>log P_{ow}</u></th> <th><u>R_f values</u></th> </tr> </thead> <tbody> <tr> <td>Benzyl alcohol</td> <td>1.1</td> <td>0.73, 0.70</td> </tr> <tr> <td>Phenol</td> <td>1.46</td> <td>0.75, 0.76, 0.73</td> </tr> <tr> <td>Naphthalene</td> <td>3.30</td> <td>0.48, 0.48</td> </tr> <tr> <td>Anthracene</td> <td>4.45</td> <td>0.32, 0.32</td> </tr> <tr> <td>Phenanthrene</td> <td>4.46</td> <td>0.33, 0.34</td> </tr> <tr> <td>DDT</td> <td>6.3</td> <td>0.28, 0.28, 0.28</td> </tr> <tr> <td>Test substance</td> <td>>6</td> <td>0, 0</td> </tr> </tbody> </table> <p>Linear regression of reference substance results: $\text{Log } P_{ow} = -10.7 \log R_f - 0.17$, ($r^2 = 0.95$, $n = 14$, $SE = 0.48$)</p> <p>Samples of the test substance showed only a single spot which had not moved from the origin. Since this position was outside the calibration range, the log P_{ow} was estimated to be >6.</p>	<u>Reference substance</u>	<u>log P_{ow}</u>	<u>R_f values</u>	Benzyl alcohol	1.1	0.73, 0.70	Phenol	1.46	0.75, 0.76, 0.73	Naphthalene	3.30	0.48, 0.48	Anthracene	4.45	0.32, 0.32	Phenanthrene	4.46	0.33, 0.34	DDT	6.3	0.28, 0.28, 0.28	Test substance	>6	0, 0
<u>Reference substance</u>	<u>log P_{ow}</u>	<u>R_f values</u>																							
Benzyl alcohol	1.1	0.73, 0.70																							
Phenol	1.46	0.75, 0.76, 0.73																							
Naphthalene	3.30	0.48, 0.48																							
Anthracene	4.45	0.32, 0.32																							
Phenanthrene	4.46	0.33, 0.34																							
DDT	6.3	0.28, 0.28, 0.28																							
Test substance	>6	0, 0																							
Conclusion (FT-CL):																									
Reliability (FT-RL):	(1) Reliable without restrictions																								
Reference (FT-RE):	Shell Research and Technology Centre. 1998. Estimation of adsorption and partition coefficients. Report No. CT.98.47133.																								
Other (FT-SO):																									

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2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Category Chemical :	Lubricating Oil Basestocks
Test Substance :	Various
Test Substance Purity/Composition and Other Test Substance Comments:	
Category Chemical Result Type :	Estimated
Test Substance Result Type :	Estimated
RESULTS	
Water Solubility Indicator :	
Water Solubility Input type:	Values
Water Solubility Value/Range : Solubility: @ Temperature: 25°C	
<p>The following water solubility values for individual hydrocarbons were either estimated by WSKOWWIN, V1.41 or were cited as empirical values in the EPI-Suite experimental database.</p>	
Modeled Compound	Water Solubility, mg/L
C15 Hydrocarbon	
Pentadecane	0.0028
Nonylcyclohexane	0.0040
4-isopropyl-1,6-dimethylnaphthalene	0.6
C20 Hydrocarbon	
icosane	9×10^{-6}
2-hexyl-6-butyl[4.4.0]bicyclodecane	1×10^{-4}
3-hexylphenanthrene	8×10^{-4}
C50 Hydrocarbon	
n-pentacontane	5×10^{-21}
2-tetracontyl[4.4.0]bicyclodecane	5×10^{-20}
2-tetratriacontyl pyrene	1×10^{-18}
pH Value :	Value or Lower Range: Upper Range :
pKa - Protein Kinase:	
pH Value at Saturation :	
Results Remarks :	It is predicted from calculations of solubility behavior that paraffinic, naphthenic and aromatic hydrocarbons in the range of C15 to C50 will have extremely low water solubility due to the hydrophobic behavior of these hydrocarbons. Estimate water solubility values for representative C15, C20 and C50 compounds

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	for paraffinic, naphthenic, and aromatic classes range from <0.001 to 0.6 mg/L.
STUDY/METHOD	
Key Study Sponsor Indicator :	
Year Study Performed :	2010
Method/Guideline Followed :	EPI-Suite estimation program WSKOWWIN, V1.41
Method/Guideline and Test Condition Remarks:	Water solubility values reported here were estimated from the Log Kow relationship used by WSKOWWIN V1.41.
GLP :	
Study Reference :	US EPA. 2010. Estimation Programs Interface for Windows (EPI-Suite). United States Environmental Protection Agency, Washington, DC.
RELIABILITY/DATA QUALITY	
Reliability :	2
Reliability Remarks :	Reliable with restrictions. The water solubility values of these individual hydrocarbons were estimated by a validated structure-activity computer model.

3.1.1 PHOTODEGRADATION

Deg. product :
Method : Calculated): Calculations by EPIWIN V3.10; AOPWIN V1.90.
Year : 2000
GLP : No
Test substance : CAS No.: Various; Unrefined and acid treated base oils.

Remark : AOPWIN V1.90 calculates atmospheric oxidation half lives of hydrocarbons in contact with hydroxyl radicals in the troposphere, under the influence of sunlight. Atmospheric oxidation rates were calculated for a range of molecular structures (paraffinic, naphthenic and aromatic hydrocarbons) and different molecular weights (i.e., C15, C20 and C50) for hydrocarbon components in lubricating base oils.

Although the low vapor pressures of these base oils indicate that volatilization will not be a very significant fate process, oxidation half-lives indicate this may be a moderate removal process if these substances were introduced to the atmosphere by adsorption to particulate matter via atmospheric emissions. The half-lives for degradation of these hydrocarbons by reaction with hydroxyl radicals, in the troposphere, under the influence of sunlight, will all be less than one day, by extrapolation from the data quoted by Atkinson (1990).

In general, most substances in the base oil category do not contain component molecules that will undergo direct photolysis. Saturated hydrocarbons (paraffins and naphthenics), and single ring aromatics, which constitute the majority of these components, do not absorb appreciable light energy above 290 nm. Therefore, direct photolysis will not contribute to a measurable degradative removal of chemical components in this category from the environment.

Result : Indirect photolysis at 25 °C
 Concentration of sensitizer: 1.50×10^6 OH radicals/cm³
 Rate constant: 18.1757×10^{-12} cm³/mol-sec
 Half-life: See following table

Modeled Compound	Half-Life, days
C15 Hydrocarbon	
Pentadecane	0.6
Nonylcyclohexane	0.5
4-isopropyl-1,6-dimethylnaphthalene	0.1
C20 Hydrocarbon	
Icosane	0.4
2-hexyl-6-butyl[4.4.0]bicyclodecane	0.3
3-hexylphenanthrene	0.3
C50 Hydrocarbon	
n-pentacontane	0.2
2-tetracontyl[4.4.0]bicyclodecane	0.1
2-tetratriacontyl pyrene	0.1

3. Environmental Fate and Pathways

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Reliability : (2) valid with restrictions
 The predicted endpoint was determined using a validated computer model.
 (21) (82) (124)

3.1.2 STABILITY IN WATER

GLP : No

Result : Measured value: N/A
 Degradation %: N/A
 Half-life: N/A
 Breakdown products: N/A

Conclusion : Hydrolysis of an organic chemical is the transformation process in which a water molecule or hydroxide ion reacts to form a new carbon-oxygen bond. Chemicals that have a potential to hydrolyze include alkylhalides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters. The chemical components that comprise the base oil category are hydrocarbons, which are not included in these chemical groups, and they are not subject to hydrolysis reactions with water.

Reliability : (1) valid without restriction

(99)

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Category Name:	Lubricating Oil Basestocks
Category Chemical :	Various
Test Substance :	Various
Test Substance Purity/Composition and Other Test Substance Comments:	
Category Chemical Result Type :	Estimated by calculation
Test Substance Result Type :	Estimated
RESULTS	
Fugacity/Distribution Result Description:	Lubricating oil basestocks are substances of variable composition containing hydrocarbons molecules typically within the range of 15 to 50 carbon atoms. Multimedia distribution was calculated for various alkyl and aryl hydrocarbons that may be found in these substances. This provided an understanding of the distribution spectrum that might be expected for these constituents.

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Test Results :

	Percent Distribution					
	air	water	soil	sediment	susp. sediment	Biota
C15 Compounds						
n-pentadecane	13	<0.1	85	2	<0.1	<0.1
iso-pentadecane	68	<0.1	31	0.7	<0.1	<0.1
Nonylcyclohexane	11	<0.1	87	2	<0.1	<0.1
2-hexylbicyclo[4.3.0]nonane	52	<0.1	47	1	<0.1	<0.1
n-nonylbenzene	19	<0.1	79	2	<0.1	<0.1
2-butyl-naphthalene	0.7	0.2	97	2	<0.1	<0.1
2-methylphenanthrene	2	1	95	2	<0.1	<0.1
C20 Compounds						
n-icosane	<0.1	<0.1	98	2	<0.1	<0.1
iso-icosane	9	<0.1	89	2	<0.1	<0.1
2-hexyl,6-butylbicyclo[4.4.0]decane	2	<0.1	96	2	<0.1	<0.1
Tetradecylbenzene	<0.1	<0.1	98	2	<0.1	<0.1
2-decyl-naphthalene	<0.1	<0.1	98	2	<0.1	<0.1
3-hexylphenanthrene	<0.1	<0.1	98	2	<0.1	<0.1
C50 Compounds						
n-pentacontane	<0.1	<0.1	98	2	<0.1	<0.1
2-tetracontylbicyclo[4.4.0]decane	<0.1	<0.1	98	2	<0.1	<0.1
tetratetracontylbenzene	<0.1	<0.1	98	2	<0.1	<0.1
2-tetracontyl-naphthalene	<0.1	<0.1	98	2	<0.1	<0.1
2-hexatriacontylphenanthrene	<0.1	<0.1	98	2	<0.1	<0.1

Temperature :

20°C

Level of Multi-media Model :

1

Model Input (Water Solubility:)

	Water solubility (mg/L)
n-pentadecane	0.0028
iso-pentadecane	0.0033
n-nonylcyclohexane	0.0040
2-hexylbicyclo[4.3.0]nonane	0.028
n-nonylbenzene	0.035
2-butyl-naphthalene	0.63
2-methylphenanthrene	0.27*
n-icosane	9×10^{-6}
2-hexyl,6-butylbicyclo[4.4.0]decane	1.1×10^{-4}
Tetradecylbenzene	4.1×10^{-4}
2-decyl-naphthalene	0.0021
3-hexylphenanthrene	8.3×10^{-4}
n-pentacontane	5×10^{-21}
2-tetracontylbicyclo[4.4.0]decane	5×10^{-20}
Tetratetracontylbenzene	2×10^{-19}
2-tetracontyl-naphthalene	1×10^{-18}
2-hexatriacontylphenanthrene	5×10^{-19}

Values denoted by * were cited in the EPI-Suite experimental database.

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Model Input (Vapor Pressure:)	Vapor Pressure (Pa)	
	n-pentadecane	0.457*
	iso-pentadecane	5.81
	n-nonylcyclohexane	0.331*
	2-hexylbicyclo[4.3.0]nonane	2.57
	n-nonylbenzene	0.761*
	2-butyl-naphthalene	0.053
	2-methylphenanthrene	0.002*
	n-icosane	0.00062*
	2-hexyl,6-butylbicyclo[4.4.0]decane	0.003
	Tetradecylbenzene	0.0032*
	2-decyl-naphthalene	0.00073
	3-hexylphenanthrene	0.00011
	n-pentacontane	2×10^{-7}
	2-tetracontylbicyclo[4.4.0]decane	2×10^{-13}
	Tetratetracontylbenzene	2×10^{-14}
	2-tetracontyl-naphthalene	3×10^{-15}
2-hexatriacontylphenanthrene	5×10^{-16}	
Values denoted by * were cited in the EPI-Suite experimental database.		
Model Input (log K_{ow}:)	Partition Coefficient (Log K _{ow})	
	n-pentadecane	7.7
	iso-pentadecane	7.6
	n-nonylcyclohexane	7.5
	2-hexylbicyclo[4.3.0]nonane	6.6
	n-nonylbenzene	7.1*
	2-butyl-naphthalene	5.7
	2-methylphenanthrene	5.1*
	n-icosane	10
	2-hexyl,6-butylbicyclo[4.4.0]decane	9.0
	Tetradecylbenzene	8.9
	2-decyl-naphthalene	8.1
	3-hexylphenanthrene	7.4
	n-pentacontane	25
	2-tetracontylbicyclo[4.4.0]decane	24
	Tetratetracontylbenzene	24
	2-tetracontyl-naphthalene	23
2-hexatriacontylphenanthrene	22	
Values denoted by * were cited in the EPI-Suite experimental database.		
Model Input (Melting Point:)	Melting Point (°C)	
	n-pentadecane	9.9*
	iso-pentadecane	1.54
	n-nonylcyclohexane	-10*
	2-hexylbicyclo[4.3.0]nonane	24.2
	n-nonylbenzene	-24*
	2-butyl-naphthalene	63
	2-methylphenanthrene	123*
	n-icosane	36.8*
	2-hexyl,6-butylbicyclo[4.4.0]decane	68.8
Tetradecylbenzene	16*	
2-decyl-naphthalene	109	

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	3-hexylphenanthrene 132 n-pentacontane 87 2-tetracontylbicyclo[4.4.0]decane 300 Tetratetracontylbenzene 305 2-tetracontyl-naphthalene 316 2-hexatriacontylphenanthrene 328 Values denoted by * were cited in the EPI-Suite experimental database.
Henry's Law Constant :	Calculated by EQC for each constituent
Model Concentration -- Air :	
Model Concentration -- Water :	
Model Concentration -- Soil :	
Model Concentration -- Sediment :	
Results Remarks :	
STUDY/METHOD	
Key Study Sponsor Indicator :	Key
Year Study Performed :	
Method/Guideline Followed :	EQC Equilibrium Criterion Model, Fugacity Based Level 1
Deviations from Method/Guideline :	
Method/Guideline Description :	The EQC model calculates the distribution of a fixed quantity of conserved (i.e., non-reacting) chemical, in a closed environment at equilibrium, with no degrading reactions, no advective processes, and no intermedia transport processes (e.g., no wet deposition or sedimentation). The medium receiving the emission is unimportant because the chemical is assumed to become instantaneously distributed.
Method/Guideline and Test Condition Remarks :	
GLP :	No
Study Reference :	Trent University. 2003. EQC fugacity-based EQC-equilibrium criterion model, Version 2.02. Canadian Environmental modeling Centre, Trent University, Ontario. URL: http://www.trentu.ca/cemc/
RELIABILITY/DATA QUALITY	
Reliability :	(2) Reliable with restrictions
Reliability Remarks :	Environmental distribution was estimated using an accepted validated model.

3.5 BIODEGRADATION

- Type** : Aerobic
Inoculum : Microorganisms were obtained from Canterbury Sewage Works (UK) and prepared according to the prescribed methods for this test.
Contact time : 28 day(s)
Method : Directive 84/449/EEC, C.5 "Biotic degradation - modified Sturm test"
Year : 1986
GLP : Yes
Test substance : CAS No. 64742-65-0; Distillates (petroleum), solvent-dewaxed heavy paraffinic
- Result** : The test substance was partially degraded to 20-26% of the theoretical CO₂ in 28 days. Degradation commenced after a lag period of 2 days. Biodegradation curve showed that degradation had virtually stopped by day 28. Test substance was therefore inherently biodegradable since it achieved >20% biodegradability based upon CO₂ evolution.

<u>Sample</u>	<u>% Degradation (day 28)</u>	<u>Mean % Degraded</u>
Test substance	26, 20	23
Na Benzoate	86, 92	89

- Test condition** : The test substance was added to test medium from a stock solution containing 2.4 g/l emulsified in Dobane PT sulphonate (2 mg/l), a non-biodegradable detergent. The final test concentration of the base oil was 20 mg/l. The test medium was dispensed into Sturm vessels, inoculated and aerated with 60 ml/min of CO₂-free air and incubated at 20 ± 1°C. Biodegradation was determined on days 1, 2, 5, 9, 14, 20, and 28 by titrating the total CO₂ released. The medium was acidified on day 27 to release the total CO₂ by day 28. Test substance, control blank, and sodium benzoate control (20 mg/l) were tested in duplicates. The empirical formula used was C_nH_{2n+1} which yielded a theoretical CO₂ evolution of 3.14 g CO₂ per g of test substance.

- Reliability** : (2) valid with restrictions
 The study report lacked an extensive description of experimental procedures but instead referenced procedures detailed in a laboratory SOP.

(116)

- Type** : Aerobic
Inoculum : Activated sludge, domestic
Contact time : 28 day(s)
Method : OECD Guide-line 301 F "Ready Biodegradability: Manometric Respirometry Test"
Year : 1995
GLP : Yes
Test substance : CAS No. 64742-54-7; Distillates (petroleum), hydrotreated heavy paraffinic

- Result** : By day 28, 31% degradation of the test material was observed and indicated that the test material was inherently biodegradable. By day 5, >60% biodegradation of positive control was observed, which meets the guideline requirement. No excursions from the protocol were noted. Biodegradation was based on net oxygen consumption and the theoretical oxygen demand of the test material as calculated using results of an elemental analysis of the test material.

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<u>Sample</u>	<u>% Degradation* (day 28)</u>	<u>Mean % Degradation (day 28)</u>
HHP	32.93, 27.2, 33.27	31.13
Na Benzoate	82.04; 72.88	77.46

* replicate data

Test condition : Fresh activated sludge was obtained one day prior to test initiation, and homogenized in a blender for two minutes. After allowing the sample to settle for approximately 30 minutes, the homogenated supernatant was decanted, avoiding carry-over of solids. Microbial activity of an aliquot of the filtered supernatant was $1E^6$ CFU/ml which was determined using microbial agar dip slides. Activated sludge supernatant was added to the test medium at 10 ml/l and the inoculated medium was continuously aerated with CO₂-free air until the next day when the test systems were prepared.

Test medium consisted of glass distilled water and mineral salts (phosphate buffer, ferric chloride, magnesium sulfate, calcium chloride). Test vessels were 1 Liter glass flasks located in a water bath and electronically monitored for oxygen consumption. Test material was tested in triplicate, controls and blanks were tested in duplicate. Test material (hydrotreated heavy paraffinic petroleum distillates, HHP) concentration was approximately 44 mg/l, equivalent to a theoretical oxygen demand (ThOD) of 148 mg/l. Test material was weighed onto a Gelman type A/E 13 mm glass fiber filter which was then added to each respirometer flask. Sodium benzoate (positive control) concentration was 53.54 mg/l, and was added using an aliquot of a stock solution. Test temperature was $22 \pm 1^\circ\text{C}$. All test vessels were stirred constantly for 28 days using magnetic stir bars and plates.

Reliability : (1) valid without restriction

(95)

Type : Aerobic

Inoculum : Activated sludge, domestic

Contact time : 28 day(s)

Method : OECD Guide-line 301 B "Ready Biodegradability: Modified Sturm Test (CO₂ evolution)"

Year : 1990

GLP : Yes

Test substance : CAS No. 64741-89-5; distillates (petroleum), solvent-refined, light paraffinic

Result : By day 28, the 10 and 20 mg C/L test flasks showed

<u>Day</u>	<u>% Degradation Reference</u>	<u>% Degradation</u>	
		<u>10 ppm Test Sub.</u>	<u>20 ppm Test Sub.</u>
10	31	0	1
21	89	25	12
28	89	29	22

The test material was not readily biodegradable. Within a period of 28 days, 22 and 29% degradation was observed. The pass limit for this test is 60% within 28 days.

The reference test substance was degraded to 89% by day 28. The pH of the test cultures (10 mg/l and 20 mg/l) and controls (sodium benzoate standard and negative control) measured on Day 27 were 4.8, 4.8, 4.9, and 5.2, respectively.

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Test condition : The test material entered the experimental containers through direct dispersion in water. Activated sludge bacteria from the Severn Trent Plc sewage treatment plant in Belper, Derbyshire was used as the inoculum. The sample sludge was homogenized in a mixer for 10 minutes prior to a solid settling phase and a subsequent filtering of the supernatant for use. The experimental containers had an inoculum concentration of 1%. The exposures lasted for a period of 28 days. The experimental containers were 5 liter glass culture vessels, containing 3 liters of a mixture of nutrient medium, test material, and inoculum. Test conditions were run in darkness at a constant temperature of 21°C. Nutrient medium was prepared according to the OECD guideline recipe using tap water purified by ion exchange and reverse osmosis. A series of both two controls and two test material concentrations were run. The controls consisted of a group with just the culture medium and the inoculum and a group with culture medium, inoculum, and 20 mg/l Sodium benzoate (C₆H₅ * COONa). The two test concentrations of test material were 10 and 20 mg/l. All culture vessels were sealed and aerated with CO₂ free air at a rate of about 2 bubbles per second. Additionally, the solution was continuously stirred by magnetic stirrers. Samples were taken from the first CO₂ absorber vessel on Days 0, 1, 2, 3, 6, 8, 10, 14, 16, 21, 23, 27, and 28. Samples were taken from the second absorber vessel on Days 0 and 28. The absorbers were made up of 500 ml Dreschel bottles filled with 350 ml of 0.05M NaOH. The solution was prepared using purified, degassed water. On day 27, the pH of each vessel was measured and 1 ml of concentrated HCl was added to drive off inorganic carbonate. CO₂ production (as inorganic carbon) was measured by an Ionics 555 TOC Analyzer in triplicate.

Reliability : (2) valid with restrictions
The study was performed following the 1981 guidelines for OECD 301B. (36)

Type : Aerobic
Inoculum : Activated sludge, domestic
Contact time : 21 day(s)
Method : CEC Method L-33-T-82 using test medium from ISO Standard 7827 and OECD 301A and 301E
Year : 1991
GLP : Yes
Test substance : CAS No. 64741-89-5; distillates (petroleum), solvent-refined, light paraffinic

Result : By day 21, biodegradation of the test substance was 63%, 65%, and 61% in the individual flasks. The mean biodegradation was 63%.

% Biodegradation

Day	Reference Material			Test Substance		
	Rep1	Rep2	Rep3	Rep1	Rep2	Rep3
21	27	29	30	63	65	61
Mean:	29			63		

Biodegradation of the reference material was 27%, 29%, and 30% in the individual flasks, and the mean biodegradation was 29%.

There were no apparent deviations from the given method.

Test condition : Settled activated sludge acquired from Buckland Sewage Treatment Works, Milber, Newton Abbot, Devon, was utilized as the inoculum. The inoculum was normally between 10⁵ and 10⁷ Colony Forming Units (CFU)/ml. Bacteria were enumerated by Dip Slide (Oxoid, TTC Red Spot) and incubated at 25 ±1°C until sufficient colonies were visible to enable counting.

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The inoculum was used in the experiment at a rate of 1 ml per flask. The test medium was prepared following the formula specified in ISO Standard 7827. Mother solutions of the test substance and reference oil were prepared by adding 150 g of test or reference substance to 1 liter of A113 (1,1,2-trichlorotrifluoroethane). The negative control reference substance was white oil, R.L. 110 (Brixham test substance #T071). The test design consisted of 5 test flasks containing 150 ml of test medium, 1 ml inoculum, and 50 ml of test substance mother solution; 5 reference flasks containing 150 ml of test medium, 1 ml inoculum, and 50 ml of reference substance mother solution; 2 blank flasks containing 150 ml of test medium and 1 ml inoculum; and 1 poisoned flask prepared identical as the test flasks but contained 1 ml of HgCl₂. Incubation flasks were 500-ml conical flasks fitted with foam plugs.

On day 0 of the test, two blank flasks, two test flasks, and two reference flasks were sacrificed for analysis of residual oil content by infrared spectrophotometry (see analysis procedure below). The remaining flasks were placed on an orbital incubator and maintained at 25 ± 1°C for 21 days. On day 21, the contents of all flasks were analyzed for residual oil content.

Analysis Procedure:

Residual oil content (%) in each flask was analyzed using a method suitable for the determination of hydrocarbon lubricants in water samples. Lubricants were extracted from water using 1,1,2 trichlorotrifluoroethane and were analyzed using infrared spectrophotometry. The samples were quantified against known standards of the lubricant using the maximum absorption of the CH₃-CH₂ band at 2930 ± 10 cm⁻¹.

Percent test substance degraded was calculated as

$$\frac{\% \text{ (ROC) poisoned flask} - \% \text{ ROC test flask}}{\% \text{ ROC poisoned flask}} \times 100$$

Reliability : (2) valid with restrictions
The CEC method is not a test of ready or inherent biodegradability, nor do the test results provide a reliable measure of the extent of ultimate biodegradability, or mineralization. These test results can only indicate primary biodegradation, i.e., some loss of oil based on concentration analysis of the parent base oil over the course of the study. (59)

Type : Aerobic
Test substance : Various base oils

Result : 28 biodegradability studies have been reported for base oils. In the preceding paragraphs a full study description is Based on the results of ultimate biodegradability tests using modified Sturm and manometric respirometry testing these base oils are expected to be, for the most part, inherently biodegradable. Results of primary biodegradability testing using the CEC test method indicate that transformation of parent base oil due to biological activity occurs to a varying extent, ranging from 13% to 79% loss of original concentrations of tested base oils.

Summarized data for all studies (including those described in the preceding

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paras) are tabulated below

Method*	Biodeg. (%)	Ref.
Distillates, solvent-refined heavy paraffinic (64741-88-4)		
OECD 301B**	22, 11	BP AT301/036
OECD 301B	15, 12	BP AT301/030
OECD 301B	8, 8	BP AT301/032
OECD 301B	3, 11	BP AT301/035
OECD 301B	12, 11	BP 301/031
OECD 301B	9, 8	BP AT301/034
CEC L-33-T-82	72	BP BL3821/B
CEC L-33-T-82	71	BP BL3822/B
CEC L-33-T-82	53	BP BL3823/B
CEC L-33-T-82	79	BP BL3820/B
CEC L-33-T-82	64	BP BL3826/B
CEC L-33-T-82	51	BP BL3825/B
Distillates, solvent-refined light paraffinic (64741-89-5)		
OECD 301B	29, 22	BP AT301/064
OECD 301B	17, 17	BP AT301/029
CEC L-33-T-82	63	BP BL3975/B
CEC L-33-T-82	75	BP BL3819/B
Solvent de-asphalted Bright stock (64741-95-3)		
OECD 301B	11, 4	BP AT301/038
CEC L-33-T-82	17	BP BL3971/B
Distillates, hydrotreated or solvent refined light naphthenic (64741-97-5)		
84\449\EEC, C5	1.5	Shell SBGR.87.259
Solvent-refined residual oil (64742-01-4)		
OECD 301B	4, 2	No Ref
OECD 301B	5, 5	BP AT301/037
CEC L-33-T-82	45	BP BL3824/B
CEC L-33-T-82	13	BP BL3970/B
Distillates, hydrotreated or solvent refined light naphthenic (64742-53-6)		
OECD 301F	42	EBSI 107194A
Distillates, hydrotreated heavy paraffinic (64742-54-7)		
OECD 301F	31	EBSI 198194A
Distillates, solvent dewaxed light paraffinic (64742-56-9)		
OECD 301F	50	EBSI107094A
Distillate, solvent-dewaxed heavy paraffinic (64742-65-0)		
84\449\EEC, C5	23	Shell SBGR.86.137
OECD 301F	38	EBSI 123694A
White oil, (8042-47-5)		
OECD 301B***-,	24	cited in CONCAWE 97/108
CEC L-33-T-82	0	cited in CONCAWE 97/108

* Methods used are:
 OECD 301B Ready, Sturm test
 OECD 301F Ready, Manometric method
 CEC L-33-T-82 CEC Test
 84\449\EEC, C5 Ready, Sturm Test

** For method OECD 301B the two values given for biodegradation are for test material concentrations of 10

*** Value only available for 20 ppm concentration
 (29) (30) (31) (32) (33) (34) (35) (36) (37) (48) (53) (54) (55) (56) (57) (58) (59)
 (60) (61) (62) (63) (91) (92) (93) (94) (116) (117)

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type : Semistatic
Species : *Salmo gairdneri* (Fish, estuary, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
Limit test : Yes
Analytical monitoring : Yes
Method : OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year : 1990
GLP : Yes
Test substance : CAS No. 64741-89-5; distillates (petroleum), solvent-refined, light paraffinic

Result : No mortality at 96 hours in the 0 and 1000 mg/l groups.

96 hrs-LL₀ = 1000 mg/l, based on nominal loading rates.

Only one concentration was tested in the limit test. The report states that water samples were taken at 0, 24, and 96 hours for analytical verification of test concentrations, but results of any analyses were not reported.

Test condition : Daily renewal of the test media ensured that test material levels were maintained at the exposure concentrations. The test media was introduced into the exposure vessels through direct dispersion in water. Shielded propeller-stirrers were utilized to aid in the dispersion of the test material. Observations indicated that the test material was well dispersed throughout the experiment. 20 ml water samples were drawn from the exposure vessels via a glass syringe and delivered to a storage vessel. The syringe was then rinsed with 20 ml of 1,1,2-trichlorotrifluoroethane. Subsequently, the rinse was mixed with the sample prior to storage. Water samples were collected at 0, 24, and 96 hours into the experiment. Samples were stored at 4°C in glass containers until BP International Limited analyzed them. Exposure vessels were glass aquaria equipped with shielded propeller-stirrers containing 20 liters of test media. The stirrers rotated at 2000 rpm. 10 fish were housed in each vessel and 20 fish were exposed at the experimental concentration. The experimental groups included a control and a group exposed to a concentration of 1000 mg/l. The exposure was conducted under a 16 hour/8 hour, light/dark photoperiod. The rainbow trout were supplied by Trafalgar Nurseries, Downton, Salisbury, U.K. The mean length and mean weight (sd) of the experimental fish were 4.8 cm (0.4 cm) and 1.33 g (0.49 g), respectively. Fish were fed commercial trout pellets on a daily basis. Feeding was discontinued 24 hours prior to the initial exposure. The fish were laboratory acclimated for 4 days prior to a one week test condition acclimation. Biomass loading in the test chambers was 0.67 g/l. Test water was tap water, dechlorinated through the addition of sodium thiosulfate. Exposures occurred at 14°C, a hardness of 50 mg/l as CaCO₃ and the D.O. level never dropped below 10.0 mgO₂/l. The pH of the control groups ranged from 7.6-7.7.

Reliability : (2) valid with restrictions
Only one concentration of the test substance was tested. Results of chemical analyses of test substance concentrations were not reported.

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Type	: Semistatic
Species	: <i>Salmo gairdneri</i> (Fish, estuary, fresh water)
Exposure period	: 96 hour(s)
Unit	: mg/l
Analytical monitoring	: Yes
Method	: OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year	: 1990
GLP	: Yes
Test substance	: Solvent-refined residual oil, CAS No. 64742-01-4
Result	: No mortality at 96 hours in the 0 and 1000 mg/l groups. 96 hrs-LL ₀ = 1000 mg/l, based on nominal loading rates. Only one concentration was tested in the limit test. The report states that water samples were taken at 0, 24, and 96 hours for analytical verification of test concentrations, but results of any analyses were not reported.
Test condition	: Daily renewal of the test media ensured that test material levels were maintained at the exposure concentrations. The test media was introduced into the exposure vessels through direct dispersion in water. Shielded propeller-stirrers were utilized to aid in the dispersion of the test material. Observations indicated that the test material was well dispersed at the beginning of the experiment. After 24 hours the test material was observed adhering to the glassware and propeller shields, as well as forming a floating scum on the water surface. This was also observed at each additional 24 hour renewal period. 20 ml water samples were drawn from the exposure vessels via a glass syringe and delivered to a storage vessel. The syringe was then rinsed with 20 ml of 1,1,2-trichlorotrifluoroethane. Subsequently, the rinse was mixed with the sample prior to storage. Water samples were collected at 0, 24, and 96 hours into the experiment. Samples were stored at 4°C in glass containers until BP International Limited analyzed them. Exposure vessels were glass aquaria equipped with shielded propeller-stirrers containing 20 liters of test media. The stirrers rotated at 2000 rpm. 10 fish were housed in each vessel and 20 fish were exposed at the experimental concentration. The experimental groups included a control and a group exposed to a concentration of 1000 mg/l. The exposure was conducted under a 16 hour/8 hour, light/dark photoperiod. The rainbow trout were supplied by Trafalgar Nurseries, Downton, Salisbury, U.K. The mean length and mean weight (sd) of the experimental fish were 4.8 cm (0.4 cm) and 1.33 g (0.49 g), respectively. Fish were fed commercial trout pellets on a daily basis. Feeding was discontinued 24 hours prior to the initial exposure. The fish were laboratory acclimated for 4 days prior to a one week test condition acclimation. Test water was tap water, dechlorinated through the addition of sodium thiosulphate. Exposures occurred at 14°C, a hardness of 50 mg/l as CaCO ₃ and the D.O. level never dropped below 10.0 mgO ₂ /l. The pH of the control groups ranged from 7.6-7.8.
Reliability	: (2) valid with restrictions Only one concentration of the test substance was tested. Results of chemical analyses of test substance concentrations were not reported.

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4. Ecotoxicity

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Type : Semistatic
Species : Oncorhynchus mykiss (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
Analytical monitoring : Yes
Method : OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year : 1994
GLP : Yes
Test substance : Distillate aromatic extract (CAS 64742-04-7)

Remark : A 24-hour WAF mixing period was selected based upon a mixing trial using a similar product. No substantial differences in the total organic carbon content in the aqueous phase were seen between 24 and 48-hour mixing periods.

Result : There was no mortality or other adverse reactions to the exposures during or after 96 h in the control and 1000 mg/l test solutions. Inspection of the data revealed the following:

Highest test concentration resulting in 0% mortality: 1000 mg/l WAF

Lowest test concentration resulting in 100% mortality: >1000 mg/l WAF

No Observed Effect Level (NOEL): 1000 mg/l WAF

Total organic carbon analyses results (mg/l):

<u>Treatment Group</u>	<u>0-h</u>	<u>24 h</u>	<u>72 h</u>	<u>96 h</u>
Control	6.020	2.813	3.760	4.011
1000 mg/l Rep 1	5.460	3.211	4.457	3.859
1000 mg/l Rep 2	4.952	2.620	3.849	3.779

Total organic carbon measurements made in the exposure solutions during the test were variable. The authors claim that the carbon analyses do not provide definitive evidence of stability of the test preparations.

Test condition : A semi-static toxicity test was conducted with daily renewal of test solutions. Test solutions were prepared as water accommodated fractions (WAF). Nominal loading rates were 0 (control) and 1000 mg/l. The 1000 mg/l WAF solution was prepared by adding 20.0 g of test substance to 20 liters of dilution water. The mixture was stirred for 24 hours, taking care to avoid the formation of a vortex or gross mixing. After the stirring period, the solution was allowed to settle for 1 hour, then the aqueous phase was removed and dispensed to a 20-liter glass exposure vessel. Duplicate exposure vessels were used for the 1000 mg/l treatment group; a single vessel was used for the control group. The WAFs for each vessel were made independently of each other (i.e., no batch preparations). Each vessel held 10 fish.
Dilution water was dechlorinated laboratory tap water having a total hardness of approximately 100 mg/l as CaCO₃.
Rainbow trout were obtained from a commercial supplier (Parkwood Trout Farm, Wigmore, Kent, U.K.) and were maintained in the laboratory approximately 6.5 weeks until use in testing. They were acclimatized to the test condition a week prior to use with no mortality during the acclimation period. During holding and acclimation, fish were fed commercial trout pellets daily up to 24 hour prior to initiation of the test. Fish were not fed during the test. Fish used in the experiment had a mean standard length of

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4.8 cm (SD=0.2) and a mean weight of 1.06 g (SD=0.14). The fish biomass loading for the test was 0.53 g/l. Mortality was defined as absence of (1) respiratory movement and (2) response to physical stimulation.

The test was conducted under a photoperiod of 16 h light and 8 h dark. Test solutions were aerated during the test by means of narrow bore glass tubes. The water pH, dissolved oxygen concentration and temperature in each test vessel was recorded daily. Water pH ranged from 7.4 to 7.5, dissolved oxygen ranged from 9.8 to 10.0 mg/l, and temperature remained a constant 14° C. Total organic carbon was measured during the test on samples of fresh (0 and 72 hours) and old (24 and 96 hours) test media.

Reliability : (1) valid without restriction (67)

Method : Acute toxicity tests

Test substance : Various base oils

Result : The following studies have been added in supporting evidence to the detailed robust summary given above for fish toxicity. Acute fish toxicity studies have been reported for 14 base oil samples (including the studies summarized in full above). The results for all 14 samples are summarized in the table below.

<u>Result</u>	<u>Reference</u>
Salmo gairdneri - semistatic test	
Distillates, solvent-refined heavy paraffinic (64741-88-4)	
7-d LL ₀ =1000 ppm dispersion	BP AT301/028
7-d LL ₀ =1000 ppm dispersion	BP AT301/022
7-d LL ₀ =1000 ppm dispersion	BP AT301/023
7-d LL ₀ =1000 ppm dispersion	BP AT301/027
7-d LL ₀ =1000 ppm dispersion	BP AT301/024
7-d LL ₀ =1000 ppm dispersion	BP AT301/025
Distillates, solvent refined light paraffinic (64741-89-5)	
96-h LL ₀ =1000 ppm dispersion	BP AT301/044
7-d LL ₀ =1000 ppm dispersion	BP AT301/021
Solvent deasphalted bright stock (64741-95-3)	
96-h LL ₀ =1000 ppm dispersion	BP AT301/043R
Solvent refined residual oil (64742-01-4)	
7-d LL ₀ =1000 ppm dispersion	BP AT301/026
96-h LL ₀ =1000 ppm dispersion	BP AT301/042
Pimephales promelas - static test	
Distillates hydrotreated heavy paraffinic (64742-54-7)	
96-h LL ₀ =100 ppm WAF	EBSI 198140
Solvent dewaxed residual oil (64742-62-7)	
96-h LL ₀ =100 ppm WAF	EBSI 198240
Distillates solvent dewaxed heavy paraffinic (64742-65-0)	
96-h LL ₀ =100 ppm WAF	EBSI 101740
(42) (43) (44) (45) (46) (47) (49) (50) (51) (52) (64) (88) (89) (90)	

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4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : Static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
Analytical monitoring : No
Year : 1988
GLP : No
Test substance : CAS No. 64742-53-6 or 64741-97-5, Distillates (petroleum), hydrotreated or solvent-refined light naphthenic

Result : After 48 hrs no daphnid immobilization was found in any of the concentrations tested.

The 48 hr EL₀ was 10 g/l.

Control survival was 100% after 48 hrs.

Test condition : Individual treatment concentrations were prepared as water accommodated fractions (WAF). Nominal loading rates in the definitive test were 0, 0.01, 0.1, 1, and 10 g/l. Control and dilution water was reconstituted hard water prepared by adding salts to glass-distilled deionized water following EPA guidelines (hardness 174 mg/ml as CaCO₃). Test substance was mixed in dilution water for 23 hrs. The mixtures were allowed to stand for 1 hr prior to siphoning off the aqueous phase for testing. Glass flasks (140 ml) were filled with each of the WAFs with 10 daphnids per vessel. The flasks were sealed with glass cover slip to minimize the loss of volatile components of the oil. Test daphnids were <24 hrs old and collected from cultures supplied by the testing laboratory that have been aged between 15 and 35 days. Two replicates per treatment and control were used. Black caps were placed over those flasks in which an oily film was visible on the surface of the test solution so the organisms would avoid the darkened zone and not be trapped in the film. Test temperature was 18 - 22 °C. Dissolved oxygen in the control and highest concentration was 8.8 to 9.1 mg/ml. pH in the control and highest concentration was 7.7 - 8.0.

Reliability : (2) valid with restrictions
Although test guidelines were not specified and the study was not conducted under GLPs, it was a well-documented study. Analytical monitoring of the oil concentration in the WAFs was not performed. An oily film was visible on the surface of some test solutions apparently as a carryover from the WAF preparations.

(118)

Type : Semistatic
Species : Gammarus pulex (Crustacea)
Exposure period : 96 hour(s)
Unit : mg/l
Analytical monitoring : No
Year : 1988
GLP : No
Test substance : CAS No. 64742-53-6 or 64741-97-5, Distillates (petroleum), hydrotreated or solvent-refined light naphthenic

Result : No dead organisms were found in any of the test vessels after 96 hours. However, some organisms disappeared from all treatments and control

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- throughout the test. It was assumed that these organisms were eaten by the remaining organisms.
The numbers of missing animals after 96 hours were 2, 1, 4, 5, and 2 in the control, 0.01, 0.1, 1, and 10 g/l WAFs. Since <50% of the organisms were missing in any concentration, and even if these lost animals died as a result of treatment, the 96-hr LL₀ was 10 g/l.
- Test condition** : Individual treatment concentrations were prepared as water accommodated fractions (WAF). Nominal loading rates in the definitive test were 0, 0.01, 0.1, 1, and 10 g/l. Control and dilution water was laboratory mains tap water obtained from bore holes, and passed through particle and activated carbon filters (alkalinity 247 mg/ml as CaCO₃, hardness 274 mg/ml as CaCO₃, conductivity 492 mS/cm, pH 7.3). Test substance was mixed in dilution water for 23 hrs. The mixtures were allowed to stand for 1 hr prior to siphoning off the aqueous phase for testing. Fresh WAFs were prepared for each 24-hr renewal. Glass crystallizing dishes (350 ml) were filled with 300 ml of each of the WAFs with 10 organisms per dish. Three replicates per treatment and control were used. Test organisms were between 1 and 2 mm in size and collected from a tributary of the River Len at Hollingbourne, Kent, UK. Test temperature was 14 - 18.2 °C.
- Reliability** : Dissolved oxygen in the control and highest concentration was 7.8 to 9.9 mg/ml. pH in the control and highest concentration was 6.8 - 8.5.
(2) valid with restrictions
Although test guidelines were not specified and the study was not conducted under GLPs, it was a well-documented study. Analytical monitoring of the oil concentration in the WAFs was not performed. (118)
- Type** : Static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
Analytical monitoring : Yes
Method : OECD Guide-line 202
Year : 1994
GLP : Yes
Test substance : Distillate aromatic extract, CAS No. 64742-04-7
- Remark** : A 24-hour WAF mixing period was selected based upon a mixing trial with the test substance. No substantial differences in the total organic carbon content in the aqueous phase was seen between 24 and 48-hour mixing periods.
- Result** : There was no immobilization or other adverse reaction to the exposure solutions during the test. Inspection of the data revealed the following:
48-H EL₅₀ = >1000 mg/l WAF
Highest test concentration resulting in 0% immobilization: 1000 mg/l WAF
Lowest test concentration resulting in 100% immobilization: > 1000 mg/l WAF
No Observed Effect Level (NOEL): 1000 mg/l WAF
- Total organic carbon analyses (mg/l):
- | <u>Treatment Group</u> | <u>0-h</u> | <u>48 h</u> |
|------------------------|------------|-------------|
| Control | 3.587 | 2.256 |
| 1000 mg/l R1 and R2 | 1.937 | 1.997 |
| 1000 mg/l R3 and R4 | 2.168 | 1.831 |
- Total organic carbon measurements made on the exposure solutions

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Test condition

during the test were variable. The authors claim that the carbon analyses do not provide definitive evidence of stability of the test preparations.

: A static 48-hour toxicity test was conducted without renewal of test solutions. Test solutions were prepared as water accommodated fractions (WAF). Nominal loading rates were 0 (control) and 1000 mg/l. The 1000 mg/l WAF solution was prepared by adding 2 g of test substance to 2 liters of dilution water. The mixture was stirred for 24 hours, taking care to avoid the formation of a vortex or gross mixing. After the stirring period, the solution was allowed to settle for 1 hour, then the aqueous phase was removed and 200 ml of the solution was dispensed into each of four replicate glass vessels. The 1000 mg/l WAF treatment used four replicate vessels, while the control treatment used two replicate vessels. Each vessels held 10 daphnids, and all vessels were covered during the test to reduce evaporation.

Dilution water was reconstituted water having a total hardness of approximately 270 mg/l as CaCO₃.

Daphnids used in the test had been cultured at 21 °C in the laboratory in reconstituted water. The original culture was obtained from the Institut National de Recherche Chimique Appliquee, France. Cultures were fed daily with a suspension of mixed algae (predominately Chlorella sp.). Gravid adults were isolated 24 hours prior to initiation of the test, and the young daphnids produced overnight were used for testing. The daphnid loading rate during the test was 20 ml solution per daphnid. Immobilization was defined as the inability to swim for approximately 15 seconds after gentle agitation.

The test was conducted under a photoperiod of 16 h light and 8 h dark. No aeration was applied during the test. Temperature was recorded daily, and pH and dissolved oxygen were recorded at initiation and termination of the test. Water pH ranged from 7.7 to 7.9, dissolved oxygen ranged from 7.8 to 8.1, and temperature remained a constant 21 °C. Total organic carbon was measured as a means to demonstrate stability of the test solutions. Measurements were made of test solutions collected at 0 and 48 hours.

Reliability

: (1) valid without restriction

(66) (82)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species : Scenedesmus subspicatus (Algae)
Endpoint : growth rate
Exposure period : 96 hour(s)
Unit : mg/l
Limit test : Yes
Analytical monitoring : Yes
Method : OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year : 1991
GLP : Yes
Test substance : CAS No. 64741-88-4; distillates (petroleum), solvent-refined, heavy paraffinic

Result

: No inhibition of growth or growth rate were measured at the single test concentration of 50% WAF. Since there were no observed effects during the study, the 96-hour "No Observed Effect Concentration" (NOEC) was 50% WAF. The 50% WAF solution was equal to a test substance loading rate of 500 mg/l.

The OECD guideline criterion for cell growth in the control group was met

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Test condition : in this experiment.
Preparation of the Water Accommodated Fraction (WAF): 2.0 grams of test material were placed on 2 Liters of culture medium and stirred via magnetic stirrer for a period of 24 hours prior to the test. Culture medium was prepared according to the guideline formula. After the 24 hour period, stirring was ceased for one hour prior to removing the aqueous phase. The aqueous phase, representing 100% WAF, was then combined with an equal volume of algal suspension. The algal suspension consisted of *Scenedesmus* cells taken from a culture in logarithmic growth phase and diluted with growth medium to a cell density of 3.70×10^4 cells/ml. The algal species *Scenedesmus subspicatus* utilized in this study was supplied by the Culture Centre of Algae and Protozoa (CCAP) c/o Institute of Freshwater Ecology, Cumbria, U.K. Sterile culture medium was inoculated with *Scenedesmus* and incubated under continuous illumination and aeration at 21°C.
10 ml samples of the 50% WAF were taken at times 0 and 96 hours. After adding 10 ml of 1,1,2-trichlorotrifluoroethane, the samples were stored at 4°C until analyzed. Analytical results were not reported.
500 ml of the algal suspension were added to 500 ml of 100% WAF to make the test solution. 100 ml of the test solution was contained in a loosely stoppered 250 ml conical flask. All flasks were incubated and shaken at approximately 100 rpm in an orbital shaker. 6 replicates of a single test concentration and 3 replicates of a control were examined in this study. The flasks were housed under a 24 hour light photoperiod at an intensity of approximately 7,000 lux and a constant temperature of 24°C. No aeration was supplied during the study, however, gas exchange and algal cell suspension was maintained by the orbital shaker. Samples were taken for the determination of algal growth every 24 hours beginning at hour 0 and ending at hour 96. Absorbances were measured at 665 nm with a Jenway 610 Spectrophotometer. At the initiation and completion of the experiment, the cell densities of the control cultures were determined through direct counting aided by a hemacytometer. The pH of all control and test flasks was taken at 0 and 96 hours. The pH at the beginning and end of the experiment in all groups ranged from 8.3 to 8.5 and 9.4 to 9.9, respectively. The area under the curve and growth rate were taken as indices of algal growth and were calculated using the absorbance readings. Percent inhibition values were calculated for area under the curve and growth rate.

Remark : Three other base oil samples have been tested for algal toxicity. The results for all three samples were similar to that described above. Samples tested at one concentration only were as follows:

<u>CAS No.</u>	<u>Result</u>	<u>Ref.</u>
64741-88-4	96-h LL ₀ = 50% WAF	BP Project 301/74
64741-89-5	96-h LL ₀ = 50% WAF	BP Project 301/70
64742-01-4	96-h LL ₀ = 50% WAF	BP Project 301/76

Reliability : (2) valid with restrictions
Only one concentration of the test substance was tested. Results of chemical analyses of test substance concentrations were not reported.
(38) (39) (40) (41)

Species : *Scenedesmus subspicatus* (Algae)
Exposure period : 72 hour(s)
Unit : mg/l
Analytical monitoring : Yes
Method : OECD Guide-line 201 "Algae, Growth Inhibition Test"

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Year : 1994
GLP : Yes
Test substance : Distillate aromatic extract, CAS No. 64742-04-7

Method : Statistical method: One-way analysis of variance
Remark : A 24-hour WAF mixing period was selected based upon a mixing trial using a similar product. No substantial differences in the total organic carbon content in the aqueous phase was seen between 24 and 48-hour mixing periods.

Result : EbLR₅₀ (72-h) = >1000 mg/l WAF
ErLR₅₀ (24-48 h) = >1000 mg/l WAF
No Observed Effect Level (NOEL) = 1000 mg/l WAF

Results of Absorbance Readings:

Absorbance values (mean)

<u>Loading Rate</u>	<u>0-h</u>	<u>24-h</u>	<u>48-h</u>	<u>72-h</u>
0 (Control)	0.026	0.043	0.333	0.574
1000 mg/l WAF	0.026	0.045	0.338	0.590

Results of Percent Inhibition Calculations:

<u>Loading Rate</u>	<u>Percent Inhibition Values</u>		<u>Growth Rate</u> (24-48 h)	<u>%</u> <u>Inhibition</u>
	<u>AUGC %</u> (72-h)	<u>Inhibition</u>		
Control	14.372	--	0.085	--
1000 mg/l WAF	14.706	-2	0.084	1

Results of Total Organic Carbon analyses (mg/l):

<u>Loading Rate</u>	<u>0-h</u>	<u>72 h</u>
0 (control)	23.27	4.636
1000 mg/l WAF	10.16	5.215

Total organic carbon measurements made on the exposure solutions during the test were variable. The authors claim that the carbon analyses do not provide definitive evidence of stability of the test preparations.

Test condition : A 72-h static toxicity test was conducted without renewal of test solutions. Test solutions were prepared as water accommodated fractions (WAF). Nominal loading rates were 0 (control) and 1000 mg/l WAF. The 1000 mg/l WAF solution was made by adding 4 g of test substance in 2 liters of algal culture medium to give a loading rate of 2000 mg/l. The mixture was stirred for 24 hours, taking care to avoid the formation of a vortex or gross mixing. After the stirring period, the solution was allowed to settle for 1 hour, then the aqueous phase was removed. The 2000 mg/l WAF was diluted 50:50 with an algal suspension to create a 1000 mg/l WAF. Algal culture medium was prepared according to the recipe given in OECD Guideline 201.

Scenedesmus subspicatus cultures originated from the Culture Centre of Algae and Protozoa (CCAP), Institute of Freshwater Ecology, Cumbria, U.K. The algal suspension used in the test was prepared by first inoculating sterile culture medium with S. subspicatus taken from a master culture. The suspension was incubated at 21 °C under continuous illumination of approximately 7000 lux until reaching log-phase growth, which was characterized by an absorbance of 0.780 (@665 nm). 300 ml of the suspension was added to 300 ml of the 2000 mg/l WAF solution to achieve 600 ml of 1000 mg/l WAF test solution. This solution had an absorbance of 0.026 and a mean cell density of 3.69×10^4 cells/ml at the start of the test.

Test vessels were 250-ml conical flasks holding 100 ml of test solution. They were loosely stoppered to reduce evaporation. Six replicate flasks of

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inoculated 1000 mg/l WAF solution and three replicate flasks holding inoculated control medium were prepared and incubated for 72 hours under continuous lighting at approximately 24 °C. Separate flasks holding culture medium and 1000 mg/l WAF solution were similarly held and used for total organic carbon analysis at 0 and 72 hours. The pH of the test and control solutions was measured at 0 and 72 hours. Test solution and control solution pH values at 0 and 72 hours ranged 8.0 to 10.0 and 8.0 to 9.8, respectively.

Samples were taken from each flask at 0, 24, 48 and 72 hours, and the absorbance at 665 nm was measured using a Jenway 6100 Spectrophotometer. Cell densities of the control cultures at 0, 24, 48 and 72 hours were measured by direct counting with the aid of a haemocytometer to confirm that absorbance values were well correlated with cell densities to be used to monitor the growth of the test cultures. Area under the growth curve (AUGC) was used as an index of growth, and percent inhibition of the AUGC and percent inhibition of growth rate were used to assess effects of the test substance. The AUGC, average maximum growth rates and the percent inhibition of the AUGC and growth rates were calculated according to OECD Guideline 201. The effective loading rate for biomass (EbLR₅₀) and growth rate (ErLR₅₀) were evaluated using the inhibition data.

Reliability : (1) valid without restriction (65) (82)

Species : *Scenedesmus subspicatus* (Algae)
Exposure period : 96 hour(s)
Unit : mg/l
Analytical monitoring : Yes
Method : Directive 87/302/EEC, part C, p. 89 "Algal inhibition test"
Year : 1991
GLP : Yes
Test substance : Solvent-refined residual oil, CAS No. 64742-01-4

Result : No inhibition of growth or growth rate were measured at the single test concentration of 50% WAF. The 50% WAF solution was equal to a test substance loading rate of 500 mg/l.

Since there was neither a 50% decline in biomass, nor a 50% decline in growth rate, the 96-hour EbC₅₀ and the 0-24 hour ErC₅₀ are reported as being greater than 50% WAF. Since there were no observed effects during the study, the "No Observed Effect Concentration" (NOEC) for the algae exposed to the test material is reported as being equal to 50% WAF. The OECD guideline criterion for cell growth in the control group was met in this experiment.

Test condition : Preparation of the Water Accommodated Fraction (WAF):
2.0 grams of test material were placed on 2 liters of culture medium and stirred via magnetic stirrer for a period of 24 hours prior to the test. After the 24 hour period, stirring was ceased for one hour prior to removing the aqueous phase. The aqueous phase, representing 100% WAF, was then combined with an equal volume of algal suspension.
10 ml samples of the 50% WAF were taken at times 0 and 96 hours. After adding 10 ml of 1,1,2-trichlorotrifluoroethane, the samples were stored at 4°C until analyzed by the sponsor. Results of any analyses were not reported.

Culture Medium:
15 mg/l NH₄Cl

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12mg/l $\text{MgCl}_2 \cdot 6\text{H}_2\text{O}$
18mg/l $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$
15 mg/l $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$
1.6 mg/l KH_2PO_4
0.08 mg/l $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$
0.1 mg/l $\text{Na}_2\text{EDTA} \cdot 2\text{H}_2\text{O}$
0.185 mg/l H_3BO_3
0.415 mg/l $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$
 3×10^{-3} mg/l ZnCl_2
 1.5×10^{-3} mg/l $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$
 10^{-5} mg/l $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$
 7×10^{-3} mg/l $\text{Na}_2\text{MoO}_4 \cdot 2\text{H}_2\text{O}$
50 mg/l NaHCO_3

The algal species *Scenedesmus subspicatus* utilized in this study was supplied by the Culture Centre of Algae and Protozoa (CCAP) c/o Institute of Freshwater Ecology, Cumbria, U.K. Sterile culture medium was inoculated with *Scenedesmus* and incubated under continuous illumination and aeration at 24°C. This produced an algal suspension in log phase growth characterized by an absorbance of 0.451 (at 665 nm). Prior to use, the suspension was diluted to an absorbance of 0.022, yielding a mean cell density of 3.69×10^4 cells/ml.

100 ml of the test solution was contained in a loosely stoppered 250 ml conical flask. All flasks were incubated and shaken at approximately 100 rpm in an orbital shaker. 6 replicates of a single test concentration and 3 replicates of a control were examined in this study. 500 ml of the algal suspension were added to 500 ml of 100% WAF to make the test solution. The flasks were housed under a 24 hour light photoperiod at an intensity of approximately 7,000 lux and a constant temperature of 24 °C. No aeration was supplied during the study, however, gas exchange and algal cell suspension was maintained by the orbital shaker. Samples were taken for the determination of algal growth every 24 hours beginning at hour 0 and ending at hour 96. Absorbances were measured at 665 nm with a Jenway 610 Spectrophotometer. At the initiation and completion of the experiment, the cell densities of the control cultures were determined through direct counting aided by a haemocytometer. The pH of all control and test flasks was taken at 0 and 96 hours. The pH at the beginning and end of the experiment in all groups ranged from 8.0 to 8.1 and 9.6 to 10.0, respectively.

The area under the curve and growth rate were taken as indices of algal growth and were calculated using the absorbance readings:

$$A = (N1 - N2)/2 \times t1 + (N1+N2 - 2N0)/2 \times (t2 - t1) \\ + (Nn-1 + Nn - 2N0)/2 \times (tn - tn-1)$$

A= area

N0 = absorbance at t0

N1 = absorbance at t1

Nn = absorbance at tn

t1 = time of first measurement (hours from start)

tn = time of nth measurement (hours from start)

Growth Rate: (determined only for 0 - 24 hour period)

$$u = (\ln Nn - \ln N1)/(tn - t1)$$

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Calculation of Inhibition:
Percentage inhibition of growth (IA) and growth rate (Iu) were calculated by the following equations:

$$IA = (Ac - At)/Ac \times 100$$

and

$$Iu = (uc - ut)/uc \times 100$$

Reliability : (2) valid with restrictions
Only one concentration of the test substance was tested. Results of chemical analyses of test substance concentrations were not reported. (27)

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Species : Daphnia magna (Crustacea)
Exposure period : 21 day(s)
Unit : mg/l
Analytical monitoring : Yes
Method : OECD Guide-line 202, part 2 "Daphnia sp., Reproduction Test"
Year : 1995
GLP : Yes
Test substance : CAS No. 64741-88-4; distillates (petroleum), solvent-refined, heavy paraffinic

Result : After 14 and 21 days of exposure, there were no statistically significant differences between the control group and the 10 and 1000 mg/ml WAF test groups in terms of survival or reproduction (young produced per adult). In addition, there were no apparent effects on the F1 generation produced during the test. The numbers of unhatched eggs and dead young were low in all treatment groups.

The NOEC for survival and reproduction was the maximum test concentration, 1000 mg/ml WAF.

The test met the validation criteria for 1) dissolved oxygen at least 60%, 2) pH deviation not greater than 0.3, 3) control mortality not greater than 20%, 4) first young (control group) within 9 days, 5) cumulative young per female (control group) at least 20 after 14 days and at control group at least 3.

Test condition : Preparation of the WAF:
20 and 2000 mg of test material were each separately placed in 2 liters of reconstituted water (water hardness approximately 270 mg/ml as CaCO₂) and stirred via magnetic stirrer for a period of 24 hours prior to the test. After the 24-hour period, stirring was ceased for one hour prior to removing the aqueous phase.

Test Organism Culture:

Adult Daphnia magna were maintained in polypropylene vessels containing approximately 2 liters of reconstituted water at a temperature of 21°C. The organisms were supplied by the Institut National de Recherche Appliquée (IRCHA) France. The lighting was held at 16:8 hour light:dark photoperiod. Gravid adults were isolated 24 hours prior to the initiation of the test, the young daphnids produced overnight were removed and utilized for testing.

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Test Procedure:

The aqueous phase of each WAF was removed and 400-ml aliquots were apportioned to five, 500-ml glass flasks. A similar number of control flasks containing reconstituted water also were prepared. The fifth flask from each group was taken for Total Organic Carbon analysis of the exposure media. At the start of the test, 10 daphnids were placed within each test flask, and all flasks were covered to reduce evaporation. Each vessel received approximately 3.75×10^9 cells/ml of a mixed unicellular algae culture as a daily feeding. Fresh WAFs were prepared on days 0, 2, 4, 7, 9, 11, 14, 16, and 18, and the adult daphnids were transferred from the old to the fresh solutions. The numbers of live and dead Daphnia of the parental generation were counted daily. At each test media renewal, Daphnia with eggs or young in the brood pouch, discarded unhatched eggs, and the number of live and dead filial Daphnia were counted.

Temperature was recorded daily for the duration of the experiment, while dissolved oxygen and pH were recorded prior to and after each media renewal. Measurements of TOC were made in the fresh and old test solutions 3 times a week over 21 days. Dissolved oxygen in the control, 10, and 1000 mg/ml WAF groups ranged from 7.9 to 8.3, from 7.9 to 8.3, and from 7.8 to 8.3, respectively. Water pH in the control, 10, and 1000 mg/ml WAF groups ranged from 7.7 to 7.8, from 7.7 to 7.8, and from 7.7 to 7.8, respectively. The temperature within all test groups remained constant at 21.0 °C. The results of the TOC analysis did not demonstrate a cases the TOC of the control water was higher than that of the test groups. The TOC in the old media tended to be higher than fresh solutions.

Reliability

: (2) valid with restrictions

The analytical results provided no definitive evidence of stability of the test preparations. Only two test concentrations were run.

(71)

Species : Daphnia magna (Crustacea)
Exposure period : 21 day(s)
Unit : mg/l
Analytical monitoring : Yes
Method : OECD Guide-line 202, part 2 "Daphnia sp., Reproduction Test"
Year : 1995
GLP : Yes
Test substance : Solvent-refined residual oil, CAS No. 64742-01-4

Result

: After 14 and 21 days of exposure, there were no statistically significant differences between the control group and the 10 and 1000 mg/l WAF test groups in terms of survival or reproduction (young produced per adult). In addition, there were no apparent effects on the F1 generation produced during the test. The numbers of unhatched eggs and dead young were low in all treatment groups.

The NOEC for survival and reproduction was the maximum test concentration, 1000 mg/l WAF.

The test met the validation criteria for

- 1) dissolved oxygen >60%
- 2) pH deviation W0.3
- 3) control mortality W
- 4) first young (control group) within 9 days
- 5) cumulative young per female (control group) D20 after 14 days and D40 after 21 days

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Test condition : 6) number of broods per control group D3.
Preparation of Reconstituted Water:
Reconstituted water was prepared by combining 25 ml of each of the following stock solutions and bringing to a volume of 1 Liter with deionized water (conductivity $<5 \text{ S cm}^{-1}$; pH = 7.8 \pm 0.2). The reconstituted water was aerated until the dissolved oxygen was approximately air saturation. The reconstituted water as prepared had a total hardness of approximately 270 mg/l as CaCO_3 .

- 1) 11.76 g/l $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$
- 2) 4.63 g/l $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$
- 3) 2.59 g/l NaHCO_3
- 4) 0.23 g/l KCl

Preparation of the WAF:
20 and 2000 mg of test material were each separately placed in 2 liters of reconstituted water and stirred via magnetic stirrer for a period of 24 hours prior to the test. After the 24-hour period, stirring was ceased for one hour prior to removing the aqueous phase.

Test Organism Culture:
Adult *Daphnia magna* were maintained in polypropylene vessels containing approximately 2 liters of reconstituted water at a temperature of 21 °C. The organisms were supplied by the Institut National de Recherche Appliquée (IRCHA) France. The lighting was held at at 16:8 hour light:dark photoperiod. Gravid adults were isolated 24 hours prior to the initiation of the test, the young daphnids produced overnight were removed and utilized for testing.

Test Procedure:
The aqueous phase of each WAF was removed and 400-ml aliquots were apportioned to five, 500-ml glass flasks. A similar number of control flasks containing reconstituted water also were prepared. The fifth flask from each group was taken for Total Organic Carbon analysis of the exposure media. The four remaining flasks of each group were used to hold test daphnids. At the start of the test, 10 daphnids were placed within each test flask, and the flasks were covered to reduce evaporation. Fresh WAFs were prepared on days 0, 2, 4, 7, 9, 11, 14, 16, and 18, and the adult daphnids were transferred from the old to the fresh solutions. The old solutions were strained through a fine mesh and any retained young daphnids (live or dead) and unhatched eggs were counted using a stereo microscope prior to being discarded.

Each vessel received approximately 3.75×10^9 cells/ml of a mixed unicellular algae culture as a daily feeding. This level allowed for continuous feeding throughout the experiment. The numbers of live and dead *Daphnia* of the parental generation were counted daily. At each test media renewal, *Daphnia* with eggs or young in the brood pouch, discarded unhatched eggs, and the number of live and dead filial *Daphnia* were counted.

Temperature was recorded daily for the duration of the experiment, while dissolved oxygen and pH were recorded prior to and after each media renewal. Measurements of TOC were made in the fresh and old test solutions. Dissolved oxygen in the control, 10, and 1000 mg/L WAF groups ranged from 7.9 to 8.5, from 7.9 to 8.5, and from 7.9 to 8.5, respectively. Water pH in the control, 10, and 1000 mg/l WAF groups ranged from 7.6 to 7.8, from 7.6 to 7.8, and from 7.6 to 7.8, respectively. The temperature within all test groups remained constant at 21.0 °C. The results of the TOC

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analysis did not demonstrate a direct relationship with WAF concentration, and in many cases the TOC of the control water was higher than that of the test groups. The TOC in the old media tended to be higher than fresh solutions.

Analytical Monitoring:

The stability of the test material (both freshly renewed and old) in the test solutions was verified by Total Organic Carbon (TOC) analysis of the control and the WAF loaded groups 3 times per week over 21 days.

Reliability : (2) valid with restrictions
The analytical results provided no definitive evidence of stability of the test preparations
(68) (79) (84) (108) (121) (125) (129)

Exposure period : 21 day(s)
Unit : mg/l

Result : In addition to the studies described above, studies have been reported for nine further base oil samples in 21 day studies with *D. magna*. These have been added as supporting evidence to the detailed robust summaries given above for chronic toxicity to aquatic invertebrates. In each case OECD guideline 202 part 2 was used as the method.
The results are summarized below:

<u>CAS No.</u>	<u>Result</u>	<u>Reference</u>
64741-88-4	21-d LL ₀ = 1000 mg/l WAF	BP 692/039
64741-88-4	21-d LL ₀ = 1000 mg/l WAF	BP 692/040
64741-88-4	21-d LL ₀ = 1000 mg/l WAF	Shell Exp. 5922
64741-89-5	21-d LL ₀ = 1000 mg/l WAF	BP 692/036
64741-89-5	21-d LL ₀ = 1000 mg/l WAF	BP 692/037
64741-95-3	21-d LL ₀ = 1000 mg/l WAF	BP 692/042
64742-01-4	21-d LL ₀ = 1000 mg/l WAF	BP 692/041
64742-53-6	21-d LL ₀ = 10 mg/l WAF	Shell Exp. 6215
64742-55-8	21-d LL ₀ = 1000 mg/l WAF	Shell Exp. 5922
64742-65-0	21-d LL ₀ = 1000 mg/l WAF	Shell Exp. 5922

(70) (72) (73) (74) (75) (76) (114) (115)

Species : *Daphnia magna* (Crustacea)
Exposure period : 21 day(s)
Unit : mg/l
Analytical monitoring : Yes
Method : OECD Guide-line 202, part 2 "*Daphnia* sp., Reproduction Test"
Year : 1995
GLP : Yes
Test substance : Distillate aromatic extract, CAS N. 64742-04-7

Remark : A 24-hour WAF mixing period was selected based upon a mixing trial using a similar product. No substantial differences in the total organic carbon content in the aqueous phase was seen between 24 and 48-hour mixing periods.

Result : Summary of Findings:

	Nominal loading rate (mg/l)		
	0	10	1000
% survival of parental generation	100	100	100

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No live young				
Total	2105	2046	2108	
per Female	53	51	53	
No. dead				
Total	0	0	0	
per Female	0	0	0	
No. unhatched eggs				
Total	2	1	0	
per Female	<1	<1	0	

Lethal Effects on Parental Generation:

21 d ELR₅₀ (survival) = >1000 mg/l WAF

Sublethal Effects on Parental Generation:

21-d ELR₅₀ (reproduction) = >1000 mg/l WAF

Effects on Filial (F1) Generation: No discernable effects noted.

No Observed Effect Level (NOEL) for the Test:

NOEL = 1000 mg/l WAF

Ranges of TOC Measurements (mg C/l):

Nominal

Loading Rate	Fresh Solutions	Old Solutions
0 (control)	1.243 - 3.161	1.438 - 3.645
10	1.492 - 5.149	0.635 - 2.753
1000	1.608 - 3.975	1.109 - 5.181

The author's claim that the total organic carbon measurements made on the control and test solutions were variable and tended to approximate the detection limit. Furthermore, the carbon analyses do not provide definitive evidence of stability of the test preparations.

Validation Criteria:

All validation criteria were met for the test. These criteria included:

- 1) control mortality 20%
- 2) dissolved oxygen concentration 60% saturation
- 3) pH deviation 0.3
- 4) time to production of first young in control group 9 days
- 5) cumulative young produced per female in control group
20 @ 14 d;
40 @ 21 d
- 6) number of broods per control group 3

Test condition

: A semi-static 21-day chronic toxicity test was conducted with renewal of test solutions three times per week. Test solutions were prepared as water accommodated fractions (WAF). Nominal loading rates were 0 (control), 10, and 1000 mg/l. The 10 and 1000 mg/l WAF solutions were prepared by adding 0.02 and 2 g, respectively of test substance to 2 liters of dilution water. The mixtures were stirred for 24 hours, taking care to avoid the formation of a vortex or gross mixing. After the stirring period, the solutions were allowed to settle for 1 hour, then the aqueous phase of each was removed and dispensed into replicate glass test vessels. Glass flasks served as replicate test vessels with each replicate holding 400 ml of test solution. There were four replicate test vessels per treatment and each vessel contained 10 daphnids at test initiation. A fifth replicate of each test level was prepared and was used for sampling for total organic carbon

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(TOC) analyses.

Dilution water was reconstituted freshwater having a total hardness of approximately 270 mg/l as CaCO₃.

Daphnids used in the test had been cultured at 21 °C in the laboratory in reconstituted water. The original culture was obtained from the Institut National de Recherche Chimique Appliquee, France. Cultures were fed daily with a suspension of mixed algae (predominately Chlorella sp.). Gravid adults were isolated 24 hours prior to initiation of the test, and the young daphnids produced overnight were used for testing. The daphnid loading rate during the test was 40 ml solution per daphnid. Daphnids were fed daily 10 l of a mixed unicellular algal suspension (equivalent to 3.3 x 10⁹ cells/ml and 0.24 mg C/daphnid/day). Live and dead daphnids of the parental generation were counted daily. At each renewal period (three times per week), the general condition and size of parental generation daphnids were evaluated, and the numbers of adults with eggs or young in the brood pouch, numbers of live and dead F1 generation daphnids, and the numbers of discarded unhatched eggs were determined. At the renewal periods, adult daphnids were transferred to fresh media by wide-bore pipette then the contents of each vessel were passed through a fine mesh. Young daphnids (live and dead) and unhatched eggs were collected in this manner and counted. Young daphnids were considered dead if no sign of movement was apparent during microscopic examination. Adult daphnids which were unable to swim for approximately 15 seconds after gentle agitation were considered dead.

The test was conducted under a photoperiod of 16 h light and 8 h dark and 21 °C. No aeration was applied during the test. Temperature was recorded daily, and dissolved oxygen, pH and temperature were recorded before and after each renewal period. TOC analyses were carried out on fresh test solutions on days 0, 2, 5, 7, 9, 12, 14, 16, and 19, and on old solutions on days 2, 5, 7, 9, 12, 14, 16, 19, and 21. Water quality in the fresh and old solutions remained consistent during the test. The pH of fresh and old solutions ranged from 7.7 to 7.9, dissolved oxygen ranged from 7.8 to 8.4 mg O₂/l, and temperature remained a constant 21.0 °C.

Reliability

: (1) valid without restriction

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5.1.1. ACUTE ORAL TOXICITY

Acute Toxicity

Test Substance

Category Chemical (CAS #):	64742-54-7
Test Substance (CAS #):	64742-54-7; Ssangyong 150N; Distillates (petroleum), hydrotreated heavy paraffinic; Viscosity was 161 SUS at 100°F and 45 SUS at 210°F.
Test Substance Purity/Composition and Other Test Substance Comments :	Ssangyong 150N (CRU 83272) No other information
Category Chemical Result Type :	Measured
Unable to Measure or Estimate Justification :	
METHOD	
Route of Administration:	Oral
Other Route of Administration:	
Type of Exposure:	Single oral gavage
Species:	Rat
Other Species:	

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Mammalian Strain:	Sprague-Dawley
Other Strain:	
Gender:	Male and female
Number of Animals per Dose:	5 per sex
Concentration:	100%
Dose:	15 g/kg body weight
Year Study Performed :	1983
Method/Guideline Followed:	Similar to guideline limit test
GLP:	Study was conducted in accordance with FDA Good Laboratory Practices.
Method/Guideline and Test Condition Remarks:	Animals were observed frequently on the day of dosing and daily afterward for 14 days. Body weights were measured on days 0, 7, and 14. Animals were sacrificed on day 14.

TEST RESULTS

Concentration (LC/LD)

LC/LD	%:	Value Description:	Value or Lower Concentration:	Upper Concentration:	Units:
LD	50	>		15,000	mg/kg body weight
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

Number of Deaths (Male):	0
Number of Deaths (Female):	0

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Number of Deaths (Total):	0
Results Remarks:	No treatment-related clinical signs were observed except for discharge covering the perineum on the day of dosing. All surviving animals gained weight during the study.
Conclusion:	The oral LD50 of the test substance was >15,000 mg/kg.
RELIABILITY/DATA QUALITY	
Reliability:	2 – Reliable with restrictions
Reliability Remarks:	Comparable to guideline limit study; no gross necropsy information reported
Key Study Sponsor Indicator:	Key
REFERENCE	
Reference:	The acute oral toxicity of hydrotreated base oil in albino rats. Test report on Mobil study 32751. Mobil Environmental and Health Science Laboratory, Princeton, NJ. 1983

5. Toxicity

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Acute Toxicity

Test Substance

Category Chemical (CAS #):	64742-65-0
Test Substance (CAS #):	64742-65-0; Stock 141; Distillates (petroleum), solvent-dewaxed heavy paraffinic Its viscosity was ~102 SUS at 100°F and 40 SUS at 210°F (18.8 cSt at 40°C and 4.0 cSt at 100°C).
Test Substance Purity/Composition and Other Test Substance Comments :	Stock 141 (Sample no. 1720811) No compositional information
Category Chemical Result Type :	Measured
Unable to Measure or Estimate Justification :	

METHOD

Route of Administration:	Oral
Other Route of Administration:	
Type of Exposure:	Single oral gavage
Species:	Rat
Other Species:	
Mammalian Strain:	Sprague-Dawley
Other Strain:	

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Gender:	Male and female
Number of Animals per Dose:	5 per sex
Concentration:	100%
Dose:	15 g/kg body weight
Year Study Performed :	1982
Method/Guideline Followed:	Other; similar to guideline limit test
GLP:	Study was conducted in accordance with FDA Good Laboratory Practices.
Method/Guideline and Test Condition Remarks:	A group of five male and five female fasted Sprague-Dawley rats were dosed once by oral gavage with the liquid test material at a dose level of 15 g/kg. They were observed frequently on the day of treatment and daily thereafter for 14days. There were no clinical signs of toxicity observed during the observation period. The animals were weighed on days 0, 7 and 14. The animals were sacrificed and discarded after the 14 day observation period.

TEST RESULTS

Concentration (LC/LD)

LC/LD	%:	Value Description:	Value or Lower Concentration:	Upper Concentration:	Units:
LD	50	>		15,000	mg/kg body weight
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

Number of Deaths (Male):	0
Number of Deaths (Female):	0
Number of Deaths (Total):	0

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Results Remarks:	All animals gained weight throughout the study. There were no deaths after administration of the test compound. No treatment-related clinical signs were observed except for that all animals had soft stool on the day of dosing, but were normal within 24 hours. The oral LD50 of the test material was judged greater than 15 g/kg.
Conclusion:	The oral LD50 of the test substance was >15,000 mg/kg.
RELIABILITY/DATA QUALITY	
Reliability:	2 – Reliable with restriction
Reliability Remarks:	Comparable to guideline limit study;; no gross necropsy information reported
Key Study Sponsor Indicator:	Key
REFERENCE	
Reference:	The acute oral toxicity of Mobil base stock 141 in albino rats. Test report on Mobil study 20801. Mobil Environmental and Health Science Laboratory, Princeton, NJ. 1982

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Acute Toxicity

Test Substance

Category Chemical (CAS #):	64742-65-0
Test Substance (CAS #):	64742-65-0; MLDW 100" PN (Stock 142); Paraffin oils (petroleum), catalytic dewaxed heavy Its viscosity was 22.33 cSt at 40°C (~100 SUS) and 4.23 cSt at 100°C.
Test Substance Purity/Composition and Other Test Substance Comments :	MLDW 100" PN; Stock 142 (Sample no. 82192) No other information
Category Chemical Result Type :	Measured
Unable to Measure or Estimate Justification :	

METHOD

Route of Administration:	Oral
Other Route of Administration:	
Type of Exposure:	Single oral gavage
Species:	Rat
Other Species:	
Mammalian Strain:	Sprague-Dawley

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Other Strain:	
Gender:	Male and female
Number of Animals per Dose:	5 per sex
Concentration:	100%
Dose:	15 g/kg body weight
Year Study Performed :	1983
Method/Guideline Followed:	Similar to guideline limit test
GLP:	Study was conducted in accordance with FDA Good Laboratory Practices.
Method/Guideline and Test Condition Remarks:	Animals were observed frequently on the day of dosing and daily afterward for 14 days. Body weights were measured on days 0, 7, and 14. Animals were sacrificed on day 14.

TEST RESULTS

Concentration (LC/LD)

LC/LD	%:	Value Description:	Value or Lower Concentration:	Upper Concentration:	Units:
LD	50	>		15,000	mg/kg body weight
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

Number of Deaths (Male):	1
Number of Deaths (Female):	0
Number of Deaths (Total):	1

5. Toxicity

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Results Remarks:	One male died on the day of dosing as a result of an injury during dosing and not from toxicity of the test substance. No treatment-related clinical signs were observed except for soft stool on the day of dosing. All surviving animals gained weight during the study.
Conclusion:	The oral LD50 of the test substance was >15,000 mg/kg.
RELIABILITY/DATA QUALITY	
Reliability:	2 – Reliable with restrictions
Reliability Remarks:	Comparable to guideline limit study; no gross necropsy information reported
Key Study Sponsor Indicator:	Key
REFERENCE	
Reference:	The acute oral toxicity of MLDW 100” PN in albino rats. Test report on Mobil study 30231. Mobil Environmental and Health Science Laboratory, Princeton, NJ. 1983

Acute Toxicity**Test Substance**

Category Chemical (CAS #):	64741-50-0
Test Substance (CAS #):	64741-50-0; API 84-01; Unrefined base oil
Test Substance Purity/Composition and Other Test Substance Comments :	No information
Category Chemical Result Type :	Measured

Type : Oral LD₅₀
Value : > 5000 mg/kg bw
Species : Rat
Strain : Sprague-Dawley
Sex : Male/female
Number of animals : 5
Vehicle : None - administered undiluted
Year : 1986
GLP : Yes
Test substance : Unrefined base oil Sample API 84-01 [CAS 64741-50-0] See section 1.1.1.

Method : A single dose of undiluted test material (5g/kg) was administered orally to 5 male and 5 female fasted rats. Food and water was made available ad-lib immediately after dosing.
 The animals were observed for clinical signs and mortality at hourly intervals for the first 6 hours post dosing and twice daily thereafter. Body weights were recorded prior to fasting, prior to dosing and at 7 and 14 days post dosing.
 At 14 days, all surviving animals were killed and subjected to a gross necropsy examination.

Result : There were no deaths during the study and growth rates were unaffected by dosing. Clinical signs that occurred during the first 3 days included: hypoactivity, diarrhea and a yellow-stained anal area. All animals returned to normal by day 14. At gross necropsy, there were no visible lesions.

Reliability : (1) valid without restriction

(13)

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(13)

American Petroleum Institute (1986)
Acute oral toxicity study in rats
Acute dermal toxicity study in rabbits
Primary dermal irritation study in rabbits
Primary eye irritation study in rabbits
Dermal sensitization study in Guinea pigs
API 84-01 Light paraffinic distillate CAS 64741-50-0
API Med. Res. Publ.: 33-30595

Acute Toxicity**Test Substance**

Category Chemical (CAS #):	64742-53-6
Test Substance (CAS #):	64742-53-6; API 83-12; Highly refined base oil
Test Substance Purity/Composition and Other Test Substance Comments :	API 83-12 No further information
Category Chemical Result Type :	Measured

Type : Oral LD₅₀
Value : > 5000 mg/kg bw
Species : Rat
Strain : Sprague-Dawley
Sex : Male/female
Number of animals : 5
Vehicle : None - administered undiluted
Year : 1986
GLP : Yes
Test substance : Highly refined Base oil Sample API 83-12 [CAS64742-53-6] See section 1.1.1.

Method : A single dose of undiluted test material (5g/kg) was administered orally to 5 male and 5 female fasted rats. Food and water was made available ad-lib immediately after dosing.
 The animals were observed for clinical signs and mortality at hourly intervals for the first 6 hours post dosing and twice daily thereafter. Body weights were recorded prior to fasting, prior to dosing and at 7 and 14 days post dosing. At 14 days, all surviving animals were killed and subjected to a gross necropsy examination.

Result : There were no deaths during the study.
 Clinical signs observed included: hypoactivity, yellow-stained anal area, hair loss in the urogenital region and swollen hind paws. All animals returned to normal by day 3 and had gained weight by day 7. At necropsy, there were no visible lesions except in one female in which the spleen was cystic, mottled red and tan and had a rough surface. In this animal the pancreas adhered to the entire surface of the spleen.

Reliability : (1) valid without restriction

(12)

5. Toxicity

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(12)

American Petroleum Institute (1986)
Acute oral toxicity study in rats
Acute dermal toxicity study in rabbits
Primary dermal irritation study in rabbits
Primary eye irritation study in rabbits
Dermal sensitization study in Guinea pigs
API 83-12 Hydrotreated light naphthenic distillate CAS
64742-53-6
API Med. Res. Publ.: 33-30592

5. Toxicity

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Acute Toxicity

Test Substance

Category Chemical (CAS #):	64742-56-9; 64742-56-0; 64742-65-0; 64741-97-5; 64741-96-4; 64742-52-5
Test Substance (CAS #):	64742-56-9; API 78-9; Solvent dewaxed light paraffinic distillate 64742-56-0; API 78-10; Solvent dewaxed heavy paraffinic distillate 64742-65-0; API 79-3; Solvent dewaxed heavy paraffinic distillate 64742-65-0; API 79-4; Solvent dewaxed heavy paraffinic distillate 64742-65-0; API 79-5 Solvent dewaxed heavy paraffinic distillate Tufflo 6056; White mineral oil 64741-97-5; API 78-5; Solvent refined light naphthenic distillate 64741-96- 4; API 79-1; Solvent refined heavy naphthenic distillate 64742-52-5; API 83-15; Hydrotreated heavy naphthenic distillate
Test Substance Purity/Composition and Other Test Substance Comments :	API 78-9 API 78-10 API 79-3 API 79-4 API 79-5 Tufflo 6056 API 78-5 API 79-1 API 83-15 No other information
Category Chemical Result Type :	Measured

Type : Oral LD₅₀
Species : Rat
Test substance : Various Base oils

Remark : CONCAWE summarized the data available on the acute oral toxicity of lubricating oil base stocks. The data are shown in the following table.

	CAS No.	Oral LD50 (g/kg)	API Report No.
Paraffinic distillates			
Solvent dewaxed, light			
API 78-9	64742-56-9	>5	29-33104
Solvent dewaxed, heavy			
API 78-10*	64742-56-0	>5	29-33105

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API 79-3	64742-65-0	>5	29-33067
API 79-4	64742-65-0	>5	29-33066
API 79-5	64742-65-0	>5	29-33068
White mineral oil			
Tufflo 6056*		>5	39-31651

Naphthenic distillates

Solvent refined, light			
API 78-5	64741-97-5	>5	29-33106
Solvent refined, heavy			
API 79-1	64741-96-4	>5	29-33065
Hydrotreated, heavy			
API 83-15	64742-52-5	>5	33-32639

* Although these materials are not included in the HPV Lubricating base stocks category, they are similar to other materials in the category and provide supportive information.

(2) (3) (4) (5) (6) (7) (8) (14) (81)

- (2) American Petroleum Institute (1982)
Acute toxicity tests of API sample 78-10 paraffinic oil (150 SUS/100 °F)
API Med. Res. Publ. 29-33105
- (3) American Petroleum Institute (1982)
Acute toxicity tests of API sample 78-5 naphthenic oil (150 SUS/100 °F)
API Med. Res. Publ. 29-33106
- (4) American Petroleum Institute (1982)
Acute toxicity tests of API sample 78-9 paraffinic oil (70 SUS/100 °F)
API Med. Res. Publ. 29-33104
- (5) American Petroleum Institute (1982)
Acute toxicity tests of API sample 79-1 naphthenic oil (90 SUS/210 °F)
API Med. Res. Publ. 29-33065
- (6) American Petroleum Institute (1982)
Acute toxicity tests of API sample 79-3 paraffinic oil (350 SUS/100 °F)
API Med. Res. Publ. 29-33067
- (7) American Petroleum Institute (1982)
Acute toxicity tests of API sample 79-4 paraffinic oil (550 SUS/100 °F)
API Med. Res. Publ. 29-33066
- (8) American Petroleum Institute (1982)
Acute toxicity tests of API sample 79-5 paraffinic oil (800 SUS/100 °F)
API Med. Res. Publ. 29-33068

5. Toxicity

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- (14) American Petroleum Institute (API).1986. Acute oral toxicity study in rats. Acute dermal toxicity study in rabbits. Primary dermal irritation study in rabbits. Primary eye irritation study in rabbits. Dermal sensitization study in guinea pigs. API sample 83-15 hydrotreated heavy naphthenic distillate. (CAS 64742-52-5). API Health Environ. Sci. Dep. Rep. 33-32639
- (81) CONCAWE (1997)
Lubricating oil basestocks
Product dossier No. 97/108
CONCAWE, Brussels

5. Toxicity

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5.1.2. ACUTE INHALATION TOXICITY

Acute Toxicity

Test Substance

Category Chemical (CAS #):	64742-65-0
Test Substance (CAS #):	64742-65-0; MLDW 100" PN (Stock 142); Paraffin oils (petroleum), catalytic dewaxed heavy Its viscosity was 22.33 cSt at 40°C (~100 SUS) and 4.23 cSt at 100°C.
Test Substance Purity/Composition and Other Test Substance Comments :	MLDW 100" PN; Stock 142; (Sample no. 82192) No other information
Category Chemical Result Type :	Measured
Unable to Measure or Estimate Justification :	
METHOD	
Route of Administration:	Inhalation
Other Route of Administration:	
Type of Exposure:	Acute (4-hour exposure)
Species:	Rat
Other Species:	

5. Toxicity

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Mammalian Strain:	Sprague-Dawley
Other Strain:	
Gender:	Male and female
Number of Animals per Dose:	10 per sex per dose
Concentration:	0 (sham-exposed), 100, 510, or 2,400 mg/m ³ aerosolized test substance
Dose:	
Year Study Performed :	1983
Method/Guideline Followed:	Comparable to guideline study
GLP:	The study was conducted in accord with EPA GLPs.
Method/Guideline and Test Condition Remarks:	Rats were exposed in whole-body chambers for 4 hours to a mean measured concentration of 0 (sham-exposed), 0.10, 0.51, or 2.40 mg/L of aerosolized test substance measured gravimetrically and with an IR backscatter detector. Mass median aerodynamic diameters were 2.5, 1.8, and 1.7 µm, respectively. Half of the animals in each group were sacrificed on the day after exposure; the remaining animals were observed daily and sacrificed at 2 weeks after exposure. Endpoints included observations during exposure, individual clinical signs pre-exposure, immediately after exposure, and daily thereafter until sacrifice. Body weights were measured on days -3, 1, 2, 4, 8, 12, and 16. All animals were necropsied and observed for macroscopic abnormalities. Weights of liver, kidney, and lung (wet and dry, right middle lobe) were measured. Histological slides were prepared of the lung, nose, liver, kidney, and mediastinal lymph nodes. Slides from the control and high-dose group were evaluated by a pathologist.

TEST RESULTS

Concentration (LC/LD)

LC/LD	%:	Value Description:	Value or Lower Concentration:	Upper Concentration:	Units:
LC	50	>		2,400	Mg/m ³
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

5. Toxicity

Id Lubricating oil
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Number of Deaths (Male):	0
Number of Deaths (Female):	0
Number of Deaths (Total):	0
Results Remarks:	No animals died during the study and there were no significant treatment-related changes in clinical signs or body weight. No treatment-related changes were seen in the other endpoints at either sacrifice.
Conclusion:	The 4-hour LC50 was >2.40 mg/L (2,400 mg/m ³) and no significant treatment-related toxicity was observed.
RELIABILITY/DATA QUALITY	
Reliability:	1 – Reliable without restrictions
Reliability Remarks:	Comparable to guideline study
Key Study Sponsor Indicator:	Key
REFERENCE	
Reference:	Acute inhalation toxicity of aerosolized MLDW 100” PN (Stock 142). Final report for Mobil study 30236. Mobil Environmental and Health Science Laboratory. 1984

5. Toxicity

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Acute Toxicity

Test Substance

Category Chemical (CAS #):	64742-65-0
Test Substance (CAS #):	64742-65-0; Stock 141; Distillates (petroleum), solvent-dewaxed heavy paraffinic Its viscosity was ~102 SUS at 100°F and 40 SUS at 210°F (18.8 cSt at 40°C and 4.0 cSt at 100°C).
Test Substance Purity/Composition and Other Test Substance Comments :	Stock 141 (CRU No. 1720811) No other information
Category Chemical Result Type :	Measured
Unable to Measure or Estimate Justification :	

METHOD

Route of Administration:	Inhalation
Other Route of Administration:	
Type of Exposure:	Acute (4-hour exposure)
Species:	Rat
Other Species:	
Mammalian Strain:	Sprague-Dawley

5. Toxicity

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Other Strain:	
Gender:	Male and female
Number of Animals per Dose:	10 per sex per dose
Concentration:	0 (sham-exposed), 110, 520, or 2,460 mg/m ³ aerosolized test substance
Dose:	
Year Study Performed :	1983
Method/Guideline Followed:	Comparable to guideline study
GLP:	The study was conducted in accord with EPA GLPs.
Method/Guideline and Test Condition Remarks:	Rats were exposed in whole-body chambers for 4 hours to a mean measured concentration of 0 (sham-exposed), 0.11, 0.52, or 2.46 mg/L of aerosolized test substance measured gravimetrically and with an IR backscatter detector. Mass median aerodynamic diameters were 2.4, 1.8, and 1.6 µm, respectively. Half of the animals in each group were sacrificed on the day after exposure; the remaining animals were observed daily and sacrificed at 2 weeks after exposure. Endpoints included observations during exposure, individual clinical signs pre-exposure, immediately after exposure, and daily thereafter until sacrifice. Body weights were measured on days -3, 1, 2, 4, 8, and 16. All animals were necropsied and observed for macroscopic abnormalities. Weights of liver, kidney, and lung (wet and dry, right middle lobe) were measured. Histological slides were prepared of the lung, nose, liver, kidney, and mediastinal lymph nodes. Slides from the control and high-dose group were evaluated by a pathologist.

TEST RESULTS

Concentration (LC/LD)

LC/LD	%:	Value Description:	Value or Lower Concentration:	Upper Concentration:	Units:
LC	50	>		2,460	mg/m ³
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

5. Toxicity

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Number of Deaths (Male):	0
Number of Deaths (Female):	0
Number of Deaths (Total):	0
Results Remarks:	No animals died during the study and there were no significant treatment-related changes in clinical signs or body weight. No treatment-related changes were seen in the other endpoints at either sacrifice.
Conclusion:	The 4-hour LC50 was >2.5 mg/L (2,500 mg/m ³) and no significant treatment-related toxicity was observed.
RELIABILITY/DATA QUALITY	
Reliability:	1 – Reliable without restrictions
Reliability Remarks:	Comparable to guideline study
Key Study Sponsor Indicator:	Key
REFERENCE	
Reference:	Acute inhalation toxicity of aerosolized stock 141. Biophase and pathology reports for Mobil study 31011. Mobil Environmental and Health Science Laboratory. 1984

5. Toxicity

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5. Toxicity

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Acute Toxicity

Test Substance

Category Chemical (CAS #):	64742-56-9
Test Substance (CAS #):	64742-56-9 ; MRD-87-099; Distillates (petroleum), solvent-dewaxed light paraffinic
Test Substance Purity/Composition and Other Test Substance Comments :	MRD -87-099 No other information
Category Chemical Result Type :	Measured
Unable to Measure or Estimate Justification :	

METHOD

Route of Administration:	Inhalation
Other Route of Administration:	
Type of Exposure:	Acute (4-hour exposure)
Species:	Rat
Other Species:	
Mammalian Strain:	Sprague-Dawley

5. Toxicity

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Other Strain:	
Gender:	Male and female
Number of Animals per Dose:	5 per sex per dose
Concentration:	0 (sham-exposed) and 5,399 mg/m ³ aerosolized test substance
Dose:	
Year Study Performed :	1987
Method/Guideline Followed:	40 CFR 798.1150 Acute Inhalation Toxicity and OECD Guideline 403 (Acute Inhalation Toxicity).
GLP:	The study was conducted in accord with EPA GLPs.
Method/Guideline and Test Condition Remarks:	Rats were exposed in whole-body chambers for 4 hours to a mean measured concentration of 5,399 mg/m ³ of aerosolized test substance. Mass median aerodynamic diameter was 4.4 µm; geometric standard deviation was 3.5. A comparable control group was sham-exposed. Animals were then observed daily and sacrificed on day 14 after exposure. Endpoints included observations during exposure, individual clinical signs pre-exposure, immediately after exposure, and daily thereafter until sacrifice. Body weights were measured on days 0, 7, and 14. All animals were necropsied and observed for macroscopic abnormalities.

TEST RESULTS

Concentration (LC/LD)

LC/LD	%:	Value Description:	Value or Lower Concentration:	Upper Concentration:	Units:
LC	50	>		5,399	mg/m ³
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

Number of Deaths (Male): 0

Number of Deaths: 0

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(Female):	
Number of Deaths (Total):	0
Results Remarks:	Abnormal clinical observations in the treated group during the 14 days after exposure included ungroomed appearance, yellow ano-genital stain, alopecia, reddened skin, and hunched posture. Both males and females lost weight after exposure between days 0 and 7, but were gaining weight comparable to controls over days 7 to 14. Abnormalities observed at necropsy were limited to discolored lungs and cervical lymph nodes in a few animals.
Conclusion:	The 4-hour LC50 was $>5,399 \text{ mg/m}^3$ and no significant treatment-related toxicity was observed.
RELIABILITY/DATA QUALITY	
Reliability:	1 – Reliable without restrictions
Reliability Remarks:	Guideline study
Key Study Sponsor Indicator:	Key
REFERENCE	
Reference:	Final report on project number 209915. Four-hour inhalation toxicity study in rats. Test material: MRD-87-099. Exxon Biomedical Sciences, Inc., East Millstone, NJ. May, 1988

5. Toxicity

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High Production Volume Information System (HPVIS)

Acute Toxicity

Test Substance

Category Chemical (CAS #):	64742-65-0
Test Substance (CAS #):	64742-65-0; MRD-87-101; distillates (petroleum), solvent-dewaxed heavy paraffinic
Test Substance Purity/Composition and Other Test Substance Comments :	MRD-87-101 (No sample number) No other information
Category Chemical Result Type :	Measured
Unable to Measure or Estimate Justification :	

METHOD

Route of Administration:	Inhalation
Other Route of Administration:	
Type of Exposure:	Acute (4-hour exposure)

5. Toxicity

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Species:	Rat
Other Species:	
Mammalian Strain:	Sprague-Dawley
Other Strain:	
Gender:	Male and female
Number of Animals per Dose:	5 per sex per dose
Concentration:	0 (sham-exposed) and 4,026 mg/m ³ aerosolized test substance
Dose:	
Year Study Performed :	1987
Method/Guideline Followed:	40 CFR 798.1150 Acute Inhalation Toxicity and OECD Guideline 403 (Acute Inhalation Toxicity).
GLP:	The study was conducted in accord with EPA GLPs.
Method/Guideline and Test Condition Remarks:	Rats were exposed in whole-body chambers for 4 hours to a mean measured concentration of 4,026 mg/m ³ of aerosolized test substance. Mass median aerodynamic diameter was 4.3 µm; geometric standard deviation was 2.2. A comparable control group was sham-exposed. Animals were then observed daily and sacrificed on day 14 after exposure. Endpoints included observations during exposure, individual clinical signs pre-exposure, immediately after exposure, and daily thereafter until sacrifice. Body weights were measured on days 0, 7, and 14. All animals were necropsied and observed for macroscopic abnormalities.

TEST RESULTS

Concentration (LC/LD)

LC/LD	%:	Value Description:	Value or Lower Concentration:	Upper Concentration:	Units:
LC	50	>		4,026	mg/m ³
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

5. Toxicity

Id Lubricating oil
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<input type="text"/>					
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Number of Deaths (Male):	0
Number of Deaths (Female):	0
Number of Deaths (Total):	0
Results Remarks:	Abnormal clinical observations in the treated group during the 14 days after exposure included ungroomed appearance and yellow ano-genital stain. All animals gained weight after exposure and body weights in the treated group were comparable to those of controls. Treatment-related abnormalities observed at necropsy appeared to be limited to enlarged cervical lymph nodes in one male and reddened cervical lymph nodes in one female.
Conclusion:	The 4-hour LC50 was >4,026 mg/m ³ and no significant treatment-related toxicity was observed.
RELIABILITY/DATA QUALITY	
Reliability:	1 – Reliable without restrictions
Reliability Remarks:	Guideline study
Key Study Sponsor Indicator:	Key
REFERENCE	
Reference:	Final report on project number 210115. Four-hour inhalation toxicity study in rats. Test material: MRD-87-101. Exxon Biomedical Sciences, Inc., East Millstone, NJ. May, 1988

5. Toxicity

Id Lubricating oil
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Acute Toxicity

Test Substance

Category Chemical (CAS #):	64741-88-4
Test Substance (CAS #):	64741-88-4; MRD-87-102; distillates (petroleum), solvent-refined heavy paraffinic
Test Substance Purity/Composition and Other Test Substance Comments :	MRD-87-102 (No sample number No other information
Category Chemical Result Type :	Measured
Unable to Measure or Estimate Justification :	

METHOD

Route of Administration:	Inhalation
Other Route of Administration:	
Type of Exposure:	Acute (4-hour exposure)
Species:	Rat
Other Species:	
Mammalian Strain:	Sprague-Dawley

5. Toxicity

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Other Strain:	
Gender:	Male and female
Number of Animals per Dose:	5 per sex per dose
Concentration:	0 (sham-exposed) and 5,530 mg/m ³ aerosolized test substance
Dose:	
Year Study Performed :	1987
Method/Guideline Followed:	40 CFR 798.1150 Acute Inhalation Toxicity and OECD Guideline 403 (Acute Inhalation Toxicity).
GLP:	The study was conducted in accord with EPA GLPs.
Method/Guideline and Test Condition Remarks:	Rats were exposed in whole-body chambers for 4 hours to a mean measured concentration of 5,530 mg/m ³ of aerosolized test substance. Mass median aerodynamic diameter was 2.7 µm; geometric standard deviation was 2.9. A comparable control group was sham-exposed. Animals were then observed daily and sacrificed on day 14 after exposure. Endpoints included observations during exposure, individual clinical signs pre-exposure, immediately after exposure, and daily thereafter until sacrifice. Body weights were measured on days 0, 7, and 14. All animals were necropsied and observed for macroscopic abnormalities.

TEST RESULTS

Concentration (LC/LD)

LC/LD	%:	Value Description:	Value or Lower Concentration:	Upper Concentration:	Units:
LC	50	>		5,530	Mg/m ³
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

Number of Deaths (Male): 0

Number of Deaths 0

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(Female):	
Number of Deaths (Total):	0
Results Remarks:	Abnormal clinical observations in the treated group during the 14 days after exposure included yellow ano-genital stain and alopecia in a few animals. All animals gained weight after exposure and body weights in the treated group were comparable to those of controls. Treatment-related abnormalities observed at necropsy appeared to be limited to enlarged cervical lymph nodes in two animals.
Conclusion:	The 4-hour LC50 was $>5,530 \text{ mg/m}^3$ and no significant treatment-related toxicity was observed.
RELIABILITY/DATA QUALITY	
Reliability:	1 – Reliable without restrictions
Reliability Remarks:	Guideline study
Key Study Sponsor Indicator:	Key
REFERENCE	
Reference:	Final report on project number 210215. Four-hour inhalation toxicity study in rats. Test material: MRD-87-102. Exxon Biomedical Sciences, Inc., East Millstone, NJ. May, 1988

5. Toxicity

Id Lubricating oil
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Acute Toxicity

Test Substance

Category Chemical (CAS #):	8042-47-5
Test Substance (CAS #):	8042-47-5; Stock 461; 80" white oil; white mineral oil Its viscosity was a nominal value of 80 SUS.
Test Substance Purity/Composition and Other Test Substance Comments :	Stock 461 (No sample number identified) No other information
Category Chemical Result Type :	Measured
Unable to Measure or Estimate Justification :	

METHOD

Route of Administration:	Inhalation
Other Route of Administration:	
Type of Exposure:	Acute (4-hour exposure)
Species:	Rat
Other Species:	
Mammalian Strain:	Sprague-Dawley

5. Toxicity

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Other Strain:	
Gender:	Male and female
Number of Animals per Dose:	10 per sex per dose
Concentration:	0 (sham-exposed), 140, 550, or 2,460 mg/m ³ aerosolized test substance
Dose:	
Year Study Performed :	1983
Method/Guideline Followed:	EPA guidelines study
GLP:	The study was conducted in accord with EPA GLPs.
Method/Guideline and Test Condition Remarks:	Rats were exposed in whole-body chambers for 4 hours to a mean measured concentration of 0 (sham-exposed), 0.14, 0.55, or 2.46 mg/L of aerosolized test substance measured gravimetrically and with an IR backscatter detector. Mass median aerodynamic diameters were 4.8, 3.0, and 2.2 µm, respectively. Half of the animals in each group were sacrificed on the day after exposure; the remaining animals were observed daily and sacrificed at 2 weeks after exposure. Endpoints included observations during exposure, individual clinical signs pre-exposure, immediately after exposure, and daily thereafter until sacrifice. Body weights were measured on days -3, 1, 2, 4, 8, and 16. All animals were necropsied and observed for macroscopic abnormalities. Weights of liver, kidney, and lung (wet and dry, right middle lobe) were measured. Histological slides were prepared of the lung, nose, liver, kidney, and thoracic lymph nodes. Slides from the control and high-dose group were evaluated by a pathologist.

TEST RESULTS

Concentration (LC/LD)

LC/LD	%:	Value Description:	Value or Lower Concentration:	Upper Concentration:	Units:
LC	50	>		2,460	mg/m ³
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

5. Toxicity

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Number of Deaths (Male):	0
Number of Deaths (Female):	0
Number of Deaths (Total):	0
Results Remarks:	No animals died during the study and there were no significant treatment-related changes in clinical signs or body weight. No treatment-related changes were seen in the other endpoints at either sacrifice.
Conclusion:	The 4-hour LC50 was >2.5 mg/L (2,500 mg/m ³) and no significant treatment-related toxicity was observed.
RELIABILITY/DATA QUALITY	
Reliability:	1 – Reliable without restrictions
Reliability Remarks:	Guideline study
Key Study Sponsor Indicator:	Key
REFERENCE	
Reference:	Acute inhalation toxicity of aerosolized 80” white oil (Stock 461). Final report for Mobil study 32421. Mobil Environmental and Health Science Laboratory. 1985

Acute Toxicity**Test Substance**

Category Chemical (CAS #):	64742-53-6
Test Substance (CAS #):	64742-53-6; API 83-12; Highly refined base oil
Test Substance Purity/Composition and Other Test Substance Comments :	API 83-12 No other information
Category Chemical Result Type :	Measured

Type : Inhalation LC₅₀
Value : 2.18 mg/l
Species : Rat
Strain : Sprague-Dawley
Sex : Male/female
Number of animals : 5
Vehicle : Air
Exposure time : 4 hour(s)
Year : 1987
GLP : Yes
Test substance : Highly refined Base oil Sample API 83-12 [CAS64742-53-6] See section 1.1.1.

Method : A group of 5 male and 5 female rats were exposed for 4 hours to an aerosol of the test material at a target concentration of 5 mg/l. Four additional groups of rats were then exposed for 4 hours to target aerosol concentrations of 1, 1.5, 2.5 and 3.5 mg/l. A control group exposed, in the chamber, to air only was also included.
 Animals were observed continuously during the first hour of exposure, hourly for the remainder of the exposure and once daily for the 14-day post exposure period. Mortalities were recorded and body weights were measured prior to exposure and again 7 and 14 days after exposure. On the 14th day post-exposure, necropsies were performed on all surviving animals. For all animals, including animals found dead, the lungs and any other abnormal tissues were removed and fixed for subsequent histopathological examination.

Result : Actual exposure concentrations and mortalities were as follows:

5. Toxicity

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Target level (mg/l)	Actual concentration		Mortality	
	mg/l	±SD	Male	Female
0	0.02	0.01	0/5	0/5
1.0	1.04	0.1	1/5	1/5
1.5	1.51	0.15	0/5	0/5
2.5	2.37	0.31	3/5	3/5
3.5	3.49	0.36	5/5	5/5
5.0	5.05	0.18	5/5	5/5

Particle size measurements confirmed that mass median aerodynamic diameter and geometric standard deviation values were in the ranges 1.7 to 2.5 µm and 1.5 to 1.61 respectively. These measurements confirm that the particles were within the respirable range.

The LC₅₀ for combined sexes was estimated to be 2.18 with 95% confidence limits of 1.80 to 2.55 mg/l.

Body weight differences did not show a consistent dose related pattern. At the highest concentration, the animals were obscured by a dense aerosol and observations could not be made during the exposure period. In other groups, there was a decreased activity, wet inguinal area, eyes partially closed, wet coat, loose stool and oily coat during exposure. During the first week post-exposure, similar signs were observed as well as signs of poor condition, respiratory distress and some deaths occurred. During test week 2, most survivors were considered to be of normal appearance. The signs that were observed occurred in a dose related manner.

At gross necropsy, dark red lungs were described for some animals. The incidence is shown below.

Dose group	Male	Female
0	0/5	0/5
1.0	1/5	1/5
1.5	0/5	0/5
2.5	3/5	3/5
3.5	5/5	5/5
5.0	5/5	5/5

At histology, affected animals exhibited diffuse pulmonary congestion and perivascular edema that were mostly moderate or marked in degree. Less consistently spotty alveolar edema was also seen. There was widespread damage to alveolar walls resulting in fibronecrotic debris resembling hyaline membranes in more marked cases and extravasation of RBCs and PMNs. Necrosis and inflammation were seen in the walls of small blood vessels and there was spotty epithelial necrosis in small bronchioles, but the most severe damage seemed to be centroacinar. The larger airways were relatively unaffected.

None of the surviving animals exhibited the above acute changes. However, most of the surviving animals exposed to 2.5 or 1.0 mg/l and above exhibited chronic inflammatory changes that were not seen in the controls and only occasionally in animals exposed at the 1.5 mg/l level, and then to a lesser degree of severity. Other findings were considered sporadic or unrelated to exposure to the test material.

Test condition

: Whole body exposures were carried out in stainless steel and glass chambers of 0.25 cubic meter volume. Aerosols were generated using a nebulizer. Concentrations of test material in the exposure chambers were determined gravimetrically by collection of the aerosol on filters. Analytical

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Reliability : samples were taken at least once per hour during the exposure period.
Particle size determinations were also carried out.
(1) valid without restriction (16)
American Petroleum Institute (1987)
(16) Acute inhalation toxicity evaluation of a petroleum derived
hydrocarbon in rats. API 83-12 Hydrotreated light naphthenic
distillate CAS 64742-53-6
API HESD Publ. 34-32775

Acute Toxicity**Test Substance**

Category Chemical (CAS #):	Not available
Test Substance (CAS #):	Solvent extracted, dewaxed paraffinic distillate; Solvent extracted, dewaxed, hydrotreated paraffinic distillate; Solvent dewaxed light paraffinic distillate
Test Substance Purity/Composition and Other Test Substance Comments :	No other information
Category Chemical Result Type :	Measured

Type : Inhalation LC₅₀
Species : Rat
Test substance : Various Base oils

Remark : CONCAWE summarized the data available on the acute inhalation toxicity of lubricating oil mists in 4 hour exposure studies in rats. The data (Original source Whitman et al, 1989) on 3 paraffinic distillates are shown in the following table.

	Inhalation LC₅₀ (mg/l)
Paraffinic distillates	
Solvent extracted, dewaxed	>4
Solvent extracted, dewaxed, hydrotreated	>4
Solvent dewaxed, light	>4

(81) (126)

(81)

CONCAWE (1997)
Lubricating oil basestocks
Product dossier No. 97/108
CONCAWE, Brussels

(126)

Whitman, F. T., Freeman, J. J., Infurna, R. N. and Phillips, R. D. (1989)
Evaluation of the acute and subacute inhalation toxicity of lubricating oil mists
The toxicologist Vol. 9., p 143

5. Toxicity

Id Lubricating oil
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5.1.3. ACUTE DERMAL TOXICITY

Acute Toxicity

Test Substance

Category Chemical (CAS #):	64742-65-0
Test Substance (CAS #):	64742-65-0; MLDW 100" PN (Stock 142); Paraffin oils (petroleum), catalytic dewaxed heavy Its viscosity was 22.33 cSt at 40°C (~100 SUS) and 4.23 cSt at 100°C.
Test Substance Purity/Composition and Other Test Substance Comments :	MLDW 100" PN; Stock 142 (Sample no. 82192) No other information
Category Chemical Result Type :	Measured
Unable to Measure or Estimate Justification :	

METHOD

Route of Administration:	Dermal
Other Route of Administration:	
Type of Exposure:	Single dermal dose
Species:	Rabbit
Other Species:	

5. Toxicity

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Mammalian Strain:	New Zealand white rabbit
Other Strain:	
Gender:	Male and female
Number of Animals per Dose:	3 per sex
Concentration:	100%
Dose:	5 g/kg body weight
Year Study Performed :	1983
Method/Guideline Followed:	Other; similar to guideline limit study, but with fewer animals.
GLP:	Study was conducted in accordance with FDA Good Laboratory Practices.
Method/Guideline and Test Condition Remarks:	Hair was clipped from the entire trunk of each animal before dosing. The skin on 2 males and one female was abraded; skin on the other three animals was left intact. After dosing, gauze and an occlusive rubber dam were covered the trunk of each animal and an Elizabethan collar was put on each animal. Animals were observed frequently on the day of dosing and daily thereafter for 14 days. Test sites were unwrapped at 24 hours after dosing and test sites were wiped with moistened cotton. Dermal irritation was evaluated at 26 and 72 hours after dosing. Animals were sacrificed on day 14.

TEST RESULTS

Concentration (LC/LD)

LC/LD	%:	Value Description:	Value or Lower Concentration:	Upper Concentration:	Units:
LD	50	>		5,000	mg/kg body weight
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

Number of Deaths (Male): 0

5. Toxicity

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Number of Deaths (Female):	0
Number of Deaths (Total):	0
Results Remarks:	No treatment-related clinical signs were observed and animals gained weight during the study.
Conclusion:	The oral LD50 of the test substance was >5,000 mg/kg.
RELIABILITY/DATA QUALITY	
Reliability:	2 – Reliable with restrictions
Reliability Remarks:	Comparable to guideline limit study; fewer animals; no gross necropsy information reported
Key Study Sponsor Indicator:	Key
REFERENCE	
Reference:	The acute dermal toxicity of MLDW 100” PN in albino rabbits. Test report on Mobil study 30232. Mobil Environmental and Health Science Laboratory, Princeton, NJ. 1983

5. Toxicity

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Acute Toxicity

Test Substance

Category Chemical (CAS #):	64742-65-0
Test Substance (CAS #):	64742-65-0; Stock 141; Distillates (petroleum), solvent-dewaxed heavy paraffinic Its viscosity was ~102 SUS at 100°F and 40 SUS at 210°F (18.8 cSt at 40°C and 4.0 cSt at 100°C).
Test Substance Purity/Composition and Other Test Substance Comments :	Stock 141 (Sample no. 1720811) No other information
Category Chemical Result Type :	Measured
Unable to Measure or Estimate Justification :	

METHOD

Route of Administration:	Dermal
Other Route of Administration:	
Type of Exposure:	Single dermal dose
Species:	Rabbit
Other Species:	
Mammalian Strain:	New Zealand white rabbit

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Other Strain:	
Gender:	Male and female
Number of Animals per Dose:	3 per sex
Concentration:	100%
Dose:	5 g/kg body weight
Year Study Performed :	1982
Method/Guideline Followed:	Other; similar to guideline limit study, but with fewer animals.
GLP:	Study was conducted in accordance with FDA Good Laboratory Practices.
Method/Guideline and Test Condition Remarks:	Hair was clipped from the entire trunk of each animal before dosing. The skin on 2 males and one female was abraded; skin on the other three animals was left intact. After dosing, gauze and an occlusive rubber dam were covered the trunk of each animal and an Elizabethan collar was put on each animal. Animals were observed frequently on the day of dosing and daily thereafter for 14 days. Test sites were unwrapped at 24 hours after dosing and test sites were wiped with moistened cotton. Dermal irritation was evaluated at 26 and 72 hours after dosing. Animals were sacrificed on day 14.

TEST RESULTS

Concentration (LC/LD)

LC/LD	%:	Value Description:	Value or Lower Concentration:	Upper Concentration:	Units:
LD	50	>		5,000	mg/kg body weight
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

Number of Deaths (Male):	0
Number of Deaths (Female):	0

5. Toxicity

Id Lubricating oil
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Number of Deaths (Total):	0
Results Remarks:	No treatment-related clinical signs were observed except for marginal dermal irritation at 24 hours. Animals gained weight during the study.
Conclusion:	The oral LD50 of the test substance was >5,000 mg/kg.
RELIABILITY/DATA QUALITY	
Reliability:	2 – Reliable with restriction
Reliability Remarks:	Comparable to guideline limit study; fewer animals; no gross necropsy information reported
Key Study Sponsor Indicator:	Key
REFERENCE	
Reference:	The acute dermal toxicity of Mobil base stock 141 in albino rabbits. Test report on Mobil study 20802. Mobil Environmental and Health Science Laboratory, Princeton, NJ. 1982

5. Toxicity

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Acute Toxicity

Test Substance

Category Chemical (CAS #):	64742-54-7
Test Substance (CAS #):	64742-54-7; Ssangyong 150N; Distillates (petroleum), hydrotreated heavy paraffinic; Viscosity was 161 SUS at 100°F and 45 SUS at 210°F.
Test Substance Purity/Composition and Other Test Substance Comments :	Ssangyong 150N (CRU 83272) No other information
Category Chemical Result Type :	Measured
Unable to Measure or Estimate Justification :	

METHOD

Route of Administration:	Dermal
Other Route of Administration:	
Type of Exposure:	Single dermal dose
Species:	Rabbit
Other Species:	
Mammalian Strain:	New Zealand white rabbit

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Other Strain:	
Gender:	Male and female
Number of Animals per Dose:	3 per sex
Concentration:	100%
Dose:	5 g/kg body weight
Year Study Performed :	1983
Method/Guideline Followed:	Similar to guideline study
GLP:	Study was conducted in accordance with FDA Good Laboratory Practices.
Method/Guideline and Test Condition Remarks:	Hair was clipped from the entire trunk of each animal before dosing. The skin on 2 males and one female was abraded; skin on the other three animals was left intact. After dosing, gauze and an occlusive rubber dam were covered the trunk of each animal and an Elizabethan collar was put on each animal. Animals were observed frequently on the day of dosing and daily thereafter for 14 days. Test sites were unwrapped at 24 hours after dosing and test sites were wiped with moistened cotton. Dermal irritation was evaluated at 26 and 72 hours after dosing. Animals were sacrificed on day 14.

TEST RESULTS

Concentration (LC/LD)

LC/LD	%:	Value Description:	Value or Lower Concentration:	Upper Concentration:	Units:
LD	50	>		5,000	mg/kg body weight
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

Number of Deaths (Male):	0
Number of Deaths (Female):	0

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Number of Deaths (Total):	0
Results Remarks:	No treatment-related clinical signs were observed and animals gained weight during the study.
Conclusion:	The oral LD50 of the test substance was >5,000 mg/kg.
RELIABILITY/DATA QUALITY	
Reliability:	2 – Reliable with restriction
Reliability Remarks:	Comparable to guideline limit study; fewer animals; no gross necropsy information reported
Key Study Sponsor Indicator:	Key
REFERENCE	
Reference:	The acute dermal toxicity of hydrotreated base oil (Ssangyong 150N) in albino rabbits. Test report on Mobil study 32752. Mobil Environmental and Health Science Laboratory, Princeton, NJ. 1983

Acute Toxicity**Test Substance**

Category Chemical (CAS #):	64741-50-0
Test Substance (CAS #):	64741-50-0; API 84-01; Unrefined base oil
Test Substance Purity/Composition and Other Test Substance Comments :	API 84-01 No other information
Category Chemical Result Type :	Measured

Type : Dermal LD₅₀
Value : > 2000 mg/kg bw
Species : Rabbit
Strain : New Zealand white
Sex : Male/female
Number of animals : 4
Vehicle : None applied undiluted
Year : 1986
GLP : Yes
Test substance : Unrefined base oil Sample API 84-01 [CAS 64741-50-0] See section 1.1.1.

Method : Undiluted test material was applied as a single dose (2g/kg) to the shorn, abraded skin of 4 male and 4 female rabbits. The treated site was covered with an occlusive dressing for 24 hours. After removal of the dressing, the skin was wiped with a wet towel to remove residual test material. The rabbits were observed for clinical signs and mortality hourly for the first 6 hours, then daily for derma irritation and twice daily for clinical signs and mortality.
 Observation was carried out for a 14-day post treatment period. Body weights were recorded prior to administration of the test material, again 7 days post dosing and at study termination (14 days). At termination, all surviving animals were killed and subjected to a gross necropsy examination.

Result : There were no mortalities during the study.
 With the exception of skin irritation, there were no clinical signs of toxicity except that on day 4 soft stool was observed in 1 male and 3 female animals. Dermal irritation ranged from slight to severe for erythema and edema, from slight to marked for fissuring and slight to moderate for atonia and desquamation. Slight coriaceousness was also observed. Body weight losses were recorded for 2 male and 3 female animals at day

5. Toxicity

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Reliability : 7. One male was less than starting weight on both day 7 and day 14.
(1) valid without restriction

(13)

(13)

American Petroleum Institute (1986)
Acute oral toxicity study in rats
Acute dermal toxicity study in rabbits
Primary dermal irritation study in rabbits
Primary eye irritation study in rabbits
Dermal sensitization study in Guinea pigs
API 84-01 Light paraffinic distillate CAS 64741-50-0
API Med. Res. Publ.: 33-30595

Acute Toxicity**Test Substance**

Category Chemical (CAS #):	64742-53-6
Test Substance (CAS #):	64742-53-6; API 83-12; Highly refined base oil
Test Substance Purity/Composition and Other Test Substance Comments :	API 83-12 No further information
Category Chemical Result Type :	Measured

Type : Dermal LD₅₀
Value : > 2000 mg/kg bw
Species : Rabbit
Strain : New Zealand white
Sex : Male/female
Number of animals : 2
Vehicle : None - applied undiluted
Year : 1986
GLP : yes
Test substance : Highly refined Base oil Sample API 83-12 [CAS64742-53-6] See section 1.1.1.

Method : Undiluted test material was applied as a single dose (2g/kg) to the shorn, abraded skin of 4 male and 4 female rabbits. The treated site was covered with an occlusive dressing for 24 hours. After dressing removal, the skin was wiped with a wet towel to remove residual test material. The rabbits were observed for clinical signs and mortality hourly for the first 6 hours, then daily for dermal irritation and twice daily for clinical signs and mortality. Observation was carried out for a 14-day post treatment period. Body weights were recorded prior to administration of the test material, again 7 days post dosing and at study termination (14 days). At termination, all surviving animals were killed and subjected to a gross necropsy examination.

Result : There were no deaths during the study.
 The only clinical observation with the exception of skin irritation was soft stool in all animals. This was observed 3 hours after dosing and returned to normal by day 2. Skin irritation was observed in all animals and ranged from slight to severe for erythema and edema, from slight to marked for atonia, desquamation and fissuring and from slight to moderate for

5. Toxicity

Id Lubricating oil
basestocks
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Reliability (12) : coriaceousness. Other dermal irritation seen included blanching and subcutaneous hemorrhage. All animals had gained weight by the end of the study. At necropsy, except for the skin lesions no other visible lesions were recorded. (1) valid without restriction (12) American Petroleum Institute (1986) Acute oral toxicity study in rats Acute dermal toxicity study in rabbits Primary dermal irritation study in rabbits Primary eye irritation study in rabbits Dermal sensitization study in Guinea pigs API 83-12 Hydrotreated light naphthenic distillate CAS 64742-53-6 API Med. Res. Publ.: 33-30592

5. Toxicity

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Acute Toxicity

Test Substance

Category Chemical (CAS #):	64742-56-9; 64742-56-0; 64742-65-0; 64741-97-5; 64741-96-4; 64742-52-5
Test Substance (CAS #):	64742-56-9; API 78-9; Solvent dewaxed light paraffinic distillate 64742-56-0; API 78-10; Solvent dewaxed heavy paraffinic distillate 64742-65-0; API 79-3; Solvent dewaxed heavy paraffinic distillate 64742-65-0; API 79-4; Solvent dewaxed heavy paraffinic distillate 64742-65-0; API 79-5 Solvent dewaxed heavy paraffinic distillate Tufflo 6056; White mineral oil 64741-97-5; API 78-5; 7Solvent refined light naphthenic distillate 64741-96- 4; API 79-1;Solvent refined heavy naphthenic distillate 64742-52-5; API 83-15; Hydrotreated heavy naphthenic distillate
Test Substance Purity/Composition and Other Test Substance Comments :	API 78-9 API 78-10 API 79-3 API 79-4 API 79-5 Tufflo 6056 API 78-5 API 79-1 API 83-15 No other information
Category Chemical Result Type :	Measured

Type : Dermal LD₅₀
Species : Rabbit
Test substance : Various Base oils

Remark : CONCAWE summarized the data available on the acute dermal toxicity of lubricating oil base stocks in rabbits. The data are shown in the following table.

	CAS No	Dermal LD ₅₀ (g/kg)	API Report No.
Paraffinic distillates			
Solvent dewaxed, light			
API 78-9	64742-56-9	>5	29-33104

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Id Lubricating oil
basestocks
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Solvent dewaxed, heavy			
API 78-10*	64742-56-0	>5	29-33105
API 79-3	64742-65-0	>5	29-33067
API 79-4	64742-65-0	>5	29-33066
API 79-5	64742-65-0	>5	29-33068
Naphthenic distillates			
Solvent refined, light			
API 78-5	64741-97-5	>5	29-33106
Solvent refined, heavy			
API 79-1	64741-96-4	>5	29-33065
Hydrotreated, heavy			
API 83-15	64742-52-5	>2	33-32639

* Although this material is not included in the HPV Lubricating base stocks category, it is similar to other materials in the category and provides supportive information.

(2) (3) (4) (5) (6) (7) (8) (14) (81)

- (2) American Petroleum Institute (1982)
Acute toxicity tests of API sample 78-10 paraffinic oil (150 SUS/100 °F)
API Med. Res. Publ. 29-33105
- (3) American Petroleum Institute (1982)
Acute toxicity tests of API sample 78-5 naphthenic oil (150 SUS/100 °F)
API Med. Res. Publ. 29-33106
- (4) American Petroleum Institute (1982)
Acute toxicity tests of API sample 78-9 paraffinic oil (70 SUS/100 °F)
API Med. Res. Publ. 29-33104
- (5) American Petroleum Institute (1982)
Acute toxicity tests of API sample 79-1 naphthenic oil (90 SUS/210 °F)
API Med. Res. Publ. 29-33065
- (6) American Petroleum Institute (1982)
Acute toxicity tests of API sample 79-3 paraffinic oil (350 SUS/100 °F)
API Med. Res. Publ. 29-33067
- (7) American Petroleum Institute (1982)
Acute toxicity tests of API sample 79-4 paraffinic oil (550 SUS/100 °F)
API Med. Res. Publ. 29-33066
- (8) American Petroleum Institute (1982)
Acute toxicity tests of API sample 79-5 paraffinic oil (800 SUS/100 °F)
API Med. Res. Publ. 29-33068

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- (14) American Petroleum Institute (1986)
Acute oral toxicity study in rats
Acute dermal toxicity study in rabbits
Primary dermal irritation study in rabbits
Primary eye irritation study in rabbits
Dermal sensitization study in guinea pigs
API sample 83-15 hydrotreated heavy naphthenic distillate
(CAS 64742-52-5)
API Health Environ. Sci. Dep. Rep. 33-32639
- (81) CONCAWE (1997)
Lubricating oil basestocks
Product dossier No. 97/108
CONCAWE, Brussels

5. Toxicity

Id Lubricating oil
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5.2. SKIN IRRITATION

Skin Irritation

Test Substance

Category Chemical (CAS #):	64741-50-0
Test Substance (CAS #):	64741-50-0; API 84-01; Unrefined base oil
Test Substance Purity/Composition and Other Test Substance Comments :	No information
Category Chemical Result Type :	Measured

Type: : Skin irritation
Species : Rabbit
Concentration : Undiluted
Exposure : Occlusive
Exposure time : 24 hour(s)
Number of animals : 6
Vehicle : None - undiluted
PDII : 4.3
Result : Moderately irritating
Method : Draize Test
Year : 1986
GLP : Yes
Test substance : Unrefined base oil Sample API 84-01 [CAS 64741-50-0] See section 1.1.1.

Method : 0.5 ml of undiluted test material was applied to the shorn dorsal skin in two areas on each of 6 male rabbits. One area was intact and the other abraded skin. The treated area was then covered with an occlusive dressing. After 24 hours, the dressing was removed and the treated skin was wiped to remove any residue of test material. The degree of erythema and edema was recorded according to the Draize scale. A second reading of skin responses was made at 72 hours and again at 96 hours, 7 and 14 days. Results of the 24 and 72-hour readings were used to determine the Primary Irritation Index.

Result : One animal died on day 10 even though there had been no signs of ill health previously. Irritation scores given below are averages from 5 animals.

5. Toxicity

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Observation period	Erythema		Edema		Average Score
	Intact	Abraded	Intact	Abraded	
24 hrs.	2.3	2.5	2.3	2.3	4.8
72 hrs.	1.8	2.0	1.7	2.0	3.8
96 hrs.	1.5	1.7	1.0	1.0	2.6
7 days	0.3	0.3	0.3	0.5	0.8
14 days	0	0	0	0	0

Reliability : Primary dermal irritation index: 4.3
(1) valid without restriction

(13)

(13)
American Petroleum Institute (1986)
Acute oral toxicity study in rats
Acute dermal toxicity study in rabbits
Primary dermal irritation study in rabbits
Primary eye irritation study in rabbits
Dermal sensitization study in Guinea pigs
API 84-01 Light paraffinic distillate CAS 64741-50-0
API Med. Res. Publ.: 33-30595

Skin Irritation**Test Substance**

Category Chemical (CAS #):	64742-53-6
Test Substance (CAS #):	64742-53-6; API 83-12; Highly refined base oil
Test Substance Purity/Composition and Other Test Substance Comments :	API 83-12 No further information
Category Chemical Result Type :	Measured

Type : Skin irritation
Species : Rabbit
Concentration : Undiluted
Exposure : Occlusive
Exposure time : 24 hour(s)
Number of animals : 6
Vehicle : None - undiluted
PDII : 5.4
Result : Moderately irritating
Method : Draize Test
Year : 1986
GLP : Yes
Test substance : Highly refined Base oil Sample API 83-12 [CAS64742-53-6] See section 1.1.1.

Method : 0.5 ml of undiluted test material was applied to the shorn skin in two areas on each of 6 male rabbits. One area was intact and the other abraded skin. The treated area was then covered with an occlusive dressing. After 24 hours, the dressing was removed and the treated was wiped to remove any residue of test material. The degree of erythema and edema was recorded according to the Draize scale. A second reading of skin responses was made at 72 hours and again at 96 hours, 7 and 14 days. Results of the 24 and 72-hour readings were used to determine the Primary Irritation Index.

Result : Average Irritation scores are given below:

Observation period	Erythema		Edema		Average Score
	Intact	Abraded	Intact	Abraded	
24 hrs.	2.3	2.3	2.7	2.7	5.0
72 hrs.	3.0	3.0	2.5	3.0	5.8
96 hrs.	2.7	2.8	2.7	3.0	5.6

5. Toxicity

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7 days	1.3	2.2	0.8	1.7	3.0
14 days	0	0	0	0	0

Reliability : Primary dermal irritation index: 5.4
(1) valid without restriction

(12)

(12)
American Petroleum Institute (1986)
Acute oral toxicity study in rats
Acute dermal toxicity study in rabbits
Primary dermal irritation study in rabbits
Primary eye irritation study in rabbits
Dermal sensitization study in Guinea pigs
API 83-12 Hydrotreated light naphthenic distillate CAS
64742-53-6
API Med. Res. Publ.: 33-30592

5. Toxicity

Id Lubricating oil
basestocks
Date March 31, 2011

Skin Irritation

Test Substance

Category Chemical (CAS #):	64742-56-9; 64742-56-0; 64742-65-0; 64741-97-5; 64741-96-4; 64742-52-5
Test Substance (CAS #):	64742-56-9; API 78-9; Solvent dewaxed light paraffinic distillate 64742-56-0; API 78-10; Solvent dewaxed heavy paraffinic distillate 64742-65-0; API 79-3; Solvent dewaxed heavy paraffinic distillate 64742-65-0; API 79-4; Solvent dewaxed heavy paraffinic distillate 64742-65-0; API 79-5 Solvent dewaxed heavy paraffinic distillate Tufflo 6056; White mineral oil 64741-97-5; API 78-5; 7Solvent refined light naphthenic distillate 64741-96- 4; API 79-1;Solvent refined heavy naphthenic distillate 64742-52-5; API 83-15; Hydrotreated heavy naphthenic distillate
Test Substance Purity/Composition and Other Test Substance Comments :	API 78-9 API 78-10 API 79-3 API 79-4 API 79-5 Tufflo 6056 API 78-5 API 79-1 API 83-15 No other information
Category Chemical Result Type :	Measured

Type : Skin irritation
Species : Rabbit
Concentration : Undiluted
Exposure time : 24 hour(s)
Test substance : Various base oils

Remark : CONCAWE summarized the data available on skin irritation for the lubricating oil base stocks. The data are shown in the following table.

	Irritation*	API Report
Paraffinic distillates		
Solvent dewaxed, light API 78-9 (64742-56-9)	Slight (0.6)	29-33104
Solvent dewaxed, heavy		

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API 78-10*** (64742-56-0)	Non (0.27)	29-33105
API 79-3 (64742-65-0)	Non (0.33)	29-33067
API 79-4 (64742-65-0)	Non (0.34)	29-33066
API 79-5 (64742-65-0)	Non (0.38)	29-33068
White mineral oil***	Slight	Hoekstra & Phillips
Naphthenic distillates		
Solvent refined, light		
API 78-5 (64741-97-5)	Slight (0.65)	29-33106
Solvent refined, heavy		
API 79-1 (64741-96-4)	Slight (0.8)	29-33065
Hydrotreated, heavy		
API 83-15 (64742-52-5)	Slight (1.3)**	33-32639

* NB Irritation described as slight, moderate or non-irritating in the original reports (Mean irritation score given in parentheses)

** Irritation index

*** Although these materials are not included in the HPV Lubricating base stocks category, they are similar to other materials in the category and provide supportive information.

(2) (3) (4) (5) (6) (7) (8) (14) (81)

- (2) American Petroleum Institute (1982)
Acute toxicity tests of API sample 78-10 paraffinic oil (150 SUS/100 °F)
API Med. Res. Publ. 29-33105
- (3) American Petroleum Institute (1982)
Acute toxicity tests of API sample 78-5 naphthenic oil (150 SUS/100 °F)
API Med. Res. Publ. 29-33106
- (4) American Petroleum Institute (1982)
Acute toxicity tests of API sample 78-9 paraffinic oil (70 SUS/100 °F)
API Med. Res. Publ. 29-33104
- (5) American Petroleum Institute (1982)
Acute toxicity tests of API sample 79-1 naphthenic oil (90 SUS/210 °F)
API Med. Res. Publ. 29-33065
- (6) American Petroleum Institute (1982)
Acute toxicity tests of API sample 79-3 paraffinic oil (350 SUS/100 °F)
API Med. Res. Publ. 29-33067
- (7) American Petroleum Institute (1982)
Acute toxicity tests of API sample 79-4 paraffinic oil (550 SUS/100 °F)
API Med. Res. Publ. 29-33066

5. Toxicity

Id Lubricating oil
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- (8) American Petroleum Institute (1982)
Acute toxicity tests of API sample 79-5 paraffinic oil (800
SUS/100 °F)
API Med. Res. Publ. 29-33068
- (14) American Petroleum Institute (1986)
Acute oral toxicity study in rats
Acute dermal toxicity study in rabbits
Primary dermal irritation study in rabbits
Primary eye irritation study in rabbits
Dermal sensitization study in guinea pigs
API sample 83-15 hydrotreated heavy naphthenic distillate
(CAS 64742-52-5)
API Health Environ. Sci. Dep. Rep. 33-32639
- (81) CONCAWE (1997)
Lubricating oil basestocks
Product dossier No. 97/108
CONCAWE, Brussels

5. Toxicity

Id Lubricating oil
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5.3 EYE IRRITATION

Eye Irritation

Test Substance

Category Chemical (CAS #):	64741-50-0
Test Substance (CAS #):	64741-50-0; API 84-01; Unrefined base oil
Test Substance Purity/Composition and Other Test Substance Comments :	No information
Category Chemical Result Type :	Measured

Type : Eye irritation
Species : Rabbit
Concentration : Undiluted
Dose : 0.1 ml
Number of animals : 9
Method : Draize Test
Year : 1986
GLP : Yes
Test substance : Unrefined base oil Sample API 84-01 [CAS 64741-50-0] See section 1.1.1.

Method : 0.1 ml of undiluted test material was applied to the corneal surface of one eye of each of 9 rabbits, the other eye was untreated and served as control. After 20 to 30 seconds, the treated eyes of 3 rabbits were washed with lukewarm water for 1 minute. Eyes of the other 6 rabbits were not washed.
Readings of ocular lesions for all animals were made at 1, 24, 48, 72 hours and 7 days after treatment. Sodium fluorescein was used to aid in revealing possible corneal injury.

Result : One animal died on day 7 but this was not considered to be treatment related. The test material did not cause a pain response, corneal or iridial irritation. The eye irritation that occurred had cleared by 48 hours.
The primary eye irritation scores (according to the standard Draize scoring procedure) were as follows:

Period	Unwashed eyes	Washed eyes
1 hour	3.0	4.0
24 hours	1.7	0

Scores of 0 were recorded at all other observation times.

Reliability : (1) valid without restriction

5. Toxicity

Id Lubricating oil
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(13)

(13)
American Petroleum Institute (1986)
Acute oral toxicity study in rats
Acute dermal toxicity study in rabbits
Primary dermal irritation study in rabbits
Primary eye irritation study in rabbits
Dermal sensitization study in Guinea pigs
API 84-01 Light paraffinic distillate CAS 64741-50-0
API Med. Res. Publ.: 33-30595

Eye Irritation**Test Substance**

Category Chemical (CAS #):	64742-53-6
Test Substance (CAS #):	64742-53-6; API 83-12; Highly refined base oil
Test Substance Purity/Composition and Other Test Substance Comments :	API 83-12 No further information
Category Chemical Result Type :	Measured

Type : Eye irritation
Species : Rabbit
Concentration : Undiluted
Dose : 0.1 ml
Number of animals : 9
Method : Draize Test
Year : 1986
GLP : Yes
Test substance : Highly refined Base oil Sample API 83-12 [CAS64742-53-6] See section 1.1.1.

Method : 0.1 ml of undiluted test material was applied to the corneal surface of one eye of each of 9 rabbits, the other eye was untreated and served as control. After 20 to 30 seconds, the treated eyes of 3 rabbits were washed with lukewarm water for 1 minute. Eyes of the other 6 rabbits were not washed. Readings of ocular lesions for all animals were made at 1, 24, 48, 72 hours and 7 days after treatment. Sodium fluorescein was used to aid in revealing possible corneal injury.

Result : There was no pain response during instillation of the test material and no corneal or iridial irritation was seen during the study. Any irritation that occurred had cleared by 48 hours. The primary eye irritation scores for the first 48 hours of the study were as follows:

Period	Unwashed eyes	Washed eyes
1 hour	2.7	2.0
24 hours	0.3	0
48 hours	0	0

Reliability : (1) valid without restriction

5. Toxicity

Id Lubricating oil
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(12)

American Petroleum Institute (1986)
Acute oral toxicity study in rats
Acute dermal toxicity study in rabbits
Primary dermal irritation study in rabbits
Primary eye irritation study in rabbits
Dermal sensitization study in Guinea pigs
API 83-12 Hydrotreated light naphthenic distillate CAS
64742-53-6
API Med. Res. Publ.: 33-30592

5. Toxicity

Id Lubricating oil
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Date March 31, 2011

Eye Irritation

Test Substance

Category Chemical (CAS #):	64742-56-9; 64742-56-0; 64742-65-0; 64741-97-5; 64741-96-4; 64742-52-5
Test Substance (CAS #):	64742-56-9; API 78-9; Solvent dewaxed light paraffinic distillate 64742-56-0; API 78-10; Solvent dewaxed heavy paraffinic distillate 64742-65-0; API 79-3; Solvent dewaxed heavy paraffinic distillate 64742-65-0; API 79-4; Solvent dewaxed heavy paraffinic distillate 64742-65-0; API 79-5 Solvent dewaxed heavy paraffinic distillate Tufflo 6056; White mineral oil 64741-97-5; API 78-5; 7Solvent refined light naphthenic distillate 64741-96- 4; API 79-1;Solvent refined heavy naphthenic distillate 64742-52-5; API 83-15; Hydrotreated heavy naphthenic distillate
Test Substance Purity/Composition and Other Test Substance Comments :	API 78-9 API 78-10 API 79-3 API 79-4 API 79-5 Tufflo 6056 API 78-5 API 79-1 API 83-15 No other information
Category Chemical Result Type :	Measured

Type : Eye irritation
Species : Rabbit
Concentration : Undiluted
Dose : 0.1 ml
Test substance : Various base oils

Remark : CONCAWE summarized the data available on eye irritation for following table.

	Irritation*	API report No.
Paraffinic distillates		
Solvent dewaxed, light API 78-9 (64742-56-9)	Slight	29-33104
Solvent dewaxed, heavy		

5. Toxicity

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API 78-10** (64742=56-0)	Non	29-33105
API 79-3 (64742-65-0)	Non	29-33067
API 79-4 (64742-65-0)	Non	29-33066
API 79-5 (64742-65-0)	Non	29-33068

Naphthenic distillates

Solvent refined, light		
API 78-5 (64741-97-5)	Non	29-33106
Solvent refined, heavy		
API 79-1 (64741-96-4)	Non	29-33065
Hydrotreated, heavy		
API 83-15 (64742-52-5)	Slight	33-32639

Other mineral oils

Paraffin oil** Slight Carpenter & Smyth

* Irritation described as slight, moderate or non-irritating

** Although these materials are not included in the HPV Lubricating base stocks category, they are similar to other materials in the category and provide supportive information.

(2) (3) (4) (5) (6) (7) (8) (14) (77) (81)

- (2) American Petroleum Institute (1982)
Acute toxicity tests of API sample 78-10 paraffinic oil (150 SUS/100 °F)
API Med. Res. Publ. 29-33105
- (3) American Petroleum Institute (1982)
Acute toxicity tests of API sample 78-5 naphthenic oil (150 SUS/100 °F)
API Med. Res. Publ. 29-33106
- (4) American Petroleum Institute (1982)
Acute toxicity tests of API sample 78-9 paraffinic oil (70 SUS/100 °F)
API Med. Res. Publ. 29-33104
- (5) American Petroleum Institute (1982)
Acute toxicity tests of API sample 79-1 naphthenic oil (90 SUS/210 °F)
API Med. Res. Publ. 29-33065
- (6) American Petroleum Institute (1982)
Acute toxicity tests of API sample 79-3 paraffinic oil (350 SUS/100 °F)
API Med. Res. Publ. 29-33067
- (7) American Petroleum Institute (1982)
Acute toxicity tests of API sample 79-4 paraffinic oil (550 SUS/100 °F)
API Med. Res. Publ. 29-33066

5. Toxicity

Id Lubricating oil
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Date March 31, 2011

- (8) American Petroleum Institute (1982)
Acute toxicity tests of API sample 79-5 paraffinic oil (800
SUS/100 °F)
API Med. Res. Publ. 29-33068
- (14) American Petroleum Institute (1986)
Acute oral toxicity study in rats
Acute dermal toxicity study in rabbits
Primary dermal irritation study in rabbits
Primary eye irritation study in rabbits
Dermal sensitization study in guinea pigs
API sample 83-15 hydrotreated heavy naphthenic distillate
(CAS 64742-52-5)
API Health Environ. Sci. Dep. Rep. 33-32639
- (77) Carpenter, C. P. and Smythe, H. F. (1946)
Chemical burns of the rabbit cornea
Am. J. Ophthal. Vol. 29, pp 1363-1372
- (81) CONCAWE (1997)
Lubricating oil basestocks
Product dossier No. 97/108
CONCAWE, Brussels

5. Toxicity

Id Lubricating oil
basestocks
Date March 31, 2011

Skin Sensitization

TEST SUBSTANCE

Category Chemical :	64742-65-0
Test Substance :	64742-65-0; Stock 141; Distillates (petroleum), solvent-dewaxed heavy paraffinic Its viscosity was ~102 SUS at 100°F and 40 SUS at 210°F (18.8 cSt at 40°C and 4.0 cSt at 100°C).
Test Substance Purity/Composition and Other Test Substance Comments :	Stock 141 (CRU 84120) No compositional information
Category Chemical Result Type :	Measured
Unable to Measure or Estimate Justification :	

METHOD

Test Method:	Buehler test
Study Type:	Dermal sensitization
Species:	Guinea Pig
Other Species:	
Mammalian Strain:	Hartley albino guinea pigs
Other Strain:	

5. Toxicity

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Route of Induction:	Topical dermal
Route of Challenge Exposure:	Topical dermal
Gender:	Male and female
Number of Animals per Dose:	5 per sex
Concentration:	100% for induction phase
Concentration:	25% for challenge and rechallenge (in Squibb mineral oil)
Year Study Performed :	1983
Method/Guideline Followed:	Ritz, HL and Buehler, EV. 1980. In Current Concepts in Cutaneous Toxicity. Ed. by Drill, VA and Lazar, T. Academic Press. pp. 25
GLP:	Study was conducted in accord with EPA GLPs.
Exposure Period:	Approximately 6 weeks: 3 weeks during challenge, followed by 2 weeks without treatment and then challenge
Induction Frequency of Treatment:	Once weekly for 3 weeks
Challenge Exposure Period:	Challenge and rechallenge doses were left on skin for 6 hours. Sites were scored at 24 and 48 hours after challenge and rechallenge doses.
Challenge Frequency of Treatment:	Challenge was at 14 days after third induction dose; rechallenge was at 21 days.
Total Volume applied and Units:	0.4 ml applied using Hill Top chambers with a 25 mm Webril swatch
Control Group Type:	Naïve control received challenge dose.
Vehicle Used:	Yes, but only during challenge

5. Toxicity

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Vehicle Name:	Squibb mineral oil
Other Vehicle Name:	
Vehicle Amount and Units:	
Positive Control Substance:	2,4-dinitrochlorobenzene
Negative Control Substance:	
Post-Exposure Period:	
Method/Guideline and Test Condition Remarks:	

TEST RESULTS

Measurement Period and Units:	Percent Sensitized Test Substance:	Percent Sensitized Positive Control:	Percent Sensitized Negative Control:	Sensitization Score:
Challenge and rechallenge	0	90	0	

Results Remarks:	
Interpretation of Results:	No evidence of contact sensitization was observed in this test.
Conclusion:	The test substance was not a contact sensitizer under conditions of this test.

RELIABILITY/DATA QUALITY

Reliability:	1 – Reliable without restrictions
Reliability Remarks:	Comparable to guideline study
Key Study Sponsor Indicator:	Key

REFERENCE

5. Toxicity

Id Lubricating oil
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Date March 31, 2011

Reference:

Delayed contact hypersensitivity study in guinea pigs (Buehler test) of Stock 141. Final report on Mobil study 30881. Mobil Environmental and Health Science Laboratory, Princeton, NJ. 1985

5. Toxicity

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Date March 31, 2011

Skin Sensitization

TEST SUBSTANCE

Category Chemical :	64742-65-0
Test Substance :	64742-65-0; MLDW 100" PN (Stock 142); Paraffin oils (petroleum), catalytic dewaxed heavy Its viscosity was 22.33 cSt at 40°C (~100 SUS) and 4.23 cSt at 100°C.
Test Substance Purity/Composition and Other Test Substance Comments :	MLDW 100" PN; Stock 142; (Sample no. 82192) No other information
Category Chemical Result Type :	Measured
Unable to Measure or Estimate Justification :	

METHOD

Test Method:	Buehler test
Study Type:	Dermal sensitization
Species:	Guinea Pig
Other Species:	
Mammalian Strain:	Hartley albino guinea pigs
Other Strain:	
Route of Induction:	Topical dermal

5. Toxicity

Id Lubricating oil
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Route of Challenge Exposure:	Topical dermal
Gender:	Male and female
Number of Animals per Dose:	5 per sex
Concentration:	100% for induction phase
Concentration:	15% for challenge and rechallenge (in Squibb mineral oil)
Year Study Performed :	1984
Method/Guideline Followed:	Ritz, HL and Buehler, EV. 1980. In Current Concepts in Cutaneous Toxicity. Ed. by Drill, VA and Lazar, T. Academic Press. pp. 25
GLP:	Study was conducted in accord with EPA GLPs.
Exposure Period:	Approximately 6 weeks: 3 weeks during challenge, followed by 2 weeks without treatment and then challenge
Induction Frequency of Treatment:	Once weekly for 3 weeks
Challenge Exposure Period:	Challenge and rechallenge doses were left on skin for 6 hours. Sites were scored at 24 and 48 hours after challenge and rechallenge doses.
Challenge Frequency of Treatment:	Challenge was at 14 days after third induction dose; rechallenge was at 21 days.
Total Volume applied and Units:	0.4 ml applied using Hill Top chambers with a 25 mm Webril swatch
Control Group Type:	Naïve control received challenge dose.
Vehicle Used:	Yes, but only during challenge
Vehicle Name:	Squibb mineral oil

5. Toxicity

Id Lubricating oil
basestocks
Date March 31, 2011

Other Vehicle Name:				
Vehicle Amount and Units:				
Positive Control Substance:	2,4-dinitrochlorobenzene			
Negative Control Substance:				
Post-Exposure Period:				
Method/Guideline and Test Condition Remarks:				
TEST RESULTS				
Measurement Period and Units:	Percent Sensitized Test Substance:	Percent Sensitized Positive Control:	Percent Sensitized Negative Control:	Sensitization Score:
Challenge and rechallenge	0		0	
Results Remarks:				
Interpretation of Results:	No evidence of contact sensitization was observed in this test.			
Conclusion:	The test substance was not a contact sensitizer under conditions of this test.			
RELIABILITY/DATA QUALITY				
Reliability:	1 – Reliable without restrictions			
Reliability Remarks:	Comparable to guideline study			
Key Study Sponsor Indicator:	Key			
REFERENCE				
Reference:	Delayed contact hypersensitivity study in guinea pigs (Buehler test) of MLDW Stock 142. Final report on Mobil study 30238. Mobil Environmental and Health Science Laboratory, Princeton, NJ. 1984			

Skin Sensitization

Test Substance

Category Chemical (CAS #):	64741-50-0
Test Substance (CAS #):	64741-50-0; API 84-01; Unrefined base oil
Test Substance Purity/Composition and Other Test Substance Comments :	No information
Category Chemical Result Type :	Measured

Type : Skin sensitization - Buehler Test
Species : Guinea pig
Concentration : 1st. Induction 25 % occlusive epicutaneous
 : 2nd. Challenge 1 % occlusive epicutaneous
Number of animals : 10
Vehicle : Paraffin oil
Result : Not sensitizing
Year : 1986
GLP : Yes
Test substance : Unrefined base other TS: Unrefined base oil Sample API 84-01 [CAS 64741-50-0] See section 1.1.1.

Method : 0.4 ml of a 25% mixture of test material and paraffin oil was applied under an occlusive dressing to the shorn skin of 10 male and 10 female animals. 6 hours after application the dressings were removed and the skin wiped to remove residues of test material. The animals received one application each weeks. The same application site was used each time. 2 weeks following the third application, a challenge dose (0.4 ml of a 1% mixture in paraffin oil) was applied in the same manner as the sensitizing doses. A previously untreated site was used for the challenge application. The application sites for sensitizing and challenge doses were read for erythema and edema 24 and 48 hours after patch removal. To assist in the reading of the response to the final challenge dose the test site was depilated 3 hours prior to reading by using a commercially available depilatory cream.

Positive control (2,4-dinitrochlorobenzene at 0.3% in 80% aqueous ethanol), vehicle control and naive control groups were included in this study and the procedure for these was the same as for the test groups.

5. Toxicity

Id Lubricating oil
basestocks
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Result : The criteria used to evaluate the responses are described in the report as follows:
Determination of sensitization was based upon reactions to the challenge dose. Grades of 1 or greater in the test animals indicate evidence of sensitization, provided grades of less than 1 are seen in the naive controls. If grades of 1 or greater are noted in the naive control animals, then the reactions of test animals that exceed the most severe naive control reaction are considered sensitization reactions.
Using these criteria, none of the test animals became sensitized following treatment with API 84-01. In contrast, all the positive control animals were sensitized by their treatment.

Reliability : (1) valid without restriction

(13)

(13)
American Petroleum Institute (1986)
Acute oral toxicity study in rats
Acute dermal toxicity study in rabbits
Primary dermal irritation study in rabbits
Primary eye irritation study in rabbits
Dermal sensitization study in Guinea pigs
API 84-01 Light paraffinic distillate CAS 64741-50-0
API Med. Res. Publ.: 33-30595

Skin Sensitization

Test Substance

Category Chemical (CAS #):	64742-53-6
Test Substance (CAS #):	64742-53-6; API 83-12; Highly refined base oil
Test Substance Purity/Composition and Other Test Substance Comments :	API 83-12 No further information
Category Chemical Result Type :	Measured

Type : Skin sensitization - Buehler Test
Species : Guinea pig
Concentration : 1st: Induction 50 % occlusive epicutaneous
 : 2nd: Challenge 1 % occlusive epicutaneous
Number of animals : 10
Vehicle : Paraffin oil
Result : Not sensitizing
Year : 1986
GLP : Yes
Test substance : Highly refined Base oil Sample API 83-12 [CAS64742-53-6] See section 1.1.1.

Method : 0.4 ml of a 50% mixture of test material and paraffin oil was applied under an occlusive dressing to the shorn skin of 10 male and 10 female animals. 6 hours after application, the dressings were removed and the skin wiped to remove residues of test material. The animals received one application each week for 3 weeks. The same application site was used each time. 2 weeks following the third application, a challenge dose (0.4 ml of a 1% mixture in paraffin oil) was applied in the same manner as the sensitizing doses. A previously untreated site was used for the challenge application. The application sites for sensitizing and challenge doses were read for erythema and edema 24 and 48 hours after patch removal. To assist in the reading of the response to the final challenge dose the test site was depilated 3 hours prior to reading by using a commercially available depilatory cream.

Positive control (2,4-dinitrochlorobenzene at 0.3% in 80% aqueous ethanol), vehicle control and naive control groups were included in this study and the procedure for these was the same as for the test groups.

5. Toxicity

Id Lubricating oil
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Date March 31, 2011

Result : The criteria used to evaluate the responses are described in the report as follows:
Determination of sensitization was based upon reactions to the challenge dose. Grades of 1 or greater in the test animals indicate evidence of sensitization, provided grades of less than 1 are seen in the naive controls. If grades of 1 or greater are noted in the naive control animals, then the reactions of test animals that exceed the most severe naive control reaction are considered sensitization reactions.

One animal had a score of 0.5 after challenge with API 83-12. In contrast, all the positive control animals were sensitized by their treatment. The sample of API 83-12 was therefore non sensitizing.

Reliability : (1) valid without restriction

(12)

(12)
American Petroleum Institute (1986)
Acute oral toxicity study in rats
Acute dermal toxicity study in rabbits
Primary dermal irritation study in rabbits
Primary eye irritation study in rabbits
Dermal sensitization study in Guinea pigs
API 83-12 Hydrotreated light naphthenic distillate CAS
64742-53-6
API Med. Res. Publ.: 33-30592

Skin Sensitization

Test Substance

Category Chemical (CAS #): 64742-56-9; 64742-56-0; 64742-65-0; 64741-97-5; 64741-96-4; 64742-52-5

Test Substance (CAS #): 64742-56-9; API 78-9; Solvent dewaxed light paraffinic distillate
 64742-56-0; API 78-10; Solvent dewaxed heavy paraffinic distillate
 64742-65-0; API 79-3; Solvent dewaxed heavy paraffinic distillate
 64742-65-0; API 79-4; Solvent dewaxed heavy paraffinic distillate
 64742-65-0; API 79-5 Solvent dewaxed heavy paraffinic distillate
 Tufflo 6056; White mineral oil

64741-97-5; API 78-5; 7Solvent refined light naphthenic distillate
 64741-96- 4; API 79-1;Solvent refined heavy naphthenic distillate
 64742-52-5; API 83-15; Hydrotreated heavy naphthenic distillate

Test Substance Purity/Composition and Other Test Substance Comments :

API 78-9
 API 78-10
 API 79-3
 API 79-4
 API 79-5
 Tufflo 6056
 API 78-5
 API 79-1
 API 83-15

No other information

Category Chemical Result Type : Measured

Type : Skin sensitization - Buehler Test
Species : Guinea pig
Test substance : Various base oils

Remark : CONCAWE summarized the data available on skin sensitization for the lubricating oil basestocks. The methods and criteria used were the same as those described in the previous two robust summaries. The data are shown in the following table.

5. Toxicity

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Paraffinic distillates

Solvent dewaxed, light			
API 78-9	64742-56-9	Non	29-33104
Solvent dewaxed, heavy			
API 78-10*	64742-56-0	Non	29-33105
API 79-3	64742-65-0	Non	29-33067
API 79-4	64742-65-0	Non	29-33066
API 79-5	64742-65-0	Non	29-33068

Naphthenic distillates

Solvent refined, light			
API 78-5	64741-97-5	Non	29-33106
Solvent refined, heavy			
API 79-1	64741-96-4	Non	29-33065
Hydrotreated, heavy			
API 83-15	64742-52-5	Non	33-32639

* Although this material is not included in the HPV Lubricating base stocks category, it is similar to other materials in the category and provides supportive information.

(2) (3) (4) (5) (6) (7) (8) (14) (81)

- (2) American Petroleum Institute (1982)
Acute toxicity tests of API sample 78-10 paraffinic oil (150
SUS/100 °F)
API Med. Res. Publ. 29-33105
- (3) American Petroleum Institute (1982)
Acute toxicity tests of API sample 78-5 naphthenic oil (150
SUS/100 °F)
API Med. Res. Publ. 29-33106
- (4) American Petroleum Institute (1982)
Acute toxicity tests of API sample 78-9 paraffinic oil (70
SUS/100 °F)
API Med. Res. Publ. 29-33104
- (5) American Petroleum Institute (1982)
Acute toxicity tests of API sample 79-1 naphthenic oil (90
SUS/210 °F)
API Med. Res. Publ. 29-33065
- (6) American Petroleum Institute (1982)
Acute toxicity tests of API sample 79-3 paraffinic oil (350
SUS/100 °F)
API Med. Res. Publ. 29-33067
- (7) American Petroleum Institute (1982)
Acute toxicity tests of API sample 79-4 paraffinic oil (550
SUS/100 °F)
API Med. Res. Publ. 29-33066

5. Toxicity

Id Lubricating oil
basestocks
Date March 31, 2011

- (8) American Petroleum Institute (1982)
Acute toxicity tests of API sample 79-5 paraffinic oil (800
SUS/100 °F)
API Med. Res. Publ. 29-33068
- (14) American Petroleum Institute (1986)
Acute oral toxicity study in rats
Acute dermal toxicity study in rabbits
Primary dermal irritation study in rabbits
Primary eye irritation study in rabbits
Dermal sensitization study in guinea pigs
API sample 83-15 hydrotreated heavy naphthenic distillate
(CAS 64742-52-5)
API Health Environ. Sci. Dep. Rep. 33-32639
- (81) CONCAWE (1997)
Lubricating oil basestocks
Product dossier No. 97/108
CONCAWE, Brussels

5. Toxicity

Id Lubricating oil
 basestocks
 Date March 31, 2011

REPEATED DOSE TOXICITY, INHALATION

Repeated Dose Toxicity

Test Substance

Category Chemical (CAS #):	Not available
Test Substance (CAS #):	No CAS number available; Highly refined base oil
Test Substance Purity/Composition and Other Test Substance Comments :	No further information
Category Chemical Result Type :	Measured

Type : 14 day Inhalation
Species : Rat
Sex : Male/female
Strain : No data
Route of admin. : Inhalation
Exposure period : 14 days
Frequency of treatm. : Six hours per day
Control group : Yes
NOAEL : > 50 mg/m³
Year : 1989
GLP : No data
Test substance : Two samples of highly refined, solvent extracted dewaxed paraffinic base oil

Method : Groups of 5 male and 5 female rats were exposed to oil mists generated from two highly refined oils. Exposures were by inhalation six hours each day for a total of 10 days. The two oils were examined in separate experiments. The dose groups were:

Group	Mean actual concentration (mg/m ³)	Mass median particle size (µm)
Controls	Air only	N/A
Oil 1	55	1.5
	507	1.9
	1507	2.2
Oil 2	Air only	N/A
	50	1.5
	513	1.9

5. Toxicity

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	1480	2.2
Remark	No further experimental details are provided.	
	: A further two week inhalation study in rats has been reported for two mineral oil mists (Skyberg et al, 1990). The results largely confirm those described by Whitman et al. with respect to liver weight changes and histological observations in respiratory tissues.	
Result	: Oil 1	
	All treated animals survived to study termination. The fur of all animals was saturated with test material and the amount of material present was clearly related to the exposure concentration. Alopecia and scabs subsequently formed in the highest 2 dose groups. Animals in the highest dose group were relatively unresponsive to auditory stimulation. Decreased body weight associated with a decrease in food consumption was recorded for the high dose animals.	
	Biologically significant increases in relative lung and liver weights were observed in the males and females in the high dose group but only in the mid dose females. An increase in white cell counts and the percentage of neutrophils and a decrease in the percentage lymphocytes was observed in the high dose groups only. There were no treatment related histopathological changes in the lowest 2 dose groups. Animals in the highest dose group exhibited the same changes as those observed in the nasoturbinates and lungs of animals exposed to oil 2 (See below)	
	Oil 2 Clinical observations were the same as for those animals exposed to Oil 1, except that there was no scabbing and no treatment related alterations in food consumption. There was a biologically significant increase in absolute and relative lung weights in males and females at the high dose and in females only at the mid dose. Apart from elevated liver alanine and aspartate transaminase levels in the high dose females there were no other treatment related effects. Histological effects considered to be treatment related consisted of an increase in the amount of perivascular and peribronchial lymphoid proliferations and an increase in mixed inflammatory cell infiltrations in the terminal bronchioles and alveolar ducts of the highest two dose groups. Increases in the appearance of focal hyperplasia and squamous cell metaplasia of the anterior nasal mucosa associated with inflammatory cell infiltration was observed in the two highest dose groups. These changes were indicative of mild irritation of the nasal mucosa.	
Reliability	: The NOELs for the two oils were >50 mg/m ³ (4) not assignable The information is taken from a poster presentation and a reliability score cannot be assigned. However, the data are supportive of the other study on inhalation of oil mist reported by Dalbey et al.	
(120)	(120) (126) Skyberg, K., Skaug, V., Gylseth, B., Pedersen, J. R. and Iversen, O. H. (1990) Subacute inhalation toxicity of mineral oils, C15-C20 alkylbenzenes, and polybutene in male rats. Environmental Research Vol. 53., pp 48-61	
(126)	Whitman, F. T., Freeman, J. J., Infurna, R. N. and Phillips, R. D. (1989) Evaluation of the acute and subacute inhalation toxicity of lubricating oil mists. The Toxicologist Vol. 9., p 143	

5. Toxicity

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Repeated Dose Toxicity

Test Substance

Category Chemical (CAS #):	64742-70-7; 8042-47-5; 64742-54-7																																																																
Test Substance (CAS #):	64742-70-7; Solvent refined oil (SRO) 8042-47-5; White mineral oil (WTO) 64742-54-7; Severely hydrotreated heavy paraffinic oil (HBO)																																																																
Test Substance Purity/Composition and Other Test Substance Comments :	<table border="1"> <thead> <tr> <th></th> <th><u>SRO</u></th> <th><u>WTO</u></th> <th><u>HBO</u></th> </tr> </thead> <tbody> <tr> <td>Viscosity at 100 °F</td> <td>106</td> <td>85</td> <td>161</td> </tr> <tr> <td>Pour point (°F)</td> <td>20</td> <td>15</td> <td>-5</td> </tr> <tr> <td>API Gravity</td> <td>32.8</td> <td>34.6</td> <td>33.6</td> </tr> <tr> <td>Furfural (ppm)</td> <td>1</td> <td>0</td> <td><1</td> </tr> <tr> <td>Nitrogen (ppm)</td> <td>44</td> <td>-</td> <td>8</td> </tr> <tr> <td>Sulfur (wt.%)</td> <td>0.20</td> <td>-</td> <td><0.06</td> </tr> <tr> <td>Composition (wt.%)</td> <td></td> <td></td> <td></td> </tr> <tr> <td> Paraffins</td> <td>36</td> <td>60</td> <td>29.7</td> </tr> <tr> <td> Mononaphthenes</td> <td>22.3</td> <td>-</td> <td>30.6</td> </tr> <tr> <td> Polynaphthenes 22.3</td> <td>-</td> <td>37.3</td> <td></td> </tr> <tr> <td> Monoaromatics</td> <td>12.8</td> <td>0</td> <td>0.6</td> </tr> <tr> <td> Diaromatics</td> <td>3.3</td> <td>0</td> <td>0.8</td> </tr> <tr> <td> Polyaromatics</td> <td>1.4</td> <td>0</td> <td>1.0</td> </tr> <tr> <td> Unidentified aromatics</td> <td>0.4</td> <td>0</td> <td>0</td> </tr> <tr> <td> Aromatic sulfur types</td> <td>1.1</td> <td>0</td> <td>0</td> </tr> </tbody> </table>		<u>SRO</u>	<u>WTO</u>	<u>HBO</u>	Viscosity at 100 °F	106	85	161	Pour point (°F)	20	15	-5	API Gravity	32.8	34.6	33.6	Furfural (ppm)	1	0	<1	Nitrogen (ppm)	44	-	8	Sulfur (wt.%)	0.20	-	<0.06	Composition (wt.%)				Paraffins	36	60	29.7	Mononaphthenes	22.3	-	30.6	Polynaphthenes 22.3	-	37.3		Monoaromatics	12.8	0	0.6	Diaromatics	3.3	0	0.8	Polyaromatics	1.4	0	1.0	Unidentified aromatics	0.4	0	0	Aromatic sulfur types	1.1	0	0
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Category Chemical Result Type :	Measured																																																																

Type : 4 week Inhalation
Species : Rat
Sex : Male/female
Strain : Sprague-Dawley
Route of admin. : Inhalation
Exposure period : 4 weeks
Frequency of treatm. : 6 hours/day, 5 days/week
Doses : 50, 220 & 1000 mg/m³
Control group : Yes, concurrent no treatment
Year : 1991
GLP : No data

5. Toxicity

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Test substance

: 3 base oils

Three materials were examined in this study. The properties of the materials designated SRO, WTO and HBO are shown in the following table.

SRO Solvent refined oil CAS # 64742-70-7

WTO White oil CAS # 8042-47-5. [Prepared by severely hydrotreating a dewaxed feedstock and then acid washing with fuming sulfuric acid.]

HBO Hydrotreated base oil CAS #64742-54-7 [Severely hydrotreated heavy paraffinic oil produced by treatment of the vacuum distillate with hydrogen at high temperature and pressure (hydrotreating and hydrocracking)].

	<u>SRO</u>	<u>WTO</u>	<u>HBO</u>
Viscosity at 100 °F	106	85	161
Pour point (°F)	20	15	-5
API Gravity	32.8	34.6	33.6
Furfural (ppm)	1	0	<1
Nitrogen (ppm)	44	-	8
Sulfur (wt.%)	0.20	-	<0.06
Composition (wt.%)			
Paraffins	36	60	29.7
Mononaphthenes	22.3	-	30.6
Polynaphthenes	22.3	-	37.3
Monoaromatics	12.8	0	0.6
Diaromatics	3.3	0	0.8
Polyaromatics	1.4	0	1.0
Unidentified aromatics	0.4	0	0
Aromatic sulfur types	1.1	0	0

Method

: Groups of 10 male and 10 female rats, 11-12 weeks of age, were exposed to aerosol concentrations of the three test materials at nominal concentrations of 0, 50, 220 and 1000 mg/m³.

Exposures were for 6 hours each day, 5 days each week for 4 weeks.

Total number of exposures for each of the three test materials was: 17, 18 and 20 days for SRO, WTO and HBO respectively. Food and water were available ad libitum during non-exposure periods. Clinical observations were made prior to each exposure and body weights were recorded weekly.

Animals were sacrificed within 72 hours of the last exposure after being fasted overnight. Blood samples were taken for a range of hematology and serum chemical parameters. The hematological parameters consisted of: Total white and red cells, hemoglobin, hematocrit, MCV, MCH, and MCHC. A differential white cell count was also conducted.

The following chemical parameters were measured: Alanine transferase, albumin, albumin/globulin ratio, alkaline phosphatase, aspartate aminotransferase, total bilirubin, calcium, chloride, cholesterol, creatinine, globulin, glucose, iron, lactate dehydrogenase, inorganic phosphorus, potassium, total protein, sodium, triglycerides, urea nitrogen and uric acid. All animals were necropsied and the following organs were weighed: gonads, heart, kidneys, liver, spleen, and thymus.

The right middle lobe of the lung was weighed immediately after removal

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and again after drying.

H&E sections were prepared and examined of the following tissues from all control and high dose group animals: heart, kidney, liver, lung, four locations in the nasal turbinates, spleen, gonads, thymus and tracheobronchial lymph nodes.

Sperm from the cauda epididymis of each control and high dose male was examined for an assessment of sperm morphology.

Statistical analysis

Data were analyzed by one-way analysis of variance.

A probability of Type I error of <5% (P<0.05) was considered to be statistically significant. Comparison of means was performed by Duncan's multiple range test or the Student-Neuman-Keuls multiple comparison.

Data obtained from exposure to a given test article were analyzed together.

No statistical procedures were carried out to compare the effects of different test articles with each other.

Result

: Chamber concentrations

The aerosol concentrations were comparable among the three base stocks.

Qualitatively, the aerosols were virtually identical to each liquid base oil.

The actual concentrations for each of the aerosols was as

	<u>Nominal</u>	<u>Actual</u>
SRO	0	0
	50	50 ±10
	220	210 ±10
	1000	1020 ±60
WTO	0	0
	50	50 ±10
	220	210 ±10
	1000	980 ±20
HBO	0	0
	50	47 ±2
	220	220 ±10
	1000	980 ±50

The mass median diameter was well under 2µm for each base stock

Toxicity assessment

Apart from occasional loose stool there were no treatment related clinical observations and body weights were unaffected by exposure.

No treatment related effects were found in any of the hematological or clinical chemical parameters that were measured.

The percent sperm with aberrant morphology, including breakage, was unaffected by exposure to any of the three base oils.

There were no treatment-related observations at necropsy and, with the exception of the lungs, there were no significant changes in organ weights .

Wet and dry lung weights increased in a dose-related manner. The percentage increases in wet weight are shown in the following table. For simplicity increases are shown to nearest whole numbers

Sex	% Increase in wet lung weight			
	Dose	SRO	WTO	HBO
<u>(mg/m³)</u>				
Female	50	3	8	2

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210	4	23*	34*
1000	38*	64*	36*

Male

50	5	-	1
210	12*	1	6
1000	33*	31*	32*

* denotes differences that are statistically significant ($P < 0.05$) compared to controls.

The ratios of wet to dry lung weights were significantly increased for both sexes at the highest dose concentration for all three base oils.

Morphologically, treatment related changes were only observed in the lungs and tracheobronchial lymph nodes.

Foamy macrophages with numerous vacuoles of varying size were present in the alveolar spaces of the lungs of many of the exposed animals. The histological changes are summarized in the following table.

No. of animals in each group with a given histopathological change

Tissue/change	Dose group		
	50	210	1000
SRO			
Lung			
1-2 Foamy macrophages (FM)	20	20	20
3-6 FM	0	0	20
Thickened alveolar wall	0	0	0
FM in alveolar interstitium	0	0	0
Mild alveolar PMN infiltrate	0	5	20
Lymph nodes			
Anterior mediastinal			
Macrophage accumulation	NE	NE	9
Tracheobronchial			
FM accumulation	NE	NE	19
Macrophage accumulation	NE	NE	0
WTO			
Lung			
1-2 Foamy macrophages (FM)	20	20	20
3-6 FM	0	0	20
Thickened alveolar wall	0	0	0
FM in alveolar interstitium	0	0	0
Mild alveolar PMN infiltrate	0	0	19
Lymph nodes			
Anterior mediastinal			
Macrophage accumulation	NE	NE	0
Tracheobronchial			
FM accumulation	NE	NE	0
Macrophage accumulation	NE	NE	19
HBO			
Lung			
1-2 Foamy macrophages (FM)	0	16	16
3-6 FM	0	0	16

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Thickened alveolar wall	0	0	16
FM in alveolar interstitium	0	0	16
Mild alveolar PMN infiltrate	0	0	0
Lymph nodes			
Anterior mediastinal			
Macrophage accumulation	NE	NE	2
Tracheobronchial			
FM accumulation	NE	NE	0
Macrophage accumulation	NE	NE	3

NE denotes Not Evaluated

Only 16 animals in the HBO high dose group were examined

In conclusion the NOAELs and LOAELs for the oils can be summarized thus:

Oil	LOAEL (mg/m³)	NOAEL (mg/m³)
SRO	210	50
WTO	210	50
HBO	210	50

Reliability

: (2) valid with restrictions

It is not clear whether the study was carried out according to GLP, but otherwise it was a well conducted and well reported study.

(83)

(83)

Dalbey, W., Osimitz, T., Kommineni, C., Roy, T., Feuston, M., and Yang, J. (1991) Four-week inhalation exposures of rats to aerosols of three lubricant base oils. J. Appl. Toxicol. Vol 11 (4), pp 297-302.

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REPEATED DOSE TOXICITY, DERMAL

Repeated-Dose Toxicity

TEST SUBSTANCE

Category Chemical:	64742-56-9
Test Substance:	64742-56-9; MRD-87-099; Distillates, petroleum, solvent-dewaxed light paraffinic.
Test Substance Purity/Composition and Other Test Substance Comments:	MRD-87-099 No other information
Category Chemical Result Type:	Measured
Unable to Measure or Estimate Justification:	

METHOD

Route of Administration:	Dermal
Other Route of Administration:	
Type of Exposure:	
Species:	Rabbit
Other Species:	None
Mammalian Strain:	New Zealand White

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Other Strain:	None
Gender:	Male and female
Number of Animals per Dose:	10 (5 per sex)
Concentration:	100%
Dose:	0 (sham dosed) and 1000 mg/kg/day
Year Study Performed:	1988
Method/Guideline Followed:	Other; comparable to OECD guideline limit test
GLP:	Study was conducted in accordance with EPA Good Laboratory Practices.
Exposure Period:	4 weeks
Frequency of Treatment:	5 days/week
Post-Exposure Period:	None
Method/Guideline and Test Condition Remarks:	<p>Hair was clipped from the backs of the rabbits three days before dosing began and Elizabethan collars were placed on the animals. Hair was clipped twice weekly during the remainder of the study. The test material was applied to the clipped, unabraded dorsal skin of each rabbit on weekdays. The test material was held in contact with the skin by an impervious sleeve and non-irritating wrap. The test material was left in contact with the skin for a minimum of 6 hours, after which the remaining test material was removed with a dry paper towel.</p> <p>Endpoints during the biophase included clinical signs (daily), body weights (twice weekly), food consumption, and irritation of the skin (twice weekly). At terminal sacrifice after 4 weeks of dosing, blood samples were taken for measurement of hematological parameters (hematocrit, hemoglobin, number of red blood cells, number and differential count of white blood cells, mean corpuscular volume, mean corpuscular hemoglobin, platelets, prothrombin time, and activated partial thromboplastin time). The following clinical chemistry parameters were analyzed: albumin, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, cholesterol, creatinine, gamma glutamyl transpeptidase, glucose, sorbitol dehydrogenase, total bilirubin, total protein,</p>

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triglycerides, urea nitrogen, calcium, chloride, phosphorus, potassium, and sodium.

All animals were then killed and necropsied. The following organs were weighed: adrenals, brain, kidneys, liver, ovaries, and testes. Histological slides were prepared from the following organs and examined microscopically by a pathologist: adrenals, brain, bone with marrow (sternum), epididymides, eye and optic nerve, heart, duodenum, ileum, jejunum, cecum, colon, kidneys, liver, lungs, mammary gland, mesenteric lymph nodes, sciatic nerve, muscle (biceps femoris), ovaries, pancreas, pituitary, prostate, rectum, salivary glands, seminal vesicles, skin (treated and untreated), cervical spinal cord, spleen, stomach, testes, thymus, thyroids, parathyroids, trachea with esophagus, urinary bladder, uterus, and vagina.

Data on hematology, serum chemistry, organ weights, relative organ weights, body weights, and food consumption were analyzed statistically first by ANOVA and Bartlett's test. If variances were equal and significant differences among the means were indicated, Dunnett's test was applied. If variances were not equal, the Kruskal-Wallis test was used to test for equality of means. If significant differences were indicated, Dunn's Summed Rank test was used to determine which group differed significantly from controls.

TEST RESULTS

Concentration (LOAEL/LOAEC/NOAEL/NOAEC)

Type	Population:	Value Description:	Value or Lower Concentration:	Upper Concentration:	Units:
NOAEL	Rabbit	=	1000		Mg/kg/day

Results Remarks:

Erythema score for treated skin ranged from very slight to severe; scores for edema ranged from very slight to moderate. Additional changes in the skin included atonia, desquamation, eschar, leathery skin, exfoliation, necrosis, and fissuring.

All animals survived to termination of the study and most animals had no abnormal clinical signs at each observation interval. Body weight was not significantly affected by treatment, but food consumption was significantly decreased in females during weeks 3 and 4. The following table shows mean weekly food consumption (grams).

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	Week 1	Week 2	Week 3	Week 4
Males				
Control	1199 ± 297	1240 ± 300	1212 ± 269	1046 ± 233
Treated	1238 ± 216	1242 ± 198	1309 ± 216	1226 ± 275
Females				
Control	1352 ± 256	1390 ± 138	1478 ± 199	1274 ± 265
Treated	1256 ± 208	1265 ± 236	1225 ± 144*	930 ± 155*

*Significantly different from controls

Organs weights were not affected by treatment except for an increase in mean relative weight of the liver in males, as shown in the following table of liver weight relative to body weight (%). No microscopic changes were observed. .

	Body weight (kg)	Relative Liver Weight
Males		
Control	3.09 ± 0.37	2.2 ± 0.1
Treated	3.21 ± 0.28	2.4 ± 0.1*
Females		
Control	3.48 ± 0.40	2.2 ± 0.1
Treated	3.21 ± 0.23	2.3 ± 0.3

*Significantly different from controls

The differential leukocyte counts and the red blood cell morphology were unremarkable for the male animals; however, the females showed a slight shift in lymphocytes and segmented neutrophils. Statistical analysis of the mean serum chemistry values revealed a significant increase in the cholesterol value for the males when compared to the control value, and an increase in platelet count in females. Both responses are not considered biologically significant.. Neither change was considered biologically significant by the author although no explanation was provided

	Platelets (10 ³ /mm ³)	Cholesterol (mg/dL)
Males		
Control	473 ± 36	21.9 ± 6.7
Treated	470 ± 65	49.2 ± 8.9*

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Females		
Control	395 ± 50	41.4 ± 8.4
Treated	612 ± 135*	49.2 ± 8.5

*Significantly different from controls

The only treatment-related change seen histologically was evidence of irritation in the treated skin (inflammation, hyperplasia of hair follicles, and hyperplasia/hyperkeratosis of epidermis).

Conclusion:

Determined by the reviewer

The systemic NOAEL for a 4 week dermal administration study in rats was determined to be 1000 mg/kg/day, based on the conclusions of the author. The LOAEL was not identified (>1000 mg/kg/day).

Skin irritation and histopathological changes were observed in all treated animals.

The systemic NOEL was not identified since a significant increase in relative liver weight and cholesterol levels were observed in males and a significant increase in platelets in females was observed at 1000 mg/kg/day. Females also had a slight shift in lymphocytes and segmented neutrophils, and significantly decreased food consumption was observed during weeks 3 and 4.

RELIABILITY/DATA QUALITY

Reliability:

1. – Reliable without restrictions

Reliability Remarks:

Comparable to a guideline limit test

Key Study Sponsor Indicator:

Key

REFERENCE

Reference:

Repeated dermal toxicity study in rabbits. Test materials: MRD-87-099, MRD-87-100, MRD-87-101. Final report for project number 209909A. Exxon Biomedical Sciences, Inc. , East Millstone, NJ. 1991

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Repeated-Dose Toxicity

TEST SUBSTANCE

Category Chemical:	64742-65-0
Test Substance:	64742-65-0; MRD-87-100; Distillates, petroleum, solvent-dewaxed heavy paraffinic
Test Substance Purity/Composition and Other Test Substance Comments:	MRD-87-100 No other information
Category Chemical Result Type:	Measured
Unable to Measure or Estimate Justification:	

METHOD

Route of Administration:	Dermal
Other Route of Administration:	
Type of Exposure:	
Species:	Rabbit
Other Species:	None
Mammalian Strain:	New Zealand White
Other Strain:	None

5. Toxicity

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Gender:	Male and female
Number of Animals per Dose:	10 (5 per sex)
Concentration:	100%
Dose:	0 (sham dosed) and 1000 mg/kg/day
Year Study Performed:	1988
Method/Guideline Followed:	Other; comparable to OECD guideline limit test
GLP:	Study was conducted in accordance with EPA Good Laboratory Practices.
Exposure Period:	4 weeks
Frequency of Treatment:	5 days/week
Post-Exposure Period:	None
Method/Guideline and Test Condition Remarks:	<p>Hair was clipped from the backs of the rabbits three days before dosing began and Elizabethan collars were placed on the animals. Hair was clipped twice weekly during the remainder of the study. The test material was applied to the clipped, unabraded dorsal skin of each rabbit on weekdays. The test material was held in contact with the skin by an impervious sleeve and non-irritating wrap. The test material was left in contact with the skin for a minimum of 6 hours, after which the remaining test material was removed with a dry paper towel.</p> <p>Endpoints during the biophase included clinical signs (daily), body weights (twice weekly), food consumption, and irritation of the skin (twice weekly). At terminal sacrifice after 4 weeks of dosing, blood samples were taken for measurement of hematological parameters (hematocrit, hemoglobin, number of red blood cells, number and differential count of white blood cells, mean corpuscular volume, mean corpuscular hemoglobin, platelets, prothrombin time, and activated partial thromboplastin time). The following clinical chemistry parameters were analyzed: albumin, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, cholesterol, creatinine, gamma glutamyl transpeptidase, glucose, sorbitol dehydrogenase, total bilirubin, total protein, triglycerides, urea nitrogen, calcium, chloride, phosphorus, potassium, and sodium.</p>

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All animals were then killed and necropsied. The following organs were weighed: adrenals, brain, kidneys, liver, ovaries, and testes. Histological slides were prepared from the following organs and examined microscopically by a pathologist: adrenals, brain, bone with marrow (sternum), epididymides, eye and optic nerve, heart, duodenum, ileum, jejunum, cecum, colon, kidneys, liver, lungs, mammary gland, mesenteric lymph nodes, sciatic nerve, muscle (biceps femoris), ovaries, pancreas, pituitary, prostate, rectum, salivary glands, seminal vesicles, skin (treated and untreated), cervical spinal cord, spleen, stomach, testes, thymus, thyroids, parathyroids, trachea with esophagus, urinary bladder, uterus, and vagina.

Data on hematology, serum chemistry, organ weights, relative organ weights, body weights, and food consumption were analyzed statistically first by ANOVA and Bartlett's test. If variances were equal and significant differences among the means were indicated, Dunnett's test was applied. If variances were not equal, the Kruskal-Wallis test was used to test for equality of means. If significant differences were indicated, Dunn's Summed Rank test was used to determine which group differed significantly from controls.

TEST RESULTS

Concentration (LOAEL/LOAEC/NOAEL/NOAEC) *

Type	Population:	Value Description:	Value or Lower Concentration:	Upper Concentration:	Units:
NOAEL	Rabbit	=	1000		mg/kg/day

*Determined by reviewer based on conclusions of the author

Results Remarks:

Erythema score for treated skin ranged from very slight to severe; scores for edema ranged from very slight to moderate. Additional changes in the skin included desquamation, eschar, leathery skin, atonia, and fissuring.

All animals survived to termination of the study and most animals had no abnormal clinical signs at each observation interval. Body weight and food consumption were not significantly affected by treatment. Organs weights were not affected by treatment except for an increase in mean relative weight of the liver in males, as shown in the following table of liver weight relative to body weight (%). There were no concomitant microscopic changes.

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	Body weight (kg)	Relative Liver Weight
Males		
Control	3.09 ± 0.37	2.2 ± 0.1
Treated	3.00 ± 0.27	2.5 ± 0.2*
Females		
Control	3.48 ± 0.40	2.2 ± 0.1
Treated	3.10 ± 0.18	2.3 ± 0.1

*Significantly different from controls

Among parameters of hematology and clinical chemistry, mean gamma-glutamyl transferase was significantly decreased in males compared to controls; but the change was not considered biologically significant by the author. No explanation was provided.

	Γ-glutamyl transferase (IU/L)
Males	
Control	4.38 ± 0.71
Treated	3.12 ± 0.89*
Females	
Control	3.65 ± 1.15
Treated	4.42 ± 0.92

*Significantly different from controls

The only treatment-related change seen histologically was evidence of irritation in the treated skin (inflammation, hyperplasia of hair follicles, and hyperplasia/hyperkeratosis of epidermis).

Conclusion:

Determined by the reviewer

The systemic NOAEL for a 4 week dermal administration study in rats was determined to be 1000 mg/kg/day, based on the conclusions of the author. The LOAEL was not identified (>1000 mg/kg/day).

Skin irritation and histopathological changes were observed in all treated animals.

The systemic NOEL was not identified since a significant increase in relative liver weight and gamma-glutamyl transferase were observed in males.

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RELIABILITY/DATA QUALITY

Reliability:	1. – Reliable without restrictions
Reliability Remarks:	Comparable to guideline study
Key Study Sponsor Indicator:	Key

REFERENCE

Reference:	Repeated dermal toxicity study in rabbits. Test materials: MRD-87-099, MRD-87-100, MRD-87-101. Final report for project number 209909A. Exxon Biomedical Sciences, Inc. , East Millstone, NJ. 1991
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Repeated-Dose Toxicity

TEST SUBSTANCE

Category Chemical:	64742-65-0
Test Substance:	64742-65-0; MRD-87-101; Distillates, petroleum, solvent-dewaxed heavy paraffinic
Test Substance Purity/Composition and Other Test Substance Comments:	MRD-87-101 No other information
Category Chemical Result Type:	Measured
Unable to Measure or Estimate Justification:	

METHOD

Route of Administration:	Dermal
Other Route of Administration:	
Type of Exposure:	
Species:	Rabbit
Other Species:	None
Mammalian Strain:	New Zealand White
Other Strain:	None

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Gender:	Male and female
Number of Animals per Dose:	10 (5 per sex)
Concentration:	100%
Dose:	0 (sham dosed) and 1000 mg/kg/day
Year Study Performed:	1988
Method/Guideline Followed:	Other; comparable to OECD guideline limit test
GLP:	Study was conducted in accordance with EPA Good Laboratory Practices.
Exposure Period:	4 weeks
Frequency of Treatment:	5 days/week
Post-Exposure Period:	None
Method/Guideline and Test Condition Remarks:	<p>Hair was clipped from the backs of the rabbits three days before dosing began and Elizabethan collars were placed on the animals. Hair was clipped twice weekly during the remainder of the study. The test material was applied to the clipped, unabraded dorsal skin of each rabbit on weekdays. The test material was held in contact with the skin by an impervious sleeve and non-irritating wrap. The test material was left in contact with the skin for a minimum of 6 hours, after which the remaining test material was removed with a dry paper towel.</p> <p>Endpoints during the biophase included clinical signs (daily), body weights (twice weekly), food consumption, and irritation of the skin (twice weekly). At terminal sacrifice after 4 weeks of dosing, blood samples were taken for measurement of hematological parameters (hematocrit, hemoglobin, number of red blood cells, number and differential count of white blood cells, mean corpuscular volume, mean corpuscular hemoglobin, platelets, prothrombin time, and activated partial thromboplastin time). The following clinical chemistry parameters were analyzed: albumin, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, cholesterol, creatinine, gamma glutamyl transpeptidase, glucose, sorbitol dehydrogenase, total bilirubin, total protein, triglycerides, urea nitrogen, calcium, chloride, phosphorus, potassium, and sodium.</p>

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All animals were then killed and necropsied. The following organs were weighed: adrenals, brain, kidneys, liver, ovaries, and testes. Histological slides were prepared from the following organs and examined microscopically by a pathologist: adrenals, brain, bone with marrow (sternum), epididymides, eye and optic nerve, heart, duodenum, ileum, jejunum, cecum, colon, kidneys, liver, lungs, mammary gland, mesenteric lymph nodes, sciatic nerve, muscle (biceps femoris), ovaries, pancreas, pituitary, prostate, rectum, salivary glands, seminal vesicles, skin (treated and untreated), cervical spinal cord, spleen, stomach, testes, thymus, thyroids, parathyroids, trachea with esophagus, urinary bladder, uterus, and vagina.

Data on hematology, serum chemistry, organ weights, relative organ weights, body weights, and food consumption were analyzed statistically first by ANOVA and Bartlett's test. If variances were equal and significant differences among the means were indicated, Dunnett's test was applied. If variances were not equal, the Kruskal-Wallis test was used to test for equality of means. If significant differences were indicated, Dunn's Summed Rank test was used to determine which group differed significantly from controls.

TEST RESULTS

Concentration (LOAEL/LOAEC/NOAEL/NOAEC)

Type	Population:	Value Description:	Value or Lower Concentration:	Upper Concentration:	Units:
NOAEL	Rabbit	=	1000		mg/kg/day

Results Remarks:

Erythema score for treated skin ranged from "very slight" to "well defined"; scores for edema ranged from "limited" to "very slight". Additional changes in the skin included atonia and desquamation.

All animals survived to termination of the study and most animals had no abnormal clinical signs at each observation interval. Body weight was not significantly affected by treatment, but food consumption was significantly decreased in females during week 3. The following table shows mean weekly food consumption (grams).

	Week 1	Week 2	Week 3	Week 4
Males				

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Control	1199 ± 297	1240 ± 300	1212 ± 269	1046 ± 233
Treated	1065 ± 267	1150 ± 249	1153 ± 230	1031 ± 212
Females				
Control	1352 ± 256	1390 ± 138	1478 ± 199	1274 ± 265
Treated	1166 ± 107	1300 ± 71	1161 ± 154*	1206 ± 200

*Significantly different from controls

Organs weights and parameters of hematology and serum chemistry were not affected by treatment. The only treatment-related change seen histologically was evidence of irritation in the treated skin (inflammation, hyperplasia of hair follicles, and hyperplasia/hyperkeratosis of epidermis).

Conclusion:

Determined by the reviewer

The systemic NOAEL for a 4 week dermal administration study in rats was determined to be 1000 mg/kg/day, based on the conclusions of the author. The LOAEL was not identified (>1000 mg/kg/day).

Skin irritation and histopathological changes were observed in all treated animals.

The systemic NOEL was not identified since a significant decrease food consumption was observed during week 3 in females.

RELIABILITY/DATA QUALITY

Reliability:

1. – Reliable without restrictions

Reliability Remarks:

Comparable to guideline limit test

Key Study Sponsor Indicator:

Key study
Repeated dermal toxicity study in rabbits. Test materials: MRD-87-099, MRD-87-100, MRD-87-101.

REFERENCE

Reference:

Repeated dermal toxicity study in rabbits. Test materials: MRD-87-099, MRD-87-100, MRD-87-101. Final report for project number 209909A. Exxon Biomedical Sciences, Inc. , East Millstone, NJ. 1991

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Repeated-Dose Toxicity

TEST SUBSTANCE

Category Chemical:	64741-88-4
Test Substance:	64741-88-4; MRD-87-102; Distillates, petroleum, solvent-refined heavy paraffinic
Test Substance Purity/Composition and Other Test Substance Comments:	MRD-87-102 No other information
Category Chemical Result Type:	Measured
Unable to Measure or Estimate Justification:	

METHOD

Route of Administration:	Dermal
Other Route of Administration:	
Type of Exposure:	
Species:	Rabbit
Other Species:	None
Mammalian Strain:	New Zealand White
Other Strain:	None

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Gender:	Male and female
Number of Animals per Dose:	10 (5 per sex)
Concentration:	100%
Dose:	0 (sham dosed) and 1000 mg/kg/day
Year Study Performed:	1988
Method/Guideline Followed:	Other; comparable to OECD guideline limit test
GLP:	Study was conducted in accordance with EPA Good Laboratory Practices.
Exposure Period:	4 weeks
Frequency of Treatment:	5 days/week
Post-Exposure Period:	None
Method/Guideline and Test Condition Remarks:	<p>Hair was clipped from the backs of the rabbits three days before dosing began and Elizabethan collars were placed on the animals. Hair was clipped twice weekly during the remainder of the study. The test material was applied to the clipped, unabraded dorsal skin of each rabbit on weekdays. The test material was then spread on the skin with a glass rod and held in contact with the skin by an impervious sleeve and non-irritating wrap. The test material was left in contact with the skin for a minimum of 6 hours, after which the remaining test material was removed with a dry paper towel.</p> <p>Endpoints during the biophase included clinical signs (daily), body weights (twice weekly), food consumption, and irritation of the skin (twice weekly). At terminal sacrifice after 4 weeks of dosing, blood samples were taken for measurement of hematological parameters (hematocrit, hemoglobin, number of red blood cells, number and differential count of white blood cells, mean corpuscular volume, mean corpuscular hemoglobin, platelets, prothrombin time, and activated partial thromboplastin time). The following clinical chemistry parameters were analyzed: albumin, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, cholesterol, creatinine, gamma glutamyl transpeptidase, glucose, sorbitol dehydrogenase, total bilirubin, total protein, triglycerides, urea nitrogen, calcium, chloride, phosphorus, potassium, and sodium.</p>

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All animals were then killed and necropsied. The following organs were weighed: adrenals, brain, kidneys, liver, ovaries, and testes. Histological slides were prepared from the following organs and examined microscopically by a pathologist: adrenals, brain, bone with marrow (sternum), epididymides, eye and optic nerve, heart, duodenum, ileum, jejunum, cecum, colon, kidneys, liver, lungs, mammary gland, mesenteric lymph nodes, sciatic nerve, muscle (biceps femoris), ovaries, pancreas, pituitary, prostate, rectum, salivary glands, seminal vesicles, skin (treated and untreated), cervical spinal cord, spleen, stomach, testes, thymus, thyroids, parathyroids, trachea with esophagus, urinary bladder, uterus, and vagina.

Data on hematology, serum chemistry, organ weights, relative organ weights, body weights, and food consumption were analyzed statistically first by ANOVA and Bartlett's test. If variances were equal and significant differences among the means were indicated, Dunnett's test was applied. If variances were not equal, the Kruskal-Wallis test was used to test for equality of means. If significant differences were indicated, Dunn's Summed Rank test was used to determine which group differed significantly from controls.

TEST RESULTS

Concentration (LOAEL/LOAEC/NOAEL/NOAEC)*

Type	Population:	Value Description:	Value or Lower Concentration:	Upper Concentration:	Units:
NOAEL	Rabbit	=	1000		mg/kg/day

*Determined by reviewer based on the interpretations of the author

Results Remarks:

One control animal died prior to the scheduled sacrifice. The death appeared to be unrelated to treatment. Most surviving animals had no abnormal clinical signs at each observation interval. Erythema score for treated skin ranged from "very slight" to "well defined" with one animal receiving a score for severe irritation with eschar. No irritation was noted in the control group.

Body weight and food consumption were not significantly affected by treatment. Organ weights at sacrifice were not affected by treatment. Among parameters of hematology and clinical chemistry, gamma-glutamyl transpeptidase was

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increased in treated males, as shown in the following table. This increase was due to a high value in one animal.

	Γ-glutamyl transpeptidase (IU/L)
Males	
Control	3.08 ± 0.61
Treated	5.97 ± 2.92
Females	
Control	4.00 ± 0.89
Treated	3.65 ± 0.61

*Significantly different from controls

The only treatment-related change seen histologically was evidence of irritation in the treated skin (inflammation in the superficial dermis, enlarged, hyperplastic hair follicles, and hyperplasia/hyperkeratosis of epidermis).

Conclusion:

Determined by the reviewer

The systemic NOAEL following a 4 week dermal administration was determined to be 1000 mg/kg/day, based on the conclusions of the report. The LOAEL was not identified (>1000 mg/kg/day).

Skin irritation was observed in all treated animals.

RELIABILITY/DATA QUALITY

Reliability:

1. – Reliable without restrictions

Reliability Remarks:

Comparable to guideline limit test

Key Study Sponsor Indicator:

Key

REFERENCE

Reference:

Repeated dermal toxicity study in rabbits. Test materials: MRD-87-102 MRD-87-103. Final report for project number 209909B. Exxon Biomedical Sciences, Inc. , East Millstone, NJ. 1991

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Repeated-Dose Toxicity

TEST SUBSTANCE

Category Chemical:	64742-62-7
Test Substance:	64742-62-7; MRD-87-103; Residual oils, petroleum, solvent-dewaxed
Test Substance Purity/Composition and Other Test Substance Comments:	MRD-87-103 No other information
Category Chemical Result Type:	Measured
Unable to Measure or Estimate Justification:	

METHOD

Route of Administration:	Dermal
Other Route of Administration:	
Type of Exposure:	
Species:	Rabbit
Other Species:	None
Mammalian Strain:	New Zealand White
Other Strain:	None
Gender:	Male and female

5. Toxicity

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Number of Animals per Dose:	10 (5 per sex)
Concentration:	100%
Dose:	0 (sham dosed) and 1000 mg/kg/day
Year Study Performed:	1988
Method/Guideline Followed:	Other; comparable to OECD guideline limit test
GLP:	Study was conducted in accordance with EPA Good Laboratory Practices.
Exposure Period:	4 weeks
Frequency of Treatment:	5 days/week
Post-Exposure Period:	None
Method/Guideline and Test Condition Remarks:	<p>Also tested in this study was MD-87-102</p> <p>Hair was clipped from the backs of the rabbits three days before dosing began and Elizabethan collars were placed on the animals. Hair was clipped twice weekly during the remainder of the study. The test material was applied to the clipped, unabraded dorsal skin of each rabbit on weekdays. The test material was then spread on the skin with a glass rod and held in contact with the skin by an impervious sleeve and non-irritating wrap. The test material was left in contact with the skin for a minimum of 6 hours, after which the remaining test material was removed with a dry paper towel. The control animals were not treated but were wrapped in a similar manner.</p> <p>Endpoints during the biophase included clinical signs (daily), body weights (twice weekly), food consumption, and irritation of the skin (twice weekly). At terminal sacrifice after 4 weeks of dosing, blood samples were taken for measurement of hematological parameters (hematocrit, hemoglobin, number of red blood cells, number and differential count of white blood cells, mean corpuscular volume, mean corpuscular hemoglobin, platelets, prothrombin time, and activated partial thromboplastin time). The following clinical chemistry parameters were analyzed: albumin, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, cholesterol, creatinine, gamma glutamyl transpeptidase, glucose, sorbitol dehydrogenase, total bilirubin, total protein, triglycerides, urea nitrogen, calcium, chloride, phosphorus, potassium, and sodium.</p>

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All animals were then killed and necropsied. The following organs were weighed: adrenals, brain, kidneys, liver, ovaries, and testes. Histological slides were prepared from the following organs and examined microscopically by a pathologist: adrenals, brain, bone with marrow (sternum), epididymides, eye and optic nerve, heart, duodenum, ileum, jejunum, cecum, colon, kidneys, liver, lungs, mammary gland, mesenteric lymph nodes, sciatic nerve, muscle (biceps femoris), ovaries, pancreas, pituitary, prostate, rectum, salivary glands, seminal vesicles, skin (treated and untreated), cervical spinal cord, spleen, stomach, testes, thymus, thyroids, parathyroids, trachea with esophagus, urinary bladder, uterus, and vagina.

Data on hematology, serum chemistry, organ weights, relative organ weights, body weights, and food consumption were analyzed statistically first by ANOVA and Bartlett's test. If variances were equal and significant differences among the means were indicated, Dunnett's test was applied. If variances were not equal, the Kruskal-Wallis test was used to test for equality of means. If significant differences were indicated, Dunn's Summed Rank test was used to determine which group differed significantly from controls.

TEST RESULTS

Concentration (LOAEL/LOAEC/NOAEL/NOAEC) *

Type	Population:	Value Description:	Value or Lower Concentration:	Upper Concentration:	Units:
NOAEL	Rabbit	=	1000		mg/kg/day

***Determined by reviewer based on interpretation of study by author**

Results Remarks:

One control animal died prior to the scheduled sacrifice. The death appeared to be unrelated to treatment. Most surviving animals had no abnormal clinical signs at each observation interval.

Erythema score for treated skin ranged from "very slight" to "moderate/severe. Two animals exhibited desquamation. No irritation was noted in the control group. Body weight and food consumption were not significantly affected by

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treatment. Organ weights at sacrifice were not affected by treatment except for a significant decrease in mean relative kidney weight in males, judged by the authors not to be biologically significant. Males also had a slight shift in lymphocytes and segmented neutrophils. Sorbitol dehydrogenase was increased in females, but this and the other hematological changes were not considered biologically significant. The basis for this decision explanation for this was not provided by the author.

	Body weight (BW in kg)	Relative kidney weight (% of BW)	Sorbitol dehydrogenase (IU/L)
Males			
Control	3.19 ± 0.27	0.52 ± 0.05	42 ± 12
Treated	3.20 ± 0.15	0.46 ± 0.04*	53 ± 4
Females			
Control	3.42 ± 0.36	0.51 ± 0.08	39 ± 6
Treated	3.49 ± 0.23	0.46 ± 0.04	50 ± 5*

*Significantly different from controls (p<0.05)

The only treatment-related change seen histologically was evidence of irritation in the treated skin (inflammation in the superficial dermis, enlarged, hyperplastic hair follicles, and hyperplasia/hyperkeratosis of epidermis).

Irritation of treated skin was apparent visibly and histologically.

Conclusion:

Determined by the reviewer

The systemic NOAEL for a 4 week dermal administration study in rats was determined to be 1000 mg/kg/day, based on the conclusions of the report. The LOAEL was not identified (>1000 mg/kg/day).

Skin irritation was observed in all treated animals.

The systemic NOEL was not identified since a significant decrease in in relative kidney weight in males and a significant increase in sorbital hydrogenase in females was observed at 1000 mg/kg/day. Males also had a slight shift in lymphocytes and segmented neutrophils.

RELIABILITY/DATA QUALITY

Reliability:

1. – Reliable without restrictions

Reliability Remarks:

Comparable to guideline limit test

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Key Study Sponsor Indicator:

Key

REFERENCE

Reference:

Repeated dermal toxicity study in rabbits. Test materials: MRD-87-102 MRD-87-103. Final report for project number 209909B. Exxon Biomedical Sciences, Inc., East Millstone, NJ. 1991.

Repeated Dose Toxicity**Test Substance**

Category Chemical (CAS #):	64741-50-0
Test Substance (CAS #):	64741-50-0; API 84-01; Unrefined base oil
Test Substance Purity/Composition and Other Test Substance Comments :	No information
Category Chemical Result Type :	Measured

Type : 4 Week Dermal Exposure
Species : Rabbit
Sex : Male/female
Strain : New Zealand white
Route of admin. : Dermal
Exposure period : 6 hours each day
Frequency of treatm. : 3 times each week for a total of 12 applications
Doses : 200, 1000 and 2000 mg/kg
Control group : Yes
Year : 1986
GLP : Yes
Test substance : Unrefined base oil Sample API 84-01 [CAS 64741-50-0] See section 1.1.1.

Method : Undiluted API 84-01 was applied at doses of 200, 1000 and 2000 mg/kg/day to the shorn dorsal skin of groups of five male and five female rabbits. The test material was applied to the skin 3 times each week for 4 weeks (12 applications total). The applied material was covered with an occlusive dressing for 6 hours, which was then removed and the skin was wiped with a dry gauze to remove any residual material. A group of five rabbits of each sex served as sham controls. The test skin site of each animal was examined and scored for irritation prior to each application of test material. Mortality and moribundity checks were performed twice daily and body weights were recorded weekly. At termination, blood samples were taken for a range of hematological and clinical chemical measurements. Urine samples were also collected and frozen for possible future examination. A complete gross necropsy was performed on all animals. Major organs were weighed and tissues were processed for subsequent histopathological examination.

Result : Three animals died during the study but these were not dose-related and were, therefore, considered unrelated to treatment. Sporadic clinical signs

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were also unrelated to treatment.

In the high dose group, body weight gains were affected by treatment. In the females, there was a group net loss in weight whereas in the males the gains were significantly less than controls. These effects were largely due to effects on growth rate during the first week of the study. A mean irritation index was calculated for each group each day and also for each treatment group overall. The value was determined from Draize scores for erythema and edema for each animal. The mean irritation scores for each group were:

Group	Irritation score
Control (male)	0
Control (female)	0
200 mg/kg (male)	0.5
200 mg/kg (female)	0.4
1000 mg/kg (male)	1.7
1000 mg/kg (female)	2.0
2000 mg/kg (male)	3.1
2000 mg/kg (female)	3.2

There were no statistical differences between treated and control groups for any of the hematological determinations. These were: Total red blood cells, total white blood cells, hemoglobin concentration and hematocrit %.

The clinical chemical data for the treated and control males was similar. In the females, there was a reduced BUN and an increased SGPT for the low dose females. Since no other differences were noted and that values were within normal limits the effects were not considered to be toxicologically significant. The clinical chemical measurements consisted of: glucose, BUN, SGOT, SGPT, ALP and total protein.

The following absolute and relative organ weight differences (compared to controls) were recorded.

	Males	Females
2000 mg/kg		
Relative liver wt.	Increased	Increased
Relative kidney wt.	Increased	Increased
Relative pituitary wt.	Increased	
Relative left testis wt.	Decreased	
Relative brain wt.		Increased
1000 mg/kg		
Abs. Rt. kidneywt.	Decreased	
Abs. Heart wt.		Decreased

None of the organ weight differences were considered treatment-related. The higher than control relative organ weights were considered as a function of the reduced body weights in the affected animals.

The only findings at gross necropsy were confined to the treated skin. These consisted of dry, scaly, rough, and/or reddened skin and thickened dermis. These findings were noted throughout the treatment groups.

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There were no treatment-related gross necropsy findings in the internal organs.

Microscopic pathology findings were also largely confined to the skin. Slight to moderate proliferative changes of the skin were present in all of the male and female rabbits in the highest dose group.

The testes of one of the five males in the high dose group had bilateral diffuse tubular hypoplasia accompanied by aspermatogenesis and hypoplasia of the epididymis. These changes were considered to represent immature testes. Similar changes were not seen in the other animals in this dose group.

Reliability

: (1) valid without restriction

(11)

(11)

American Petroleum Institute (1986)
28 day dermal toxicity study in the rabbit
API 84-01 Light paraffinic distillate CAS 64741-50-0
API Med. Res. Publ. 33-31642

Repeated Dose Toxicity

Test Substance

Category Chemical (CAS #):	64742-53-6
Test Substance (CAS #):	64742-53-6; API 83-12; Highly refined base oil
Test Substance Purity/Composition and Other Test Substance Comments :	API 83-12 No further information
Category Chemical Result Type :	Measured

Species : Rabbit
Sex : Male/female
Strain : New Zealand white
Route of admin. : Dermal
Exposure period : 6 hours each day
Frequency of treatm. : 3 times each week for a total of 12 applications
Doses : 200, 1000 and 2000 mg/kg
Control group : Yes
Year : 1986
GLP : Yes
Test substance : Highly refined Base oil Sample API 83-12 [CAS64742-53-6] See section 1.1.1.

Method : Undiluted API 83-12 was applied at doses of 200, 1000 and 2000 mg/kg/day to the shorn dorsal skin of groups of five male and five female rabbits. The test material was applied to the skin 3 times each week for 4 weeks (12 applications total). The applied material was covered with an occlusive dressing for 6 hours, which was then removed and the skin was wiped with a dry gauze to remove any residual material. A group of five rabbits of each sex served as sham controls. The test skin site of each animal was examined and scored for irritation prior to each application of test material. Mortality and moribundity checks were performed twice daily and body weights were recorded weekly. At termination, blood samples were taken for a range of hematological and clinical chemical measurements. Urine samples were also collected and frozen for possible future examination. A complete gross necropsy was performed on all animals. Major organs were weighed and tissues were processed for subsequent histopathological examination.

Result : No deaths occurred during the study. Skin irritation occurred to varying degrees in all animals treated with API

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83-12. There was moderate irritation in the high dose males and females. In the mid dose group moderate irritation occurred in the females and slight irritation in the males. In the low dose group minimal irritation occurred in both sexes. The overall mean irritation scores were:

Dose level (mg/kg)	Males	Females
Control 0	0	0
200	0.1	0.4
1000	2.0	2.2
2000	2.6	3.1

Soft stool was also observed in several animals but this also occurred in a control male was not considered to be dose related. All high dose females appeared thin and this was considered to be treatment related. Body weight gains were reduced in the high dose males and females and in the mid dose females when compared to their respective controls. Overall weight changes (kg) are shown in the following table

Dose level (mg/kg)	Males	Females
Control 0	+0.5	+0.3
200	+0.3	+0.4
1000	+0.3	0.0*
2000	+0.1*	-0.2*

* statistically significant ($p \leq 0.05$)

Clinical chemical and hematological values were considered to be unaffected by treatment. A low value (cf control) for white cell count in the low dose female group was considered incidental since the value was within a normal range and was not a dose-related effect.

Although there were some organ weight differences, they were considered incidental to treatment. The exception was for the absolute testis weights, which were lower in the high dose males and the relative weights of the right testis which were also lower than controls.

At gross necropsy, findings for the skin consisted of dry, scaly, rough, fissured, crusted and/or thickened skin. This was a common finding in all treatment groups.

Histopathological examination revealed slight to moderate proliferative changes in the skin in all rabbits in the high dose group. These changes were accompanied by an increased granulopoiesis of the bone marrow. The testes of 3 of the 5 males in the high dose group had bilateral diffuse tubular hypoplasia accompanied by aspermatogenesis changes observed in either the testes or epididymes of the male rabbits in the mid or low dose groups.

No other treatment-related histopathological changes were recorded.

Reliability

: (1) valid without restriction

(10)

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(10)

American Petroleum Institute (1986)
28 day dermal toxicity study in the rabbit
API 83-12 Hydrotreated light naphthenic distillate CAS
64742-53-6
API Med. Res. Publ. 33-30499

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Repeated Dose Toxicity

Test Substance

Category Chemical (CAS #):	64742-56-9; 64742-56-0; 64742-65-0; 64741-97-5; 64741-96-4; 64742-52-5
Test Substance (CAS #):	64742-56-9; API 78-9; Solvent dewaxed light paraffinic distillate 64742-56-0; API 78-10; Solvent dewaxed heavy paraffinic distillate 64742-65-0; API 79-3; Solvent dewaxed heavy paraffinic distillate 64742-65-0; API 79-4; Solvent dewaxed heavy paraffinic distillate 64742-65-0; API 79-5 Solvent dewaxed heavy paraffinic distillate 64741-97-5; API 78-5; 7Solvent refined light naphthenic distillate 64741-96- 4; API 79-1;Solvent refined heavy naphthenic distillate 64742-52-5; API 83-15; Hydrotreated heavy naphthenic distillate
Test Substance Purity/Composition and Other Test Substance Comments :	API 78-9 API 78-10 API 79-3 API 79-4 API 79-5 API 78-5 API 79-1 API 83-15 No other information
Category Chemical Result Type :	Measured

- Type** : Various exposure periods; repeated dose dermal
Route of admin. : Dermal
Test substance : Various Base oils
- Remark** : Data on repeated dose dermal studies in rabbits have been summarized elsewhere (CONCAWE 1997).
The attached tabulated summary of information is taken from the CONCAWE publication.
- Attached document** : Attachment 2: Summary of dermal repeat dose studies.doc
(2) (3) (4) (5) (6) (7) (8) (15) (81) (123)
- (2) American Petroleum Institute (1982) Acute toxicity tests of API sample 78-10 paraffinic oil (150 SUS/100 °F) API Med. Res. Publ. 29-33105
- (3) American Petroleum Institute (1982) Acute toxicity tests of API sample 78-5 naphthenic oil (150 SUS/100 °F). API Med. Res. Publ. 29-33106

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- (4) American Petroleum Institute (1982) Acute toxicity tests of API sample 78-9 paraffinic oil (70 SUS/100 °F). API Med. Res. Publ. 29-33104
- (5) American Petroleum Institute (1982) Acute toxicity tests of API sample 79-1 naphthenic oil (90 SUS/210 °F). API Med. Res. Publ. 29-33065
- (6) American Petroleum Institute (1982) Acute toxicity tests of API sample 79-3 paraffinic oil (350 SUS/100 °F) API Med. Res. Publ. 29-33067
- (7) American Petroleum Institute (1982) Acute toxicity tests of API sample 79-4 paraffinic oil (550 SUS/100 °F). API Med. Res. Publ. 29-33066
- (8) American Petroleum Institute (1982) Acute toxicity tests of API sample 79-5 paraffinic oil (800 SUS/100 °F). API Med. Res. Publ. 29-33068
- (15) American Petroleum Institute (1987) 28-Day dermal toxicity study in the rabbit. API sample 83-15 hydrotreated heavy naphthenic distillate (CAS 64742-52-5). API Health Environ. Sci. Dep. Rep. 35-32430
- (81) CONCAWE (1997) Lubricating oil basestocks. Product dossier No. 97/108. CONCAWE, Brussels
- (123) Trimmer, G. W. et al (1989) Evaluation of the dermal toxicity of paraffinic lube oils. Toxicologist Vol 9, pp 162

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Repeated-Dose Toxicity

TEST SUBSTANCE

Category Chemical:	64742-54-7
Test Substance:	64742-54-7; Ssangyong 150N; Distillates (petroleum), hydrotreated heavy paraffinic; Viscosity was 161 SUS at 100°F and 45 SUS at 210°F.
Test Substance Purity/Composition and Other Test Substance Comments:	Ssangyong 150N (CRU 83272) No other information
Category Chemical Result Type:	Measured
Unable to Measure or Estimate Justification:	

METHOD

Route of Administration:	Dermal
Other Route of Administration:	
Type of Exposure:	Non-occluded
Species:	Rat
Other Species:	None
Mammalian Strain:	Sprague-Dawley

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Other Strain:	None
Gender:	Male and female
Number of Animals per Dose:	30 (15 per sex)
Concentration:	100%
Dose:	0 (sham-treated), 800 mg/kg/day, and 2000 mg/kg/day
Year Study Performed:	1985
Method/Guideline Followed:	Other; similar to OECD guideline, but with fewer dose levels
GLP:	Study was conducted in accordance with EPA Good Laboratory Practices.
Exposure Period:	13 weeks
Frequency of Treatment:	5 days/week (weekdays)
Post-Exposure Period:	None
Method/Guideline and Test Condition Remarks:	<p>Hair was clipped from the entire trunk of each rat as needed (at least weekly) and the test substance was applied to the back of each animal with a syringe. The test substance was spread evenly over the back of each animal with the end of the syringe. Controls were handled in the same manner, but no material was applied to the skin. The treated skin was left uncovered and the rats were fitted with cardboard Elizabethan collars to minimize ingestion of the test substance. Residual test material was wiped off on Saturday morning and the collars were removed for 2 days until dosing was performed on each Monday.</p> <p>Endpoints during the biophase included daily observation of clinical signs and body weights measured weekly. Skin irritation was assessed weekly. Blood and urine samples were collected from fasted rats before treatment began and during weeks 5, 9, and 13. Samples during week 13 were taken at sacrifice. Measured hematological parameters were hematocrit, hemoglobin, number and morphology of red blood cells, and the number and differential count of white blood cells. The following clinical chemistry parameters were analyzed: albumin, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, cholesterol, creatinine, glucose,</p>

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lactate dehydrogenase, total bilirubin, total protein, triglycerides, urea nitrogen, uric acid, calcium, chloride, iron, phosphorus, potassium, and sodium. Urine samples were also collected for analysis of specific gravity, pH, glucose, occult blood, ketone bodies, albumin, urobilinogen, and bilirubin. Sperm head morphology was also examined in the control and high dose animals.

All animals were then killed and necropsied. The following organs were weighed: adrenals, brain, epididymides, gonads, heart, kidneys, liver, prostate, spleen, thymus, thyroid, and uterus. Histological slides were prepared from the following organs of both controls and animals treated with 2000 mg/kg/day: adrenals, bone and marrow, brain, eyes and optic nerve, gonads, duodenum, colon, kidneys, liver, lung, pancreas, skin (2 sections of treated skin), spleen, stomach, thymus, thyroid, urinary bladder, and any gross lesions. All slides were examined microscopically by a pathologist.

Statistical analysis: Quantitative data were analyzed for homogeneity of variances followed by ANOVA and Dunnett's test or Duncan's Multiple Range Test. Data with non-homogeneous variances were analyzed by nonparametric means. Categorical data were analyzed by a test based on the chi-square distribution.

TEST RESULTS

Concentration (LOAEL/LOAEC/NOAEL/NOAEC)*

Type	Population:	Value Description:	Value or Lower Concentration:	Upper Concentration:	Units:
NOAEL	Rat	=	2000		mg/kg/day
LOEL	Rat	=	800		mg/kg/day

*Determined by reviewer

Results Remarks:

No treatment-related deaths occurred and no treatment-related abnormal clinical signs were noted. Slight erythema and flaking of the skin were observed during the dosing phase and minimal epidermal thickening and chronic inflammation of the dermis were present microscopically in about half of the treated males and 2/3 of treated females.

Body weights in treated males were significantly reduced at both doses by approximately 10%. No dose-response

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was apparent and the lower weight was judged not to be toxicologically significant. Parameters of hematology and urinalysis were not affected by treatment. Among parameters of serum chemistry, serum albumin, cholesterol, triglycerides, and calcium were slightly lower in males treated with 2000 mg/kg/day; alanine aminotransferase was slightly higher than in controls.

Mean liver weight in females at 2000 mg/kg was significantly higher than controls by 14%. Liver weight in females at 800 mg/kg tended to be higher than controls weight (NS) by 7%. (See following table.) Liver weight was unaffected in males. In high-dose males, liver weight relative to body weight was about 5% larger than in controls ($p < .05$). Relative liver weight was also increased in females at both doses. No treatment-related abnormalities were seen during gross examination of organs. Histologically, livers of 3 females treated with 2000 mg/kg/day had an increased frequency of mitotic figures. This frequency of mitotic figures is regarded as a test material effect, although found in only 3 animals and because it occurred in the absence of liver lesions that might have stimulated a reactive hyperplasia, and such high frequency is not found in the liver of control animals. It is interpreted simply as confirmation that test material was reaching the liver cells. The slight increase in liver size was considered by the authors to represent a nonpathologic adaptation to the presence of a foreign material.

Adrenals in exposed females were slightly larger than controls, based on organ weight analysis, by about 10% (NS) and 16% ($p < .05$) in the low- and high-level groups, respectively. No abnormalities were found that might explain the slightly large adrenal weight in the high-level females. It was concluded by the authors that the slightly increased adrenal weight in the high-level females was test material-related but was probably a nonpathologic adaptive change.

The mean thymus weight was smaller than controls in both groups of exposed males, by about 12% (NS) and 24% ($p < .05$) in low- and high-level groups, respectively. The authors indicated that much of this reduction in mass was simply a result of reduced body growth, as the group differences in relative thymus weight were not significant. No microscopic abnormalities were found. It was concluded by the authors that the test material had no direct effect on the thymus, and that the decrease in mass was expected from the reduction in body growth.

Increases in the relative weight of the brain, epididymides, kidneys, liver, prostate and testes, in the males of one or both exposed groups, are adequately explained as manifestations of the reduced body growth and/or as random variations. A nonsignificant increase in relative weights of thyroid and uterus in the high-level females was regarded by the authors as random variation without pathologic significance. None of these changes was regarded as evidence of a test material effect.

	Sham-Exposed Controls	800 mg/kg/day	2,000 mg/kg/day
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Males			
Body weight (BW in g)	488 ± 39	445 ± 35 *	440 ± 46 *
Liver weight (g)	13.91 ± 1.65	13.03 ± 1.26	13.14 ± 1.74
Liver weight/BW (%)	2.84 ± 0.14	2.93 ± 0.14 *	2.98 ± 0.17 *
Thymus weight (g)	0.375 ± 0.093	0.332 ± 0.091	0.284 ± 0.061 *
Thymus/BW (%)	0.077 ± 0.019	0.074 ± 0.018	0.064 ± 0.012
Adrenal weight (g)	0.055 ± 0.010	0.056 ± 0.008	0.056 ± 0.009
Adrenal weight/BW (%)	0.011 ± 0.002	0.013 ± 0.002	0.013 ± 0.002
Kidney weight (g)	3.609 ± 0.353	3.682 ± 0.300	3.608 ± 0.447
Kidney/BW (%)	0.741 ± 0.067	0.830 ± 0.057*	0.822 ± 0.094*
Epididymides	1.32 ± 0.132	1.340 ± 0.032	1.314 ± 0.093
Epididymides/BW (%)	0.271 ± 0.027	0.302 ± 0.032*	0.301 ± 0.036*
Brain	2.027 ± 0.083	2.015 ± 0.106	2.035 ± 0.073
Brain /BW (%)	0.417 ± 0.036	0.455 ± 0.025*	0.467 ± 0.052*
Testes	3.44 ± 0.249	3.469 ± 0.249	3.324 ± 0.276
Testes/BW (%)	0.709 ± 0.082	0.784 ± 0.083*	0.762 ± 0.101
Prostate (g)	0.835 ± 0.199	0.968 ± 0.296*	0.806 ± 0.139
Prostate/BW (%)	0.172 ± 0.044	0.218 ± 0.068	0.183 ± 0.027
Platelets (10 ⁹ /L)			
Hemoglobin (g/dL)	16.1 ± 0.9	16.3 ± 0.6	16.3 ± 0.6
Females			
Body weight (BW in g)	258 ± 24	259 ± 18	254 ± 28
Liver weight (g)	7.29 ± 0.62	7.78 ± 0.89	8.32 ± 0.95 *
Liver weight/BW (%)	2.83 ± 0.17	3.001 ± 0.231 *	3.28 ± 0.24 *
Thymus weight (g)	0.259 ± 0.059	0.259 ± 0.064	0.254 ± 0.074
Adrenal weight (g)	0.061 ± 0.009	0.067 ± 0.008 *	0.071 ± 0.012 *
Adrenal weight/BW (%)	0.024 ± 0.004	0.026 ± 0.005	0.028 ± 0.005 *
Platelets (10 ⁹ /L)			
Hemoglobin (g/dL)	16.1 ± 0.6	16.3 ± 0.6	16.3 ± 0.6

* Statistically significantly different from controls, p<0.05

No differences among the groups were found for any urinalysis parameter examined. No consistent differences among the groups were found that would suggest that the test material had an effect on any of the hematologic

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parameters examined. No differences in sperm head morphology or general sperm morphology were observed between control and high-dose rats.

Clinical chemistry parameters affected are listed in the following table: These values were not addressed in the final report.

	Sham-Exposed Controls	800 mg/kg/day	2,000 mg/kg/day
Males			
Albumin (g/dl)	3.8	3.6	3.5*
Albumin/Globulin	1.2	1.2	1.1*
Cholesterol (mg/dl)	78	64*	68*
Triglyceride (mg/dl)	65	47*	47*
Alanine Aminotransferase (IU/L)	33	36	46*
Calcium (mg/dl)	10.1	9.8	9.6*
Females			
Albumin (g/dl)	4.1	4.0	4.1
Albumin/Globulin	1.4	1.4	1.4
Cholesterol (mg/dl)	99	98	102
Triglyceride (mg/dl)	43	39	44
Alanine Aminotransferase (IU/L)	39	34	51
Calcium (mg/dl)	10.3	10.0	10.1

* Statistically significantly different from controls, $p < 0.05$

Conclusion:

Dermal administration of Ssangyong 150N to adult rats for 13 weeks resulted in minimal effects. Liver weights were increased in females, but histological changes were minimal. Thymus weight was decreased in males and adrenal weight was increased in males. No histological changes were observed in either organ and the differences in weight were not judged to represent an adverse effect. The NOAEL for systemic effects was determined by the study director to be 2000 mg/kg/day based on the conclusion that the observed effects were not biologically significant.

A LOEL of 800 mg/kg was assigned by the reviewer based on lower body weights in males at that dose.

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Slight visible dermal irritation was seen in males and slight histopathological changes in the skin were observed in treated animals of both sexes.

RELIABILITY/DATA QUALITY

Reliability:

1. – Reliable without restrictions

Reliability Remarks:

Similar to guideline study; fewer dose levels; sufficient detail provided in appendices and tables.

Key Study Sponsor Indicator:

Key

REFERENCE

Reference:

Thirteen-week dermal administration of Ssangyong 150N to rats. Final Report on study 32761 from Mobil Environmental and Health Science Laboratory, Princeton, NJ. 1988

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Repeated-Dose Toxicity

TEST SUBSTANCE

Category Chemical:	64742-65-0
Test Substance:	64742-65-0; Mineral oil base stock; Stock 141; Sample no. 527981-2 (CRU 89040)
Test Substance Purity/Composition and Other Test Substance Comments:	No information
Category Chemical Result Type:	Measured
Unable to Measure or Estimate Justification:	

METHOD

Route of Administration:	Dermal, non-occluded
Other Route of Administration:	Not applicable
Type of Exposure:	Repeated dose
Species:	Rat
Other Species:	Not applicable
Mammalian Strain:	Sprague-Dawley (Taconic Farms, Germantown, NY)
Other Strain:	Not applicable
Gender:	Male and female

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Number of Animals per Dose:	10/sex/dose
Concentration:	
Dose:	0, 2000 mg/kg
Year Study Performed:	1983
Method/Guideline Followed:	Other; Comparable to OECD guideline limit test
GLP:	FDA GLP
Exposure Period:	13 weeks
Frequency of Treatment:	Daily, 5 days/week for 13 weeks
Post-Exposure Period:	None
Method/Guideline and Test Condition Remarks:	<p>The study was designed to determine if there were any toxic effects from repeated skin application of Stock 141 (a mineral oil base stock used in metalworking fluids).</p> <p>The treatment groups and time exposure periods were as follows:</p> <ol style="list-style-type: none"> 1. Sham control (water – 2000 mg/kg) – 13 weeks – 20 animals (10/sex) 2. Stock 141 - 2000 mg/kg/day – 13 weeks – 20 animals (10/sex) <p>Animals in group 1 served as controls and were treated with water throughout the study. Animals in group 2 received Stock 141. Lot No. 527981-2 at a dose level of 2000 mg/kg/day. Fresh samples of Stock 141 were dispensed weekly and were used as received.</p> <p>Within 24 prior to treatment, hair was clipped from the entire trunk of each animal; this was repeated at weekly intervals. The test material dose, calculated from each rat's most recent body weight. Each treatment day, the test material dose was applied once daily by volume from a syringe and dosing needle. The dosage was spread uniformly over the site using the side of the dosing needle. The test site was left uncovered. To minimize ingestion of test material rats were fitted with Elizabethan collars. The neck area of each collar was lined with rubber tubing in order to prevent or minimize any irritation or the development of lesions. Similarly, the controls</p>

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received collars. were handled daily and had their backs rubbed with the side of a dosing needle after the water was applied. The animals were dosed for 5 consecutive days/week; 24 hours after the fifth dose, residual test article was wiped off and the collars removed for 2 days.

The animal s were observed once daily for reaction to treatment and twice daily for morbidity and mortality.

The body weight of each animal was measured 5 days before treatment, the first day of treatment (day 1), and at weekly intervals during the treatment period. Body weights were rounded to the nearest gram and recorded.

Blood samples were obtained from all animals (non-anesthetized), via the orbital venous sinus through a non-heparinized capillary tube, on the day of sacrifice. Hematologic evaluation was performed and parameters measured included red blood cell count and morphology, hematocrit, hemoglobin content, white blood cell count and WBC differential count. Blood samples were collected, allowed to clot and centrifuged; the serum was analyzed for glucose, urea nitrogen, uric acid, creatinine, total protein, albumin, albumin/globulin ratio, alkaline phosphatase, alanine aminotransferase (SGPT), aspartate aminotransferase (SGOT), lactate dehydrogenase, cholesterol, triglycerides, calcium, phosphorus, sodium, potassium and chloride. On days 91, 92 and 93, freshly voided urine samples were collected on plastic from approximately 50% of the animals scheduled for sacrifice. Values for pH, occult blood, glucose, protein, ketenes, bilirubin and urobilinogen were obtained, and specific gravity was determined.

After 13 weeks of treatment, the animals were fasted overnight, anesthetized with CO2 gas, and exsanguinated in an order that rotated through the treatment groups and sexes. Each animal was necropsied by a pathologist immediately after sacrifice. The following organs were weighed to the nearest mg: adrenals*, gonads*, heart, kidneys*, liver, lungs, spleen, and thymus (* items indicated that total weight of pooled organs was used, not separate weights).

TEST RESULTS

Concentration (LOAEL/LOAEC/NOAEL/NOAEC) *

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Type	Population:	Value Description:	Value or Lower Concentration:	Upper Concentration:	Units:
NOAEL	Rat	=	2000		mg/kg/day
LOEL	Rat	=	2000		mg/kg/day

***Determined by author**

Results Remarks:

Mortality: One treated male, died during week 6. He died from spontaneous segmental infarctoid necrosis of the jejunum. This death was judged not to be treatment related.

Daily Observations: No abnormal behavior patterns were noted during daily observations. In general a dry dark exudate around the eyes and nose; a dry clear exudate around the eyes and hair loss around the eyes occurred in the control and treated animals with equal frequency as a result of the restriction of preening activity by the collars. This was groomed off each weekend when the collars were removed. In a few animals, sores developed on the skin where the collar rubbed. No effects occurred which were attributed to the application of Stock 141.

Skin Irritation: One male animal in the control group had slight edema on day 64 which was absent at the next scheduled scoring interval. Two male animals in the 2000 mg/kg/day group had barely perceptible edema on day 64 which was absent at the next scheduled scoring time and did not recur. Stock 141 did not cause visible skin irritation during this study.

Body Weights: The administration of Stock 141 did not result in any changes in body weight.

Hematology: Hematologic values for the treated and control rats were within the normal range. No treatment-related effects occurred.

Serum Clinical Chemistry: In treated males, there was a statistically significant decrease in albumin (6%) and an increase in urea (18%). The values for the treated and control animals were within the normal range and the differences between control and treated animals were small; therefore these differences are judged not to be toxic responses to Stock 141.

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Urinalysis: The urine from treated rats was not different than the urine of the control rats for any parameter measured.

[Note: the following findings from the pathologist's report were not addressed by the author in the main body of the report –see table below]

Organ Weights/Pathology: Treatment-related pathologies included liver enlargement and microscopic skin changes. The absolute liver weight was 19% larger in the 2000 mg/kg/day males than in control males ($p < 0.05$). The relative liver weight was 17% larger ($p < 0.05$). In females, only the relative liver weights were significantly larger than controls ($p < 0.05$). Microscopic examination revealed no major liver pathology in any animal, no treatment-related changes, and no explanation for the liver enlargement. All other organ weights were not significantly different from controls.

The skin of the controls (sham-treated) showed epidermal thickening (hyperplasia), slight in males and trace in females. The skin of most test-treated animal, showed epidermal hyperplasia (trace to mild, in excess of that in the controls) and/or trace chronic inflammation of the superficial dermis. Epidermal hyperplasia and chronic inflammation were very minimal in the treated group.

	Sham-Exposed Controls	2,000 mg/kg/day
Males		
Body weight (BW in g)	366 ± 28	372 ± 34
Liver weight (g)	12.46 ± 1.48	14.78 ± 2.04*
Liver weight/BW (%)	3.41 ± 0.29	3.98 ± 0.47*
Thymus weight (g)	0.35 ± 0.07	0.35 ± 0.12
Platelets	ND	ND
Hemoglobin (g/dL)	16.7 ± 0.5	16.4 ± 0.7
Females		
Body weight (BW in g)	252 ± 27	239 ± 24
Liver weight (g)	8.12 ± 1.01	8.77 ± 0.78
Liver weight/BW (%)	3.23 ± 0.29	3.68 ± 0.17*
Thymus weight (g)	0.33 ± 0.12	0.30 ± 0.11
Platelets	ND	ND
Hemoglobin (g/dL)	15.8 ± 0.9	16.2 ± 0.6

*Statistically significantly different from controls ($p < 0.05$)

ND indicates “not determined”.

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Conclusion:

Dermal administration of Stock 141 to adult rats for 13 weeks resulted in minimal effects. Liver weight was increased in males, but no histological changes were observed. The study director did not discuss a NOAEL in the final report, but stated that the test substance elicited no toxic responses in the treated animals. Given this statement and the lack of systemic effects that were judged by the reviewer to be adverse, the dose of 2,000 mg/kg is judged to be a NOAEL for systemic effects.

Reviewer's Note: The systemic NOEL could not be determined (<2000 mg/kg/day); LOEL was determined to be 2000 mg/kg/day based on increased absolute and relative liver weight in males and increased relative liver weight in females.

Skin irritation was not observed visibly and histopathological changes in treated animals were minimal.

RELIABILITY/DATA QUALITY

Reliability:

Valid Without Restrictions (KS=1)

Reliability Remarks:

Comparable to guideline limit test

Key Study Sponsor Indicator:

Key

REFERENCE

Reference:

Thirteen-Week Toxicity Study by Dermal Application of Metalworking Fluid Components to Rats (Stock 141) 1983. Mobil Environmental and Health Sciences Laboratory Report 1451-81.

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Repeated-Dose Toxicity

TEST SUBSTANCE

Category Chemical:	64742-70-7																								
Test Substance:	64742-70-7; Stock 142; MLDW 100 SPN; Paraffin Oils (Petroleum), Catalytic Dewaxed Heavy; CRU 82191																								
Test Substance Purity/Composition and Other Test Substance Comments:	Paraffin Oils (Petroleum), Catalytic Dewaxed Heavy (CRU No. 82191)																								
	PAC Content – report no. 65841-ZH (Mobil, 1994)																								
	<table border="1"> <thead> <tr> <th>Sample #</th> <th>DMSO wt.%¹</th> <th>1-ARC (%)²</th> <th>2-ARC (%)</th> <th>3-ARC (%)</th> <th>4-ARC (%)</th> <th>5-ARC (%)</th> <th>6-ARC (%)</th> <th>7-ARC (%)</th> </tr> </thead> <tbody> <tr> <td>82191</td> <td>0.14</td> <td>0.01</td> <td>0.09</td> <td>0.40</td> <td>0.20</td> <td>0.08</td> <td>0.09</td> <td>0.0</td> </tr> </tbody> </table>								Sample #	DMSO wt.% ¹	1-ARC (%) ²	2-ARC (%)	3-ARC (%)	4-ARC (%)	5-ARC (%)	6-ARC (%)	7-ARC (%)	82191	0.14	0.01	0.09	0.40	0.20	0.08	0.09
Sample #	DMSO wt.% ¹	1-ARC (%) ²	2-ARC (%)	3-ARC (%)	4-ARC (%)	5-ARC (%)	6-ARC (%)	7-ARC (%)																	
82191	0.14	0.01	0.09	0.40	0.20	0.08	0.09	0.0																	
Category Chemical Result Type:	Measured																								
Unable to Measure or Estimate Justification:																									
METHOD																									
Route of Administration:	Dermal, non-occluded																								
Other Route of Administration:	Not applicable																								
Type of Exposure:	Repeated dose																								
Species:	Rat																								

1) Percent of DMSO-extractable materials (mostly PACs), determined by the PAC 2 method as described in API (2008).
 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.

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Other Species:	Not applicable
Mammalian Strain:	Sprague-Dawley (Taconic Farms, Germantown, NY)
Other Strain:	Not applicable
Gender:	Male and female
Number of Animals per Dose:	10/sex/dose
Concentration:	
Dose:	0, 1720 mg/kg
Year Study Performed:	1986
Method/Guideline Followed:	Other; Comparable to OECD guideline limit test
GLP:	No information
Exposure Period:	13 weeks
Frequency of Treatment:	Daily, 5 days/week for 13 weeks
Post-Exposure Period:	None
Method/Guideline and Test Condition Remarks:	<p>The study was designed to determine if there were any toxic effects from repeated skin application of Stock 142 (a mineral oil base stock used in metalworking fluids).</p> <p>The treatment groups and time exposure periods were as follows:</p> <ol style="list-style-type: none"> 1. Sham control (water – 1720 mg/kg) – 13 weeks – 20 animals (10/sex) 2. Stock 142 1720 mg/kg/day – 13 weeks – 20 animals (10/sex) <p>Animals in group 1 served as controls and were treated with water throughout the study. Animals in group 2</p>

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received Stock 142 at a dose level of 1720 mg/kg/day. Fresh samples of Stock 142 were dispensed weekly and were used as received.

Within 24 hours prior to treatment, hair was clipped from the entire trunk of each animal; this was repeated at weekly intervals. The test material dose, calculated from each rat's most recent body weight. Each treatment day, the test material dose was applied once daily by volume from a syringe and dosing needle. They received Stock 142 at an intended dose of 2000 mg/kg/day. The rats were actually dosed at a rate of 2 ml/kg/day; therefore the actual dose was 1720 mg/kg/day. The dosage was spread uniformly over the site using the side of the dosing needle. The test site was left uncovered. To minimize ingestion of test material rats were fitted with Elizabethan collars. The neck area of each collar was lined with rubber tubing in order to prevent or minimize any irritation or the development of lesions. Similarly, the controls received collars. were handled daily and had their backs rubbed with the side of a dosing needle after the water was applied. The animals were dosed for 5 consecutive days/week; 24 hours after the fifth dose, residual test article was wiped off and the collars removed for 2 days.

The animals were observed once daily for reaction to treatment and twice daily for morbidity and mortality.

The body weight of each animal was measured at 12, 6 and 3 days before treatment, the first day of treatment (day 1), and at weekly intervals during the treatment period. Body weights were rounded to the nearest gram and recorded.

Blood samples were obtained from all animals (ether-anesthetized), via the orbital venous sinus through a non-heparinized capillary tube, on study days 93, 94, or 95. Hematologic evaluation was performed and parameters measured included red blood cell count and morphology, hematocrit, hemoglobin content, white blood cell count and WBC differential count. Blood samples were collected, allowed to clot and centrifuged; the serum was analyzed for glucose, urea nitrogen, uric acid, total protein, albumin, albumin/globulin ratio, alkaline phosphatase, alanine aminotransferase (SGPT), aspartate aminotransferase (SGOT), lactate dehydrogenase, cholesterol, triglycerides, calcium, phosphorus, sodium, potassium and chloride. On day 86, freshly voided urine samples were collected on plastic from all animals scheduled for sacrifice and analyzed by visual appearance and for color and clarity. Values for pH, occult blood, glucose, protein, ketones, bilirubin and urobilinogen were obtained, and specific gravity was determined.

After 13 weeks of treatment, the animals were fasted overnight, anesthetized with CO₂ gas, and exsanguinated in an order that rotated through the treatment groups and sexes. Each animal was necropsied under the supervision of a pathologist immediately after sacrifice. The following organs were weighed to the nearest mg: adrenals*, gonads*, heart, kidneys*, liver, lungs, spleen, and thymus (* items indicated that total weight of pooled organs

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was used, not separate weights.

From all control and treated rats. the following tissues were processed and stained with hematoxylin and eosin: adrenal, colon. duodenum, testis. ovary, kidney, liver. lung, spleen, stomach, thymus, thyroid, treated skin and gross lesions.

TEST RESULTS

Concentration (LOAEL/LOAEC/NOAEL/NOAEC) *

Type	Population:	Value Description:	Value or Lower Concentration:	Upper Concentration:	Units:
NOAEL -Dermal	Rat	=	1720		mg/kg/day
LOEL -Dermal	Rat	=	1720		mg/kg/day

***Determined by reviewer**

Results Remarks:

Mortality: No rats died during the study; however, 1 treated male was killed because of a severe head tilt which interfered with his maneuverability about the cage and with eating. This was caused by compression of the brain from a "malignant neurinoma" of the cranial nerve.

Physical Examinations: Weekly physical examinations revealed no treatment-related effects on behavior, posture, activity, or reflexes.

Clinical Observations: Dry red crusty material was observed around the eyes and nose, clear exudate around the eyes, and hair loss around the eyes; these observations were seen with equal frequency in both treated and control animals. These incrustations apparently resulted from the restriction of the collars on preening activity.

Body weights in treated males were significantly reduced during the last 4 weeks of dosing and fasted body weights at the time of sacrifice were also significantly reduced. (See table below.) This difference is judged to result from a larger than normal body weight for the controls, because: 1) after 13 weeks, the body weights of males treated with Stock 142 were essentially identical to the body weights of the control males from eight

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previous 13-week studies, and 2) the control values were clearly higher than that of the previous studies (472 g after 13 weeks compared to 382-432 g in previous studies).

Skin Irritation: Barely perceptible to slight erythema and flaking skin were observed in 50% of the male rats after 1 week of treatment. During the remainder of the study, only occasional instances of barely perceptible erythema and/or flaking of skin were observed on the treated animals.

Hematology: The treated male rats had statistically significantly lower hematocrit and hemoglobin concentrations than the control males; however, these were judged to be of no biologic or toxicological significance since all the values were within the normal range.

Serum Chemistry: There were no treatment-related differences between the control and treated rats.

Urinalysis: There were no differences between treated and control animals for any urine parameter analyzed.

Organ Weights: Treated females had adrenal weights which were slightly, but statistically significantly, larger than the control females. Since there was no evidence of a toxic effect from serum chemical analyses or gross or microscopic examination of these tissues, the difference in adrenal weight is judged not to represent a toxic response.

The absolute liver weight in the 1720 mg/kg/day males was comparable to the controls. In treated females, the absolute liver weight was increased relative to the controls ($p < 0.05$). The relative liver weight was increased in both treated males and females ($p < 0.05$).

Gross Necropsy: No treatment-related abnormalities were observed during the gross examination of the animals. One treated male had an enlarged nerve, which caused a depression in the brain.

Histopathology: The enlarged nerve in a treated male animal was diagnosed as a "malignant neurinoma". Although this is a rare tumor, it is judged that the tumor was not caused by treatment with Stock 142.

In the liver of the treated females, but not controls, there were occasional small aggregates of cells with foamy appearing cytoplasm (vacuolar degeneration). This involved only a very small portion of the liver and does not explain the increase in liver weight. The increased liver weights may have resulted from efforts by the liver to metabolize/detoxify components of the test material which penetrated through the skin. Only a very small portion of the liver was involved; the increase in liver weight was not explained by this observation. The pathological significance of these changes was considered minimal by the study pathologist, but was regarded

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as evidence that the test material reached the liver and caused a degenerative cellular change, albeit very minimal. No histological changes were observed in the adrenals or in the skin.

	Sham-Exposed Controls	1,720 mg/kg/day
Males		
Body weight (BW in g)	443 ± 39	392 ± 24 *
Liver weight (g)	12.61 ± 1.83	13.14 ± 1.30
Liver weight/BW (%)	2.84 ± 0.21	3.35 ± 0.25 *
Thymus weight (g)	0.313 ± 0.086	0.268 ± 0.041
Adrenal weight (g)	0.050 ± 0.007	0.055 ± 0.013
Adrenal weight/BW (%)	0.011 ± 0.002	0.014 ± 0.003
Platelets (10 ⁹ /L)	438 ± 183	449 ± 206
Hemoglobin (g/dL)	16.2 ± 0.5	15.4 ± 1.0 *
Females		
Body weight (BW in g)	234 ± 12	233 ± 12
Liver weight (g)	6.52 ± 0.60	7.91 ± 0.43 *
Liver weight/BW (%)	2.80 ± 0.28	3.40 ± 0.18 *
Thymus weight (g)	0.205 ± 0.035	0.215 ± 0.049
Adrenal weight (g)	0.057 ± 0.006	0.071 ± 0.009 *
Adrenal weight/BW (%)	0.025 ± 0.003	0.031 ± 0.005 *
Platelets (10 ⁹ /L)	433 ± 201	497 ± 251
Hemoglobin (g/dL)	15.9 ± 0.4	15.8 ± 0.5

* Statistically significantly different from controls, p<0.05

Only a few, scattered abnormalities were found during the microscopic examination of the tissues; no other treatment-related changes were found.

Conclusion:

Dermal administration of Stock 142 to adult rats for 13 weeks resulted in minimal effects. Liver and adrenal weights were increased in females, but no histological changes were minimal in the liver and not observed in the adrenals. The study director did not discuss a NOAEL in the final report. However, given the lack of systemic effects that were judged by the Petroleum HPV Testing Group to be adverse, the dose of 1,720 mg/kg is judged to be a NOAEL for systemic effects.

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The Testing Group also determined the LOEL to be 1,720 mg/kg due to higher liver weight in females.

Mild skin irritation was observed visibly among treated males.

RELIABILITY/DATA QUALITY

Reliability:

Valid With Restrictions (KS=1)

Reliability Remarks:

Comparable to guideline limit test

Key Study Sponsor Indicator:

Key

REFERENCE

Reference:

Thirteen-Week Dermal Administration to Rats of a 100 Solvent Refined Paraffinic Neutral Oil Dewaxed by the Mobil Lube Dewaxing Process (Stock 142). 1986. Mobil Environmental and Health Sciences Laboratory Report 30237.

Mobil. 1994. Characterization and Quantitation of Polynuclear Aromatic Compounds in MLDW 100”PN. Mobil Environmental and Health Sciences Laboratory Report No. 65841-ZH.

API. 2008. PAC Analysis Task Group, “The relationship between the aromatic ring class content and selected endpoints of repeat-dose and developmental toxicity of high-boiling petroleum substances.”
<http://www.petroleumhpv.org/pages/pac.html>, accessed 31 Dec 2009.

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Repeated-Dose Toxicity

TEST SUBSTANCE

Category Chemical:	CAS No. 64742-65-0
Test Substance:	64742-65-0 ; Stock 300; Distillate (petroleum), solvent-dewaxed heavy paraffinic
Test Substance Purity/Composition and Other Test Substance Comments:	Stock 300 (Sample #1710811) Viscosity was ~290 SUS at 100°F and 52 SUS at 210°F. No other information
Category Chemical Result Type:	Measured
Unable to Measure or Estimate Justification:	

METHOD

Route of Administration:	Dermal
Other Route of Administration:	
Type of Exposure:	Non-occluded
Species:	Rat
Other Species:	None
Mammalian Strain:	Sprague-Dawley

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Other Strain:	None
Gender:	Male and female
Number of Animals per Dose:	20 (10 per sex)
Concentration:	100%
Dose:	0 and 2000 mg/kg/day
Year Study Performed:	1981 and 1982
Method/Guideline Followed:	Other; Comparable to OECD guideline limit test
GLP:	Study was conducted in accordance with FDA Good Laboratory Practices.
Exposure Period:	13 weeks
Frequency of Treatment:	5 days/week
Post-Exposure Period:	None
Method/Guideline and Test Condition Remarks:	<p>Hair was clipped from the entire trunk of each animal within 24 hours prior to initial treatment; the clipping was repeated weekly throughout the study. The test substance was applied to the back with a syringe and dosing needle; the test substance was spread evenly over the site with the side of the dosing needle. The site was left uncovered and the rats were fitted with cardboard Elizabethan collars to minimize ingestion of the test substance. Water was applied and spread on the backs of sham-exposed controls on the same procedure and schedule as the treated animals. Animals were dosed on 5 consecutive days per week. At 24 hours after the fifth dose, residual test substance was wiped off and the collars were removed for two days.</p> <p>Endpoints during the biophase included daily observation of clinical signs and body weights measured weekly. After 13 weeks of treatment, blood samples were taken for measurement of hematological parameters (hematocrit, hemoglobin, number and morphology of red blood cells, and the number and differential count of white blood cells). The following clinical chemistry parameters were analyzed: albumin, alkaline phosphatase, alanine aminotransferase (glutamic puruvic transaminases), aspartate aminotransferase (glutamic oxaloacetic</p>

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transaminases), cholesterol, creatinine, glucose, lactate dehydrogenase, total bilirubin, total protein, triglycerides, urea nitrogen, uric acid, calcium, chloride, iron, phosphorus, potassium, and sodium. Urine samples were also collected for analysis of specific gravity, pH, glucose, occult blood, ketone bodies, albumin, urobilinogen, and bilirubin. All animals were then killed and necropsied. The following organs were weighed: lungs, kidneys, adrenals, liver, heart, spleen, thymus, testis, ovary. Histological slides were prepared from the following organs and examined microscopically by a pathologist: adrenal, colon, duodenum, testis, ovary, kidney, liver, lung, spleen, stomach, thymus, thyroid, treated skin, and any gross lesions.

Statistical analysis: Quantitative data were analyzed for homogeneity of variance. If variances were homogeneous, data were analyzed by analysis of variance followed by multiple t tests or Duncan's multiple range tests. Categorical data were analyzed by a test based on the chi-squared distribution.

This study was conducted simultaneously with a parallel study on "Stock 141" (CAS #64742-70-7) and shared a common group of control animals with that study.

TEST RESULTS

Concentration (LOAEL/LOAEC/NOAEL/NOAEC)*

Type	Population:	Value Description:	Value or Lower Concentration:	Upper Concentration:	Units:
NOAEL	Rat	=	2000		mg/kg/day
LOEL	Rat	=	2000		mg/kg/day

*Determined by reviewer

Results Remarks:

No treatment-related deaths occurred and no treatment-related abnormal clinical signs were noted. No irritation of the skin at the treatment site was visible. Body weights, hematology, and urinalysis were not affected by treatment. Among parameters of serum chemistry, serum inorganic iron decreased (25%) in treated females and urea increased (13%) in treated males, but all values were within normal range and the differences were not judged to be a response to treatment.

The thickness of the epidermis at the treatment site was approximately doubled in sham-exposed males (epidermal hyperplasia), with an equivocal or trace thickening in females. This change was considered normal in rats treated with weekly clipping and daily wetting. Epidermal hyperplasia was noted in animals treated with Stock 300 and chronic inflammation in the superficial dermis was also seen (increased numbers of mixed inflammatory cells, endothelial, and connective tissue cells).

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Relative liver weight was higher in treated females than in controls, but no changes were observed microscopically.

Data (mean ± standard deviation) for endpoints used in the PAC model are summarized in the following table. The PAC model is described in the document on Category Analysis and Hazard Characterization for Lubricating Oil Basestocks submitted to the EPA by API. The information is provided here because of the use of these endpoints in the PAC model.

	Sham-Exposed Controls	2,000 mg/kg/day
Males		
Body weight (BW in g)	366 ± 28	359 ± 31
Liver weight (g)	12.46 ± 1.48	13.15 ± 1.90
Liver weight/BW (%)	3.41 ± 0.29	3.67 ± 0.47
Thymus weight (g)	0.35 ± 0.07	0.37 ± 0.14
Platelets	ND	ND
Hemoglobin (g/dL)	16.7 ± 0.5	16.5 ± 0.7
Females		
Body weight (BW in g)	252 ± 27	247 ± 16
Liver weight (g)	8.12 ± 1.01	8.91 ± 0.84
Liver weight/BW (%)	3.23 ± 0.29	3.61 ± 0.32*
Thymus weight (g)	0.33 ± 0.12	0.350.12
Platelets	ND	ND
Hemoglobin (g/dL)	15.8 ± 0.9	15.9 ± 1.0

*Statistically significantly different from controls (p,0.5)

ND indicates "not determined".

Conclusion:

Dermal administration of Stock 300 to adult rats for 13 weeks resulted in minimal effects. Relative liver weight was increased in females, but no histological changes were observed. The study director did not discuss a NOAEL in the final report, but did state that Stock 300 elicited no toxic response in the treated animals. Given this statement and the lack of systemic effects that were judged by the Petroleum HPV Testing Group to be adverse, the dose of 2,000 mg/kg is judged to be a NOAEL for systemic effects.

The Testing Group also determined the LOEL to be 2,000 mg/kg due to higher relative liver weight in females.

No dermal irritation was seen during the biophase and minimal effects were seen histologically in treated skin.

RELIABILITY/DATA QUALITY

Reliability:

1. – Reliable without restrictions

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Reliability Remarks:	
Key Study Sponsor Indicator:	Key study Thirteen-week toxicity study by dermal application of metalworking fluid components to rats. Stock 300.
REFERENCE	
Reference:	Thirteen-week toxicity study by dermal application of metalworking fluid components to rats. Stock 300. Final Report on study 1461-81 from Mobil Environmental and Health Science Laboratory, Princeton, NJ. 1983.

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Repeated-Dose Toxicity

TEST SUBSTANCE

Category Chemical:	64742-65-0
Test Substance:	64742-65-0; Stock 335; Distillates (petroleum), solvent-dewaxed heavy paraffinic Viscosity was ~640 SUS at 100°F and 71 SUS at 210°F.
Test Substance Purity/Composition and Other Test Substance Comments:	Stock 335 (Sample #1470811) No other information
Category Chemical Result Type:	Measured
Unable to Measure or Estimate Justification:	
METHOD	
Route of Administration:	Dermal
Other Route of Administration:	
Type of Exposure:	Non-occluded
Species:	Rat
Other Species:	None
Mammalian Strain:	Sprague-Dawley
Other Strain:	None

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Gender:	Male and female
Number of Animals per Dose:	20 (10 per sex)
Concentration:	100%
Dose:	0 and 2000 mg/kg/day
Year Study Performed:	1981 and 1982
Method/Guideline Followed:	Other; comparable to OECD guideline limit test
GLP:	Study was conducted in accordance with FDA Good Laboratory Practices.
Exposure Period:	13 weeks
Frequency of Treatment:	5 days/week
Post-Exposure Period:	None
Method/Guideline and Test Condition Remarks:	<p>Hair was clipped from the entire trunk of each animal within 24 hours prior to initial treatment; the clipping was repeated weekly throughout the study. The test substance was applied to the back with a syringe and dosing needle; the test substance was spread evenly over the site with the side of the dosing needle. The site was left uncovered and the rats were fitted with cardboard Elizabethan collars to minimize ingestion of the test substance. Water was applied and spread on the backs of sham-exposed controls on the same procedure and schedule as the treated animals. Animals were dosed on 5 consecutive days per week. At 24 hours after the fifth dose, residual test substance was wiped off and the collars were removed for two days.</p> <p>Endpoints during the biophase included daily observation of clinical signs and body weights measured weekly. After 13 weeks of treatment, blood samples were taken for measurement of hematological parameters (hematocrit, hemoglobin, number and morphology of red blood cells, and the number and differential count of white blood cells). The following clinical chemistry parameters were analyzed: albumin, alkaline phosphatase, alanine aminotransferase (glutamic pyruvic transaminases), aspartate aminotransferase (glutamic oxaloacetic transaminases), cholesterol, creatinine, glucose, lactate dehydrogenase, total bilirubin, total protein, triglycerides, urea nitrogen, uric acid, calcium, chloride, phosphorus, potassium, and sodium. Urine samples</p>

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were also collected for analysis of specific gravity, pH, glucose, occult blood, ketone bodies, albumin, urobilogen, and bilirubin. All animals were then killed and necropsied. The following organs were weighed: lungs, kidneys, adrenals, liver, heart, spleen, thymus, testis, ovary. Histological slides were prepared from the following organs and examined microscopically by a pathologist: colon, kidney, lung, liver, lymph node, ovary, skin, small intestine, spleen, stomach, testis and any gross lesions.

Statistical analysis: Quantitative data were analyzed for homogeneity of variance. If variances were homogeneous, data were analyzed by analysis of variance followed by multiple t tests or Duncan's multiple range tests. Categorical data were analyzed by a test based on the chi-squared distribution.

This study was conducted simultaneously with a parallel study on "Stock 345" (CAS #72623-83-7) and shared a common group of control animals with that study.

TEST RESULTS

Concentration (LOAEL/LOAEC/NOAEL/NOAEC)*

Type	Population:	Value Description:	Value or Lower Concentration:	Upper Concentration:	Units:
NOAEL	Rat	=	2000		mg/kg/day
LOEL	Rat	=	2000		mg/kg/day

Results Remarks:

No treatment-related deaths occurred and no treatment-related abnormal clinical signs were noted. No irritation of the skin at the treatment site was visible. Body weights, hematology, and urinalysis were not affected by treatment. No significant treatment-related effects were observed among parameters of serum chemistry except for a decrease in direct bilirubin in treated females. However, values were within normal range and the differences were not judged to be a response to treatment.

Histologically, the thickness of the epidermis at the treatment site was approximately doubled in 7 of 10 sham-exposed males (epidermal hyperplasia) and 1 of 10 females, with an equivocal or trace thickening in 3 other females. This change was considered normal in rats treated with weekly clipping and daily wetting. Epidermal hyperplasia was noted in animals treated with Stock 335 and chronic inflammation in the superficial dermis was also seen (increased numbers of mixed inflammatory cells, endothelial, and connective tissue cells). These changes were slight.

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Mean absolute liver weight was 7.2% higher in treated females than in controls (not statistically significant) and relative liver weight was increased in females by 8% (statistically significant). This reflects very minor decrease in final body weight combined with a nonsignificant absolute liver weight increase of 7.2%. No changes were observed microscopically and the slight changes in liver weight were not regarded as biologically significant.

	Sham-Exposed Controls	2,000 mg/kg/day
Males		
Body weight (BW in g)	379 ± 35	378 ± 36
Liver weight (g)	11.23 ± 1.66	11.40 ± 1.51
Liver weight/BW (%)	2.96 ± 0.23	3.01 ± 0.20
Thymus weight (g)	0.36 ± 0.09	0.38 ± 0.13
Platelets	ND	ND
Hemoglobin (g/dL)	16.5 ± 0.7	16.8 ± 0.9
Females		
Body weight (BW in g)	252 ± 18	250 ± 18
Liver weight (g)	6.99 ± 0.72	7.49 ± 0.52
Liver weight/BW (%)	2.77 ± 0.16	3.00 ± 0.16*
Thymus weight (g)	0.31 ± 0.09	0.29 ± 0.11
Platelets	ND	ND
Hemoglobin (g/dL)	16.0 ± 1.0	16.0 ± 1.2

*Statistically significantly different from controls (p<0.05)

ND indicates “not determined”.

Conclusion:

Dermal administration of Stock 335 to adult rats for 13 weeks resulted in minimal effects. Relative liver weight was increased in females, but no histological changes were observed. The study director did not discuss a NOAEL in the final report, but did state that Stock 335 elicited no toxic responses in the treated animals. Given this statement and the lack of systemic effects that were judged by the Petroleum HPV Testing Group to be adverse, the dose of 2,000 mg/kg was judged to be the NOAEL for systemic effects.

The Testing Group also determined the LOEL to be 2,000 mg/kg due to higher relative liver weight in females.

No visible dermal irritation was observed during the biophase, but slight histopathological changes were observed in the skin of both sham-treated and treated animals.

RELIABILITY/DATA QUALITY

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Reliability:	1. – Reliable without restrictions
Reliability Remarks:	Comparable to guideline limit test
Key Study Sponsor Indicator:	Key study
REFERENCE	
Reference:	Thirteen-week toxicity study by dermal application of metalworking fluid components to rats. Stock 335. Final Report on study 1471-81 from Mobil Environmental and Health Science Laboratory, Princeton, NJ. 1983.

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Repeated-Dose Toxicity

TEST SUBSTANCE

Category Chemical:	72623-83-7
Test Substance:	72623-83-7; Stock 345; Lubricating oils (petroleum) C ₂₅ , hydrotreated bright stock-based Viscosity was ~2550 SUS at 100°F and 152 SUS at 210°F.
Test Substance Purity/Composition and Other Test Substance Comments:	Stock 345 (Sample # 1480811) No other information
Category Chemical Result Type:	Measured
Unable to Measure or Estimate Justification:	
METHOD	
Route of Administration:	Dermal
Other Route of Administration:	
Type of Exposure:	Non-occluded
Species:	Rat
Other Species:	None
Mammalian Strain:	Sprague-Dawley

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Other Strain:	None
Gender:	Male and female
Number of Animals per Dose:	20 (10 per sex)
Concentration:	100%
Dose:	0 and 2000 mg/kg/day
Year Study Performed:	1981 and 1982
Method/Guideline Followed:	Other; comparable to OECD guideline limit test
GLP:	Study was conducted in accordance with FDA Good Laboratory Practices.
Exposure Period:	13 weeks
Frequency of Treatment:	5 days/week
Post-Exposure Period:	None
Method/Guideline and Test Condition Remarks:	<p>Hair was clipped from the entire trunk of each animal within 24 hours prior to initial treatment; the clipping was repeated weekly throughout the study. The test substance was applied to the back with a syringe and dosing needle; the test substance was spread evenly over the site with the side of the dosing needle. The site was left uncovered and the rats were fitted with cardboard Elizabethan collars to minimize ingestion of the test substance. Water was applied and spread on the backs of sham-exposed controls on the same procedure and schedule as the treated animals. Animals were dosed on 5 consecutive days per week. At 24 hours after the fifth dose, residual test substance was wiped off and the collars were removed for two days.</p> <p>Endpoints during the biophase included daily observation of clinical signs and body weights measured weekly. After 13 weeks of treatment, blood samples were taken for measurement of hematological parameters (hematocrit, hemoglobin, number and morphology of red blood cells, and the number and differential count of white blood cells). The following clinical chemistry parameters were analyzed: albumin, alkaline phosphatase, alanine aminotransferase (glutamic puruvic transaminases), aspartate aminotransferase (glutamic oxaloacetic</p>

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transaminases), cholesterol, creatinine, glucose, lactate dehydrogenase, total bilirubin, total protein, triglycerides, urea nitrogen, uric acid, calcium, chloride, phosphorus, potassium, and sodium. Urine samples were also collected for analysis of specific gravity, pH, glucose, occult blood, ketone bodies, albumin, urobilogen, and bilirubin. All animals were then killed and necropsied. The following organs were weighed: lungs, kidneys, adrenals, liver, heart, spleen, thymus, testis, ovary. Histological slides were prepared from the following organs and examined microscopically by a pathologist: colon, kidney, lung, liver, lymph node, ovary, skin, small intestine, spleen, stomach, testis and any gross lesions.

Statistical analysis: Quantitative data were analyzed for homogeneity of variance. If variances were homogeneous, data were analyzed by analysis of variance followed by multiple t tests or Duncan's multiple range tests. Categorical data were analyzed by a test based on the chi-squared distribution.

This study was conducted simultaneously with a parallel study on "Stock 335" (CAS #64742-65-0) and shared a common group of control animals with that study.

TEST RESULTS

Concentration (LOAEL/LOAEC/NOAEL/NOAEC)

Type	Population:	Value Description:	Value or Lower Concentration:	Upper Concentration:	Units:
NOAEL	Rat	=	2000		mg/kg/day
LOEL	Rat	=	2000		mg/kg/day

Results Remarks:

No treatment-related deaths occurred and no treatment-related abnormal clinical signs were noted. No irritation of the skin at the treatment site was visible. Body weights, hematology, and urinalysis were not affected by treatment. No significant treatment-related effects were observed among parameters of serum chemistry except for a decrease in direct bilirubin in treated females. However, values were within normal range and the differences were not judged to be a response to treatment.

Histologically, the thickness of the epidermis at the treatment site was approximately doubled in 7 of 10 sham-exposed males (epidermal hyperplasia) and 1 of 10 females, with an equivocal or trace thickening in 3 other females. This change was considered normal in rats treated with weekly clipping and daily wetting. Epidermal hyperplasia was noted in animals treated with Stock 345 and chronic inflammation in the superficial dermis was also seen (increased numbers of mixed inflammatory cells, endothelial, and connective tissue cells). These changes were slight.

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Mean absolute liver weight was 7.6% higher in treated females than in controls (not statistically significant) and relative liver weight was increased in females by 11.2% (statistically significant). This reflects very minor decrease in final body weight combined with a nonsignificant absolute liver weight increase of 7.6% . No changes were observed microscopically and the slight changes in liver weight were not regarded as biologically significant. A relative weight increase (9.4%) was found for kidneys in treated males, primarily reflecting the 6.9% decrease in final body weight of this group.

	Sham-Exposed Controls	2,000 mg/kg/day
Males		
Body weight (BW in g)	379 ± 35	353 ± 34
Liver weight (g)	11.23 ± 1.66	10.58 ± 1.62
Liver weight/BW (%)	2.96 ± 0.23	2.99 ± 0.23
Kidney weight (g)	3.06 ± 0.18	3.13 ± 0.27
Kidney weight/BW (%)	0.81 ± 0.05	0.89 ± 0.06*
Thymus weight (g)	0.36 ± 0.09	0.36 ± 0.10
Platelets	ND	ND
Hemoglobin (g/dL)	16.5 ± 0.7	16.7 ± 0.7
Females		
Body weight (BW in g)	252 ± 18	243 ± 19
Liver weight (g)	6.99 ± 0.72	7.52 ± 1.21
Liver weight/BW (%)	2.77 ± 0.16	3.08 ± 0.34*
Kidney weight (g)	1.84 ± 0.19	1.91 ± 0.27
Kidney weight/BW (%)	0.73 ± 0.06	0.78 ± 0.05
Thymus weight (g)	0.31 ± 0.09	0.26 ± 0.08
Platelets	ND	ND
Hemoglobin (g/dL)	16.0 ± 1.0	16.2 ± 0.6

*Statistically significantly different from controls (p<0.05) ND indicates “not determined”.

Conclusion:

Dermal administration of Stock 345 to adult rats for 13 weeks resulted in minimal effects. Relative liver weight was increased in females, but no histological changes were observed. The study director did not discuss the NOAEL in the final report, but did state that Stock 345 elicited no toxic responses in the treated animals. Given this statement and the

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lack of systemic effects that were judged by the reviewer to be adverse, the dose of 2,000 mg/kg was judged by the Petroleum HPV Testing Group to be a NOAEL for systemic effects.

The NOEL was not identified since a statistically significant increase in relative liver weight in males and in relative kidney weight in females was observed at 2,000 mg/kg/day. These observations were judged by the author not to be biologically significant. The Petroleum HPV Testing Group assigned a LOEL of 2,000 mg/kg based on these differences in relative organ weights.

No visible dermal irritation was observed during the biophase, but slight histopathological changes were observed in treated skin that were attributed to clipping and rubbing during dosing..

RELIABILITY/DATA QUALITY

Reliability: 1. – Reliable without restrictions

Reliability Remarks: Comparable to guideline limit test

Key Study Sponsor Indicator: Key

REFERENCE

Reference: Thirteen-week toxicity study by dermal application of metalworking fluid components to rats. Stock 345. Final Report on study 1481-81 from Mobil Environmental and Health Science Laboratory, Princeton, NJ. 1983.

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High Production Volume Information System (HPVIS)

Repeated-Dose Toxicity

TEST SUBSTANCE

Category Chemical:	White mineral oil (petroleum) CAS No. 8042-47-5
Test Substance:	Test substance was Stock 461 (80" white oil). Viscosity was a nominal value of 80 SUS.
Test Substance Purity/Composition and Other Test Substance Comments:	Lubricant Oil Basestocks are complex mixture of hydrocarbons rather than single compounds with identifiable purity.

Category Chemical Result Type:	Measured
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Unable to Measure or Estimate Justification:	
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METHOD

Route of Administration:	Dermal
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Other Route of Administration:	
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Type of Exposure:	Non-occluded
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Species:	Rat
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Other Species:	None
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Mammalian Strain:	Sprague-Dawley
Other Strain:	None
Gender:	Male and female
Number of Animals per Dose:	20 (10 per sex)
Concentration:	100%
Dose:	0 (untreated), 0 (sham-treated), and 125, 500, or 2000 mg/kg/day
Year Study Performed:	1985
Method/Guideline Followed:	Although not specified in the study records, the study design generally followed US and EU guidelines with the exception of the use of rats (justified elsewhere) and an unusually high dose of 2000 mg/kg/day.
GLP:	Study was conducted in accordance with EPA Good Laboratory Practices.
Exposure Period:	13 weeks
Frequency of Treatment:	5 days/week (weekdays)
Post-Exposure Period:	None
Method/Guideline and Test Condition Remarks:	<p>Hair was clipped from the dorsal skin of each rat as needed and the test substance was applied to the back of each animal with a syringe. The test substance was spread evenly over the back of each animal with the tip of the syringe. The treated skin was left uncovered and the rats were fitted with cardboard Elizabethan collars to minimize ingestion of the test substance. Excess test material was wiped from the skin with a gauze pad four hours after dosing. Sham-exposed controls were clipped and collared just as treated animals were and their dorsal skin was stroked with the tip of a syringe without application of any test material. Untreated controls were not clipped, collared, or given any treatments.</p> <p>Endpoints during the biophase included daily observation of clinical signs and body weights measured weekly. Skin irritation was assessed weekly.</p>

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At sacrifice at week 13, animals were fasted overnight and weighed the following morning. Blood samples were taken for measurement of the following hematological endpoints: hematocrit, hemoglobin, number and morphology of red blood cells, platelet count, and the number and differential count of white blood cells. In addition, the following clinical chemistry parameters were analyzed: albumin, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, cholesterol, creatinine, glucose, lactate dehydrogenase, sorbitol dehydrogenase, total bilirubin, total protein, triglycerides, urea nitrogen, uric acid, calcium, chloride, iron, phosphorus, potassium, and sodium. Urine samples were also collected for analysis of specific gravity, pH, glucose, occult blood, ketone bodies, albumin, urobilinogen, and bilirubin.

All animals were then killed and necropsied. The following organs were weighed: adrenals, brain, epididymides, gonads, heart, kidneys, liver, prostate, seminal vesicles, spleen, thymus, thyroid, and uterus. Histological slides were prepared from the following organs of both control groups and the high-dose animals: adrenals, bone and marrow, brain, epididymides, eyes and optic nerve, gonads, heart, duodenum, colon, kidneys, liver, lung, pancreas, prostate, salivary glands, seminal vesicles, skin (2 sections of treated skin), spleen, stomach, thymus, thyroid, urinary bladder, uterus, vagina, and any gross lesions. All slides were examined microscopically by a pathologist.

Statistical analysis: Quantitative data were analyzed by ANOVA followed by group comparisons using Fisher's Exact Test or Dunnett's test.

Histopathological examination of tissues from this study was given low priority because the study was originally designed to validate the test protocol. A complete histopathological evaluation was not needed for that validation. In 1995, the testing laboratory was closed and the pathology effort was terminated. A final pathology report was not prepared.

TEST RESULTS

Concentration (LOAEL/LOAEC/NOAEL/NOAEC)

Type	Population:	Value Description:	Value or Lower Concentration:	Upper Concentration:	Units:

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Results Remarks:

No treatment-related deaths occurred and no treatment-related abnormal clinical signs were noted except for the skin. Erythema, scabs, and flaking of the skin were observed in nearly all of the animals treated with Stock 461. A few sham-treated females also had flaking and scabs on the back.

Body weights in males decreased in a dose-related manner, with a 14% decrease in the high-dose group for mean unfasted weight in week 13. Body weight of only the high-dose females was lower than that of controls (11% versus untreated controls and 9% versus sham-exposed controls at week 13). Selected mean body weights are in the following table.

	Untreated Controls	Sham-Treated Controls	125 mg/kg/day	500 mg/kg/day	2000 mg/kg/day
Males					
Week 0	245	258	253	244	244
Week 4	425	414	410	379 ^{bd}	354 ^{bd}
Week 9	532	519	513	475 ^v	446 ^{bd}
Week 13	565	560	550	512 ^{bd}	486 ^{bd}
Females					
Week 0	174	172	172	176	167
Week 4	252	238 ^b	245	245	228 ^b
Week 9	293	279 ^b	289	287	272 ^b
Week 13	320	312	325	306	285 ^a

Significantly different from untreated: a = P<0.05 b=P<0.01

Significantly different from sham-treated: c = P<0.05 d=P<0.01

Parameters of hematology and urinalysis were not affected by treatment. Among parameters of serum chemistry, Significant differences were observed between the sham-treated controls and treated animals for alanine aminotransferase, albumin, and albumin/globulin ratio in males and for glucose and triglycerides in females. When historical values were considered, albumin and albumin/globulin ratio in males were below the historical range. The study director concluded that these parameters were marginally affected in males by treatment and females were not affected. Means for these parameters are in the following table.

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	Untreated Controls	Sham-Exposed Controls	125 mg/kg/day	500 mg/kg/day	2,000 mg/kg/day
Males					
Albumin	3.8	3.7	3.6	3.5 ^a	3.4 ^a
Alanine aminotransferase (IU/L)	30	30	30	32	40 ^a
Albumin/globulin ratio	1.1	1.1	1.1	1.0 ^a	0.9 ^a
Glucose (mg/dL)	140.1 ^a	115.1	116.7	110.2	104.5
Triglycerides	129.8	86.3	84.0	71.5	35.9
Females					
Albumin	4.1	4.1	4.1	3.8	3.9
Albumin/globulin ratio	1.4	1.3	1.3	1.2	1.2
Alanine aminotransferase	27	50	44	37	40
Glucose	118.9	131.9	121.3	119.4	106.3 ^a
Triglycerides	50.4	60.3	51.1	42.5 ^a	35.8 ^a

Significantly different from sham-treated: a = P<0.05

Although the data on organ weights were not compiled in a formal report, the raw data still existed in the study files. Therefore these data were compiled for this summary and statistical analyses on the data were performed. Details of this process are in a summary report (API, 2010). Statistical analyses were based on a parametric analysis of variance (ANOVA) followed by Dunnett's test for mean differences from sham control. Statistically significant differences from the sham-treated control were not reported at a level more significant than the ANOVA significance level.

No significant treatment-related effects were seen on absolute organ weights in either sex. Several relative organ weights, expressed as a percent of final body weight, were greater than in sham-treated controls. Given the number of relative organ weights that were higher in treated animals (including relative brain weight), the lack of treatment-related effects on absolute organ weights, and the lower body weights in treated animals, the toxicological relevance of the differences in relative organ weights is very questionable (API, 2010).

Although data on organ weights, gross observations at necropsy, and histopathology of organs were not available to the study director at the end of the biophase, the study director concluded that the NOAEL for this study was 125 mg/kg/day based on lower body weights and marginally lower serum albumin in males at 500 and 2000 mg/kg/day.

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Conclusion:	<p>Dermal administration of Stock 461 to adult rats for 13 weeks resulted in dermal irritation and decreased body weights. The study director assigned a NOAEL of 125 mg/kg on the basis of lower body weights at higher doses during the biophase. For reasons discussed in the Category Assessment Document on Lubricating Oil Basestocks, the reviewer considered the lower body weights in treated animals to be a treatment-related effect, but not an adverse systemic effect related to the test substance. The marginally lower serum albumin in one sex was not judged to be sufficient to establish a NOAEL. Given the lack of histopathology, a NOAEL for systemic effects could not be established for this study.</p> <p>Dermal irritation (erythema, flaking, and scabs) was seen during the biophase in almost all animals of both sexes.</p>
RELIABILITY/DATA QUALITY	
Reliability:	2 – Reliable with restrictions
Reliability Remarks:	Study was well designed and conducted. However, the testing laboratory was closed before microscopic evaluation of tissues was performed and a pathology report was not prepared. Therefore critical data on histopathology are not available. The utility of the study is limited as a result.
Key Study Sponsor Indicator:	Key study Stock 461 rat subchronic study
REFERENCE	
Reference:	<p>Stock 461 rat subchronic study. Interim (biophase) report on study 40921B from Mobil Environmental and Health Science Laboratory, Princeton, NJ. 1988</p> <p>American Petroleum Institute (API). 2010. Summary of Mobil Study 40921-A (Stock 461 rat reproduction study) and Mobil 40921-B (Stock 461 rat subchronic study). API, Washington, DC. Dated December 2, 2010.</p>

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High Production Volume Information System (HPVIS)

Repeated-Dose Toxicity

TEST SUBSTANCE

Category Chemical:

64742-65-0

Test Substance:

64742-65-0; Solvent-dewaxed heavy paraffinic distillate (SDHP)

Test Substance Purity/Composition and Other Test Substance Comments:

Solvent-dewaxed heavy paraffinic distillate (Site #23, Sample #7); Batch no. TA-125503/ CRU Nos. 30961 and 60901.

PAC Content – report no. PTI 2009-0303 (API, 2009a); PTI 2009-0602 (API, 2009b)

Sample #	DMSO wt.% ¹	1-ARC (%) ²	2-ARC (%)	3-ARC (%)	4-ARC (%)	5-ARC (%)	6-ARC (%)	7-ARC (%)
30961	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
60901	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

1) Percent of DMSO-extractable materials (mostly PACs), determined by the PAC 2 method as described in API (2009a; 2009b).

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.

Category Chemical Result Type:

64742-65-0

Unable to Measure or Estimate Justification:

64742-65-0; Solvent-dewaxed heavy paraffinic distillate (SDHP)

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METHOD

Route of Administration:	Dermal, non-occluded
Other Route of Administration:	Not applicable
Type of Exposure:	90-day repeat dose
Species:	Rat
Other Species:	None
Mammalian Strain:	Sprague-Dawley (Charles River Laboratories, Inc., Raleigh, NC)
Other Strain:	None
Gender:	Male and female
Number of Animals per Dose:	10 animals/sex/dose
Concentration:	100%
Dose:	0 (sham-treated), and 1000 mg/kg/day
Year Study Performed:	2009
Method/Guideline Followed:	USEPA Health Effects Test Guidelines OPPTS 870.3250; OECD 411 -limit study
GLP:	Study was conducted in accordance with EPA Good Laboratory Practices.
Exposure Period:	90 days
Frequency of Treatment:	5 days/week (weekdays)

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Post-Exposure Period:

None

**Method/Guideline
and Test Condition Remarks:**

Animals were approximately 10 weeks at the beginning of dosing following a 20 day week acclimation period. The treatment groups and time exposure periods were as follows:

1. Sham control (0 mg/kg/day) – 90 days, 20 animals
2. SDHP 1000 mg/kg/day – 90 days, 20 animals

Clinical examinations were performed twice daily during the dosing period (Monday through Friday), at the time of dose administration and approximately 1 to 2 hours following dose administration. On nondosing days the animals were observed once daily. The absence or presence of findings was recorded for individual animals at the scheduled intervals. Detailed physical examinations were conducted on all animals weekly, beginning approximately 2 weeks prior to randomization and prior to the scheduled necropsy. Any observations noted outside of the above-specified intervals were also recorded.

The application site was scored daily (prior to dose administration during the treatment period) for erythema and edema in accordance with a 4-step grading system (Draize). Other remarkable dermal findings, if present, were recorded.

Ocular examinations were conducted on all animals prior to randomization (3 October, 2009; study week 2), and near the end of the dosing period (6 January, 2010; study week 12). All ocular examinations were conducted using an indirect ophthalmoscope and slit lamp biomicroscope) preceded by pupillary dilation with an appropriate mydriatic agent.

TEST RESULTS

Concentration (LOAEL/LOAEC/NOAEL/NOAEC)*

Type	Population:	Value Description:	Value or Lower Concentration:	Upper Concentration:	Units:
NOAEL	Rat	=	1000		mg/kg/day

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LOEL	Rat	=	1000		mg/kg/day

*Determined by reviewer

Results Remarks:

A treatment-related lower mean cholesterol value was noted in the 1000 mg/kg/day group males when compared to the control group (33.3% lower), with a smaller, non-significant reduction present in females (10.0% lower). While this finding in males was outside of the WIL historical control reference range (version 2.9), it was considered to be toxicologically irrelevant due to the direction and small magnitude of change in both sexes. A higher mean serum phosphorus value was noted in the 1000 mg/kg/day group males at study week 12. Although the mean value was 13% higher than the control group mean and was outside of the historical control range, this higher phosphorus value was not observed in the females, and therefore may be secondary to the body weight effect observed in the males. There were no other definite treatment-related effects on serum chemistry parameters; however, a statistically significantly higher mean alkaline phosphatase value was noted in the 1000 mg/kg/day group males when compared to the control group. This difference was within the range of WIL historical control data.

	Sham-Exposed Controls	1,000 mg/kg/day
Males		
Body weight (BW in g)	506 \pm 34.2	442 \pm 38.9b
Cholesterol (mg/dL)	57 \pm 14.3	38 \pm 6.6b
Phosphorus (mg/dL)	9.2 \pm 0.89	10.4 \pm 1.36a
Liver weight (g)	14.35 \pm 1.149	12.99 \pm 1.267b
Liver weight/BW (%)	2.841 \pm 0.228	2.938 \pm 0.085
Thymus weight (g)	0.3123 \pm 0.07381	0.2544 \pm 0.06306
Thymus/BW (%)	0.062 \pm 0.0152	0.058 \pm 0.0142
Brain (g)	2.16 \pm 0.126	2.22 \pm 0.116
Brain/BW (%)	0.429 \pm 0.0339	0.505 \pm 0.0423b
Heart (g)	1.73 \pm 0.143	1.66 \pm 0.151
Heart/BW (%)	0.341 \pm 0.0190	0.377 \pm 0.0321b
Kidney weight (g)	3.92 \pm 0.376	3.88 \pm 0.408

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Kidney/BW (%)	0.773±0.0443	0.879±0.0628b
Spleen weight (g)	0.84±0.064	0.73±0.094a
Spleen/BW (%)	0.165±0.0109	0.166±0.0232
Females		
Body weight (BW in g)	293±27.1	293±22.3
Cholesterol (mg/dL)	60±13.8	54±11.6
Phosphorus (mg/dL)	9.2±1.49	9.6±1.08
Liver weight (g)	8.59±1.070	9.62±0.980a
Liver weight/BW (%)	2.928±0.2228	3.294±0.2751b
Thymus weight (g)	0.2430±0.04282	0.3164±0.11062
Thymus/BW (%)	0.083±0.0135	0.107±0.0330a
Brain (g)	1.98±.071	1.97±0.063
Brain/BW (%)	0.680±0.0612	0.678±0.0490
Heart (g)	1.12±0.106	1.20±0.169
Heart/BW (%)	0.384±0.0239	0.411±0.0655
Kidney weight (g)	2.39±0.238	2.41±0.099
Kidney/BW (%)	0.819±0.0648	0.828±0.0755
Spleen weight (g)	0.197±0.0275	0.217±0.0304
Spleen/BW (%)	29.042±3.8635	31.947±3.5733

a)Statistically significantly different from controls, p<0.05

b)Statistically significantly different from controls, p<0.01

Conclusion:

Authors of the laboratory's final report did not identify a specific NOAEL or LOAEL. Their conclusion in the report is presented here.

“Based on the results of this study, dermal administration of a highly refined SDHP over an area of approximately 10% of the shaved body surface area to CrI:CD(SD) rats over a period of 13 weeks was well tolerated at a dosage level of 1000 mg/kg/day and did not cause lethality or any overt toxicity. Definitive test substance-related findings were limited to lower mean final body weights and a lower mean cholesterol value in the 1000 mg/kg/day group males and a higher mean liver weight in the 1000 mg/kg/day group females; however, no histologic correlates to the higher liver weights were observed. A higher mean serum phosphorus value was noted in the 1000 mg/kg/day group males; however, this effect may have been due to the lower mean body weight gains observed in the 1000 mg/kg/day group males and therefore, was not considered definitively test substance-related. The extent of the body weight change in the 1000

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mg/kg/day group males (12.8% lower than the control group at study week 13) was considered to be test substance-related and potentially adverse.”

Overall, the main effects of treatment appeared to be lower body weight in males and higher absolute and relative liver weights in females. The Petroleum HPV Testing Group considered the lower body weight to be treatment-related, but not an adverse effect of the test substance. The increased liver weight in females was interpreted as a possible adaptive change. Therefore the Working Group assigned a NOAEL of 1000 mg/kg/day and, based on lower body weights in treated males, a LOEL of 1000 mg/kg/day.

RELIABILITY/DATA QUALITY

Reliability:

1. – Reliable without restrictions

Reliability Remarks:

Similar to guideline study; fewer dose levels; sufficient detail provided in appendices and tables.

Key Study Sponsor Indicator:

Key

REFERENCE

Reference:

API. 2009a. Characterization and quantitation of polynuclear aromatic compounds (PAC) in three HPV solvent-dewaxed heavy paraffinic distillates by PRR (Mobil-Method 2) PAC. Port Royal Research, PTI 2009-0303.

API. 2009b. Characterization and quantitation of polynuclear aromatic compounds (PAC) in three HPV solvent-dewaxed heavy paraffinic distillates by PRR (Mobil-Method 2) PAC. Port Royal Research, PTI 2009-0602.

API, 2010. A 90-Day Repeat-Dose Dermal Toxicity Study of Solvent Dewaxed Paraffinic Distillates (Petroleum) (CAS# 64742-65-0) in Sprague Dawley Rats . WIL Research Laboratories, WIL-402009

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REPEATED DOSE TOXICITY, ORAL

Repeated Dose Toxicity

Test Substance

Category Chemical (CAS #):	Not available
Test Substance (CAS #):	No CAS number available; Food grade white mineral oil N10(A); N15(H); P15(H); N70(A); N70(H); P100(H)
Test Substance Purity/Composition and Other Test Substance Comments :	N10(A); N15(H); P15(H); N70(A); N70(H); P100(H) No other information
Category Chemical Result Type :	Measured

Type : Oral 90 day
Species : Rat
Sex : Male/female
Strain : Fischer 344
Route of admin. : Oral feed
Exposure period : 90 days
Frequency of treatm. : Continuous in food
Doses : 0.002, 0.02, 0.2 & 2.0% in the diet
Control group : Yes
Method : OECD Guide-line 408 "Subchronic Oral Toxicity - Rodent: 90-day Study"
Year : 1992
GLP : Yes
Test substance : Six White oils

Six white oils examined in this study were characterized.
Only the average molecular weight and viscosity at 100 °C are shown below:

Sample	Viscosity (cSt)	Average Molecular Weight
N10(A)	3.08	320
N15(H)	3.45	330
P15(H)	3.52	350
N70(A)	7.88	410
N70(H)	7.65	420
P100(H)	11	510

Method : Three related, but separate studies were carried out at the same time on 6

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different food grade white oils and 3 food grade waxes. Only the information on the oils is included here. The information on waxes is included in the Waxes and Related Materials HPV Test Plan.

In the main study, groups of 20 male and 20 female rats were fed diets containing one of 6 different white oils at dietary concentrations of 0.002, 0.02, 0.2 and 2.0% for 90 days. Further groups of 60 male and 60 females were fed untreated control diet. Additionally groups of 20 rats of each sex were fed diets containing 2.0% coconut oil.

The second study was a reversibility study. Groups of 10 rats of each sex were fed diets for 90 days containing one of the 6 different oils at the 2.0% level or coconut oil at 2%. These animals were then fed control diet for 28 days following the 90-days treatment. Groups of 30 rats of each sex served as controls for this reversibility study.

A third study was designed to determine tissue levels of hydrocarbons. In this study, 5 rats of each sex were fed diets containing one of the 6 oils or coconut oil at the 2.0% dietary level for 90 days. Extra groups of rats (5 of each sex) were fed control diet or coconut oil or one of the six oils for 90 days followed by exposure to control diet only for a further 28 days.

In all three studies, animals were monitored for weight, food intakes and clinical condition throughout. An ophthalmic examination was performed prior to treatment and prior to necropsy on the animals in the main study and those for the study of reversibility.

A full necropsy was performed on the main and reversibility were measured on blood samples taken from the animals. Clinical chemical measurements were also made on serum separated from the blood samples. A selection of organs was weighed and a range of tissues retained for subsequent histopathological examination. All tissues from the high dose group and control groups were examined by light intermediate dose groups.

Mineral hydrocarbon levels were measured in a limited number determinations.

Remark : While only one report (three studies) is described here, numerous repeat dose studies on white oils destined for use in foods have been conducted and reported in the open literature.

Recent studies with a low molecular weight white oil have demonstrated that the F 344 rat is more sensitive in its response to mineral hydrocarbons than the Sprague Dawley rat (Firriolo et al). Indeed other studies on white oils with Sprague Dawley rats (McKee et al) and beagle dogs (Bird et al) have also not resulted in any reported effects .

Result : The six oils tested had average molecular weights ranging from 320 to 510. The effects observed in the study were inversely related to the oil's molecular weight. Thus the oil with the lowest molecular weight caused the most severe effects and at lower dose levels than the higher molecular weight materials. For simplicity, only the results of the highest and lowest molecular weight oils are summarized below. Furthermore, the results of the reversibility study are not given in detail here. In general, there was evidence of reversibility of the effects but reversibility was not complete for all of the parameters measured.

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P 100 H (Average molecular weight 510)

There were no treatment-related clinical signs, nor was there an effect on body weight. Food consumption was increased in the males of the highest dose group but this was less than 10% greater than for the controls.

Ophthalmic examination did not reveal any effects. Organ weights, hematology and clinical chemistry were unaffected except for a 10% increase in ASAT in the males in the highest dose group.

There were no treatment-related findings at necropsy and the histological examination did not reveal any treatment-related effects.

A small amount of mineral hydrocarbon was found in the livers of the male rats in the highest dose group.

N 10 A (Average molecular weight 320)

There were no treatment-related clinical signs, nor was there an effect on body weight. Food consumption was increased in the males of the highest dose group but this was less than 10% greater than for the controls.

Ophthalmic examination did not reveal any effects.

Organ weights

Increases in organ weights are as shown below, other organ weights were unaffected.

Organ	Increases (%) at Dietary concentration			
	Males		Females	
	0.2%	2.0%	0.2%	2.0%
Kidney (abs.)	4	6		5
(rel.)		7		7
Liver (abs)	8	11	6	21
(rel.)	6	12	8	23
Spleen (abs.)				17
(rel.)		5		19
MLN* (abs.)		224		220
(rel.)		224		226

* NB Mesenteric Lymph Node weights only determined for the 2% dose group in the reversal group of animals and not for the main study animals.

Hematology

In the males in the highest dose group there were increases in Neutrophils (41%), monocytes (28%) and basophils (200%) In the females, changes occurred in the 2% and 0.2% dose groups. These were as follows:

	Change (% + or -) at dose level	
	0.2%	2%
RBC	- 2	- 3
Hemoglobin	- 2	- 3
WBC		+ 23
Differential WBC Neutrophils		+ 75

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Monocytes	+ 51
Eosinophils	+ 38

Clinical chemistry

In the males there was a reduction in Alkaline phosphatase of 8 and 2% in the 2 and 0.2% dose groups respectively.

Changes in clinical chemical parameters in the females were as follows:

	Change (% + or -) at dose level	
	0.2%	2%
ALKP	- 12	- 13
ASAT		+ 12
Gamma GT		+ 91
A/G ratio		- 8

Histopathology

Liver

Liver lesions comprised microgranuloma or granuloma, the distinction between being purely related to size. Lesions were classified as microgranuloma if the average diameter was less than 25% of the average hepatic lobule. The histological features of the two were similar and consisted of collections of macrophages, some with necrotic cells surrounded by inflammatory cells and variable fibrosis.

No lesions were observed in the males whereas granulomas were seen in the females in the highest dose group.

In females in the recovery group 28 days after cessation of exposure, the incidence was unchanged but the severity of the lesions had decreased.

Mesenteric Lymph node

The lymph node lesions comprised focal collections of macrophages, often in the cortical region. The macrophages were lightly vacuolated, giving a slightly foamy appearance to their cytoplasm. Some macrophages had a yellowish-brown pigmentation of varied intensity. The focal collections of macrophages were classified as histiocytosis and were scored as minimal, mild, moderate or marked based on size and abundance. The foci of histiocytosis were not homogeneously distributed; they were often restricted to one node or even to part of one node. Histiocytosis was also found in control rats but was generally restricted to isolated foci and was always classified as minimal. Compared to controls, in males histiocytosis increased down to the 0.2% dose group. In the females, histiocytosis was also observed in the 0.02% dose group.

In the reversibility group the severity and incidence was reduced after being fed control diet for 28 days.

Ileum and jejunum

There was a significant increase in vacuolation of the lamina propria in the high dose female group.

In summary, the NOELs and LOELs for the six oils that were tested are as follows.

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Oil	LOEL (histiocytosis) Dietary concentration	NOAEL
N10A	0.02%	
N15H	0.002%	
P15H	0.02%	
N70A	0.02%	
N70H	0.02%	
P100H	-	2.0%

Reliability

: (1) valid without restriction

(22) (98) (105)

(22)

BIBRA (1992)

A 90-day feeding study in the rat with six different mineral oils (N15(H), N70(H), N70(A), P15(H), N10(A) and P100(H), three different mineral waxes (a low melting point wax, a high melting point wax and a high sulphur wax) and coconut oil.

BIBRA project No. 3.1010

(98)

Firriolo, J. M., Morris, C. F., Trimmer, G. W., Twitty, L. D., Smith, J. H. and Freeman, J. J. (1995)

Comparative 90-day feeding study with low-viscosity white mineral oil in Fischer-344 and Sprague-Dawley-derived CRL:CD rats.

Toxicologic Pathology Vol 23, No. 1, pages 26-33

(105)

McKee, R. H., Plutnick, R. T. and Traul, K. A. (1987)

Assessment of the potential reproductive and subchronic toxicity of EDS coal liquids in Sprague-Dawley rats.

Toxicology Vol 46, pp 267-280

Genetic Toxicity – in vitro**Test Substance**

Category Chemical (CAS #):	Not applicable
Test Substance (CAS #):	Various base oils
Test Substance Purity/Composition and Other Test Substance Comments :	The base oils tested had PAC contents ranging from 0.2 to 12%.
Category Chemical Result Type :	Measured

Type : Modified Ames Assay
System of testing : Salmonella typhimurium strain TA98
Metabolic activation : With
Year : 1984
Test substance : Various base oils

Method : The method differed from the standard pre- incubation Ames assay in the following respects.

A DMSO extract of the test materials was tested in the assay.

The S9 fraction was obtained from Araclor-induced hamsters.

An eightfold concentration of S-9 was used in the assays.

Twofold concentration of cofactor NADP was used.

The DMSO extracts were tested over a range of concentrations that permitted the construction of a dose-response curve.

A Mutagenicity Index was determined for each assay. This was the tangent to the dose response curve at zero dose.

An assay was judged to be positive if the Mutagenicity Index was greater than 1.0

Result : Roy describes the mutagenicity results for a range of petroleum-derived materials, 28 of which were lubricating oil base stocks. A Mutagenicity Index (MI) was determined for each test material and this was compared to the PAC content and to a carcinogenicity index that had also been determined for each material.

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The results were as follows.

Sample	MI*	%PAC**	%T***	%T/LP****
5	0.9	0.9	0	4.17
6	0	0.3	0	0
7	0.9	0.9	2	4.17
8	0	0.6	0	0
9	0	0.3	0	0
10	0	0.7	2	3.28
12	2.4	3.1	4	5.93
13	9.1	10	26	71
14	0	0.7	2	3.45
15	0	0.2	0	0
16	3.9	3.7	6	1.6
17	4	3.1	8	14.3
18	3.6	4.9	10	21.7
19	6.5	5.2	10	23.4
20	9.2	7.7	40	138
26	0	0.5	2	2
27	0	0.5	2	3.92
28	0	0.3	0	0
29	0	0.6	0	0
30	0	0.6	0	0
32	10	12	54	154
33	5.9	7.8	42	73.7
34	4.1	4.1	50	104
35	1.2	1.2	4	6.25
36	2.1	1.5	18	38.3
37	0	0.7	2	2.13
38	4.5	4.6	24	46.2
39	0	1.2	0	0

* MI denotes Mutagenicity index.

** %PAC is weight% of 3-7 ring PNAs in the oil.

*** %T is the percentage of mice with tumors in skin carcinogenicity studies reported elsewhere.

**** %T/LP is the percentage of mice with tumors multiplied by the reciprocal of the latency period. The author describes this as a carcinogenic potency index.

Test substance : The baseoils tested had PAC contents ranging from 0.2 to 12%. It is generally recognized that those base oils with PAC contents less than 3% are highly refined oils whereas those with greater values are considered to be poorly refined. This distinction was recognized and used by the EU in its classification of base oils. (EU, 1994; CONCAWE 1994)

Conclusion : Base stocks with no or low concentrations of PACs have low Mutagenicity indices. Also, those oils that were negative in the modified Ames assay (MI < 1.0) were not carcinogenic in mouse skin painting studies. Those oils which were positive in the modified Ames assay had significant levels of PACs and were carcinogenic.

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Reliability : (1) valid without restriction

(24) (26) (111)

(24)

Blackburn, G. R., Deitch, R. A., Schreiner, C. A. and
Mackerer, C. R. (1986)
Predicting tumorigenicity of petroleum distillation
fractions using a modified Salmonella Mutagenicity assay.
Cell Biol. Toxicol. Vol. 2. pp 63-84

(26)

Blackburn, G.R., Deitch, R.A., Schreiner, C.A., Mehlman, M.
A. and Mackerer, C.R. (1984)
Estimation of the dermal carcinogenic activity of petroleum
fractions using a modified Ames assay.
Cell Biol. and Toxicol. Vol 1, No 1, pp 67-80

(111)

Roy, T.A., Johnson, S.W., Blackburn, G.R., and Mackerer,
C.R. (1988)
Correlation of mutagenic and dermal carcinogenic activities
of mineral oils with polycyclic aromatic compound content.
Fund. Appl. Toxicol. Vol 10, pp 466-476

Genetic Toxicity – in vitro**Test Substance**

Category Chemical (CAS #):	Not available
Test Substance (CAS #):	CAS No. not available; Canthus 1000; deasphalted, dewaxed residual oil
Test Substance Purity/Composition and Other Test Substance Comments :	Canthus 1000 No other information
Category Chemical Result Type :	Measured

Type : Modified Ames Assay
System of testing : Salmonella typhimurium strain TA98
Metabolic activation : With
Result : Negative
GLP : No data
Test substance : Residual base oils

Method : The test substance (Canthus 1000, a deasphalted, dewaxed residual oil) was diluted 1:5 in DMSO and then shaken, centrifuged and separated into 2 fractions. Two assays were conducted for the test substance: an initial assay and a repeat assay. All plates were evaluated following approximately two days of incubation. Test volumes of 5, 10, 15, 20, 30, 40, 50 and 60 µl/plate were prepared by dilution of the DMSO fraction in DMSO and dosed at a final volume of 60 µl. The volumes were added to each plate with metabolic activation (hamster S9) and tester strain TA98 following the procedures outlined by Blackburn et al., (1986) and the methods described in the American Society for Testing Materials (ASTM) document, "The Standard Test Method for Determining Carcinogenic Potential of Virgin Base Oils in Metalworking Fluids". The same test volumes were used in the repeat assay. A positive control and vehicle control were tested concurrently.

Linear regression analysis (ASTM: E 1687-95) was performed on the test substances which caused an increase in the mean number of revertant colonies when compared to the vehicle control. Only data from the linear portion of the dose response curve was used to generate the mutagenicity index (MI). If the increase in revertant colonies was not statistically significant or if there was no increase in the mean number of revertant colonies, then the MI value was considered to be 0 (revertants/µl DMSO extract).

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Result : Data from both the initial and repeat assays on the test material (Canthus 1000) were pooled to generate a single linear MI value. With this procedure, an MI value > 1.0 (revertants/ μ l DMSO extract) is considered indicative of a potential dermal carcinogen in mice (Blackburn et al, 1996). Conversely, a test substance is considered unlikely to be carcinogenic in mouse skin when the MI value is < 1.0 (revertants/ μ l DMSO extract).
: The MI for Canthus 1000 was determined to be 0.2 revertants/ μ l DMSO extract.
Thus, under the conditions of this study, Canthus 1000 was considered negative for inducing frameshift mutations in Salmonella typhimurium.

Reliability : (4) not assignable
This summary is based on a summary of the results of a study.
It is not possible, therefore to assign a reliability to this study.
The data however are useful, together with other similar data to demonstrate that residual base oils are not mutagenic in a modified Ames assay.

(20) (24) (25) (97)
)

(24) Blackburn, G. R., Deitch, R. A., Schreiner, C. A. and Mackerer, C. R. (1986)
Predicting tumorigenicity of petroleum distillation fractions using a modified Salmonella Mutagenicity assay.
Cell Biol. Toxicol. Vol. 2. pp 63-84

(20) American Society of Testing Materials (ASTM)
The standard test method for determining carcinogenic potential of virgin base oils in metalworking fluids
E-1687-98, Conshohocken, PA

(25) Blackburn, G. R., Roy, T. A., Bleicher Jr., W. T., Reddy, M. V. and Mackerer, C. R. (1996)
Comparisons of biological and chemical predictors of dermal carcinogenicity of petroleum oils
J. Polycyclic aromatic compounds Vol 11 pp 201-210

(97) Exxonmobil Biomedical Sciences Inc.
(00MRL 18)

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Genetic Toxicity – in vitro

Test Substance

Category Chemical (CAS #):	Not available
Test Substance (CAS #):	CAS numbers not available Vacuum residuum Bright stock 150 SUS Bright stock 150 Solvent Bright stock
Test Substance Purity/Composition and Other Test Substance Comments :	No other information
Category Chemical Result Type :	Measured

Type : Modified Ames Assay
System of testing : Salmonella typhimurium strain TA98
Metabolic activation : With
Result : Negative

Remark : Summaries are available on Modified Ames assays that have been carried out on 3 additional residual base oils and a vacuum residuum. The results and references to the studies are shown below. Under the conditions of this study, the test materials were considered negative for inducing frameshift mutations in Salmonella typhimurium.

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	Material	Mutagenicity Index (MI)	Reference
	Vacuum residuum	0.8	Petrolabs (1998)
	Bright stock	0.11	Petrolabs (2000)
	150 SUS Bright stock	0	EMBSI
	150 Solvent Bright stock	0	EMBSI
Reliability	: (4) not assignable This summary is based on a summary of the results of a study. It is not possible, therefore, to assign a reliability to this study. The data, however, are useful, together with other similar data, to demonstrate that residual base oils are not mutagenic in a modified Ames assay.		
			(85) (109) (110)
(109)	Petrolabs (1998) H-Mobil-67763-Vacuum Resid.		
(110)	Petrolabs (2000) H-Mobil-68351-Bright stock		
(85)	EMBSI 01.MRL.66		

Genetic Toxicity – in vitro**Test Substance**

Category Chemical (CAS #):	64742-56-9; 64742-56-0; 64742-65-0; 64741-97-5; 64741-96-4; 64742-52-5
Test Substance (CAS #):	64742-56-9; API 78-9; Solvent dewaxed light paraffinic distillate 64742-56-0; API 78-10; Solvent dewaxed heavy paraffinic distillate 64742-65-0; API 79-3; Solvent dewaxed heavy paraffinic distillate 64742-65-0; API 79-4; Solvent dewaxed heavy paraffinic distillate 64742-65-0; API 79-5 Solvent dewaxed heavy paraffinic distillate 64741-97-5; API 78-5; 7Solvent refined light naphthenic distillate 64741-96- 4; API 79-1;Solvent refined heavy naphthenic distillate
Test Substance Purity/Composition and Other Test Substance Comments :	API 78-9 API 78-10 API 79-3 API 79-4 API 79-5 API 78-5 API 79-1 No other information
Category Chemical Result Type :	Measured

Type : Mouse lymphoma assays - General comments

Remark : The mouse lymphoma assays that have been described have been compromised, either because there was no dose-related response or there was a limitation due to poor solubility of the test material. For these reasons, no mouse lymphoma assays have been described in detail in this robust summary.

However, the results of these mouse lymphoma assays (with and without metabolic activation) carried out on seven different lubricating base oils are summarized in the following table.

Sample Paraffinic base oils	Result	Reference (API report No.)
API 78-9	Equivocal No dose response	28-31864

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API 78-10	Equivocal No dose response	28-31868
API 79-3	Equivocal No dose response	28-31865
API 79-4	Equivocal No dose response	28-31866
API 79-5	Equivocal No dose response	28-31867
Naphthenic base oils		
API 78-5	Negative ^(a)	28-32359
API 79-1	Negative ^(a)	29-32360

Reliability : ^(a) Solubility limited the evaluation
(1) valid without restriction

NO REFERENCE
LISTED

Genetic Toxicity – in vivo**Test Substance**

Category Chemical (CAS #):	64741-97-5
Test Substance (CAS #):	64741-97-5; API 78-5; Solvent refined light naphthenic distillate
Test Substance Purity/Composition and Other Test Substance Comments :	API 78-5 No other information
Category Chemical Result Type :	Measured

Type : Cytogenetic assay
Species : Rat
Sex : Male/female
Strain : Sprague-Dawley
Route of admin. : Gavage
Exposure period : 5 days
Doses : 0.5, 1.67 & 5.0 g/kg/day
Result : Negative
Year : 1982
GLP : No
Test substance : Highly refined base oil

Method : Test material was administered orally to groups of five male and five female rats daily for 5 days. The dose groups were 0.5, 1.67 and 5.0 g/kg/day. Additionally five animals of each sex were orally dosed with 0.9% saline daily for five days; these animals served as negative controls. Positive controls consisted of ten males and ten females that were given a single i.p. dose of triethylenmelamine (TEM) in saline at a dose level of 1.0 mg TEM /kg. This positive control substance was administered six hours before termination of the study.

Three hours prior to kill, the animals were injected i.p. with 4 mg/kg of colchicine to arrest cell division.

The animals were killed with CO₂ and the adhering tissue and epiphyses of both tibiae were removed. The marrow was removed and transferred to Hank's balanced salt solution. The marrow button was collected by centrifugation and resuspended in 0.075M KCl. The centrifugation was repeated and the pellet resuspended in fixative (methanol:acetic acid, 3:1). The fixative was changed once and the cells left overnight at 4 °C. Cells in fixative were dropped onto glass slides which were air-dried and

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stained with Giemsa.

Each slide was scored for chromosomal aberrations. Scoring was for gaps, breaks, fragments and reunion figures. Routinely 50 spreads were read for each animal. A mitotic index based on at least 500 cells was recorded. This index was calculated by scoring the number of cells in mitosis per 500 cells on each slide read.

Result : The results of the assay are summarized in the following table.

Group size	Frequency of aberrations		% cells 1+ 2+ aberrations		Mitotic index
	Str*	Num**			
-ve control (saline)					
10 (male)	0.002	0.018	0.2	0	3.8
9 (female)	>0.007	0.047	0.7	0.2	2.6
+ve control (TEM @1.0 mg/kg)					
10 (male)	>0.791*	0.032	21.7**	12.8**	2.6
9 (female)	>1.211**	0.048	26.6**	18.8**	1.6
API 78-5 (0.5 g/kg/day)					
8 (male)	0.008	0.030	0.5	0.3	2.4
9 (female)	0.004	0.011	ss0.4	0	4.0
API 78-5 (1.67 g/kg/day)					
9 (male)	0.004	0.018	0.4	0	2.0
10 (female)	>0.008	0.028	0.8	0.2	4.3
API (5 g/kg/day)					
10 (male)	0.002	0.008	0.2	0	6.9
10 (female)	0.006	0.006	ss0.6	0	4.5

It was concluded that the aberration frequency of groups treated with test material did not differ from that of the negative controls at any tested dose. Furthermore, there was no increase in the percentage of cells showing one or more structural or numerical aberrations. Therefore it was concluded that the test material was negative in this assay.

Reliability : (1) valid without restriction
Although there is no statement relating to GLP compliance, the study was subjected to a QA audit. (9)

(9) American Petroleum Institute (1982)
Mutagenicity evaluation of API 78-5, 100 SUS/100 °F naphthenic oil.
API Med. Res. Publ. 29-32359

Genetic Toxicity – in vivo**Test Substance**

Category Chemical (CAS #):	Not available
Test Substance (CAS #):	Various paraffinic and naphthenic base oils
Test Substance Purity/Composition and Other Test Substance Comments :	No other information
Category Chemical Result Type :	Measured

Type : Cytogenetic assay
Species : Rat
Sex : Male/female
Strain : Sprague-Dawley
Route of admin. : Gavage
Exposure period : 5 days
Result : Negative
GLP : No
Test substance : Lubricating base oils (various)

Remark : Conaway et al published a summary of the results of cytogenetics assays that had been carried out on 5 naphthenic and 2 paraffinic base oils. A full description of the experimental protocol for one of the studies is given above for sample API 78-5. The results for all seven samples are summarized briefly here.

Result : The results tabulated in the publication are as follows:

Sample	Dose (mg/kg)	No. animals	No. cells	Aberrant cells (%)
Paraffinic oils				
<u>64 SUS</u>	Corn oil	8	400	4.3
	500	10	500	3.8
	1000	9	450	2
	2000	10	500	2.8
<u>133 SUS</u>	Corn oil	10	500	3
	500	8	400	1.3
	1000	10	500	2
	2000	10	500	1
<u>331 SUS</u>	Corn oil	10	500	4
	500	9	450	3.8

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	1000	8	450	5.6
	2000	10	500	7*
<u>485 SUS</u>	Corn oil	7	350	4
	500	9	450	4.9
	1000	8	400	4.3
	2000	7	350	5.7
<u>990 SUS</u>	Corn oil	8	400	1
	500	6	300	1.3
	1000	9	450	1.6
	2000	8	400	2.5
Naphthenic oils				
<u>80 SUS</u>	Saline	19	950	0.4
	500	17	850	0.4
	1670	19	950	0.6
	5000	20	1000	0.4
<u>2000 SUS</u>	Saline	19	950	0.7
	500	18	874	0.7
	1670	18	900	1.6
	5000	15	750	0.4
TEM	0.4-1.0			24.2-41.8*

* denotes significant by Wilcoxon rank test

Source : The data summarized by Conaway et al originated from an API program. The reports from which the data were summarized are:

API Report No

Paraffinic oils	.
64 SUS	28-31864
133 SUS	28-31868
331 SUS	28-31865
485 SUS	28-31866
990 SUS	28-31867
Naphthenic oils	
80 SUS	29-32359
2000 SUS	29-32360

Test substance : Two naphthenic and 5 paraffinic base stocks were tested. The characteristics of the samples tested are as follows:

Sample	Initial boiling point (° F)	Aromatics (%)	PNAs (%)
Paraffinic oils			
SUS at 100 °F			
64	536	10.2	0.4
133	639	13.8	0.7
331	636	28.1	3.0
485	572	27.8	4.1
990	515	31.9	4.8
Naphthenic oils			
SUS at 100 °F			
80	470	23.8	0.8
2000	611	37.7	4.5

Reliability : (1) valid without restriction

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- (78) Conaway, C. C., Schreiner, C. A. and Cragg, S. T. (1984)
Mutagenicity evaluation of petroleum hydrocarbons
In: Advances in modern experimental toxicology Volume VI:
Applied toxicology of hydrocarbons, pp 89-107.
Eds MacFarland et al., Princeton Scientific Publishers

Carcinogenicity**Test Substance**

Category Chemical (CAS #):	Not available
Test Substance (CAS #):	No CAS numbers available
Test Substance Purity/Composition and Other Test Substance Comments :	Lubricating base oils No other information
Category Chemical Result Type :	Measured

5.7 CARCINOGENICITY

Species : Mouse
Sex : Male/female
Route of admin. : Dermal
Exposure period : Up to 84 weeks
Frequency of treatm. : Once or twice weekly
Doses : Various
Control group : Yes, concurrent no treatment
Test substance : Distillate base oils

Remark : Numerous skin carcinogenicity studies have been carried out on lubricating base oils derived from distillates. Data from these studies have been summarized and reviewed elsewhere.
 No single study is summarized here but the general conclusions that may be drawn from the numerous studies are:
 Highly refined base oils are not skin carcinogens.
 Poorly refined or unrefined base oils are skin carcinogens.
 A good correlation exists between skin carcinogenic potential and level of DMSO extractables and polycyclic aromatic compounds present in the base oil.
 The degree of carcinogenicity is dependent on the level of polycyclic aromatic compounds present in the base oil.
 When applied repeatedly to the skin, carcinogenic base oils are

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associated only with skin tumors and not with an increase in systemic tumors.

There is a good correlation between skin carcinogenicity and Mutagenicity Index as determined in a modified Ames assay.

- (81) (23) (26) (80) (81) (101) (111)
CONCAWE (1997)
Lubricating oil basestocks
Product dossier No. 97/108
CONCAWE, Brussels
- (101) IARC (1984)
IARC Monographs on the evaluation of the carcinogenic risk of chemicals to humans, Volume 33: Polynuclear aromatic hydrocarbons, part 2, carbon blacks, mineral oils (lubricant base oils and derived products) and some nitroarenes.
International Agency for Research on Cancer, Lyon.
- (80) CONCAWE (1994)
The use of the dimethyl sulphoxide (DMSO) extract by the IP 346 method as an indicator of the carcinogenicity of lubricant base oils and distillate aromatic extracts.
CONCAWE Report No. 94/51
CONCAWE, Brussels.
- (23) Bingham, E. Trosset, R. P., Warshawsky, D. (1980)
Carcinogenic potential of petroleum hydrocarbons, a critical review of the literature.
J. Environmental Pathology and Toxicology, Vol 3, pp 483-563.
- (111) Roy, T.A., Johnson, S.W., Blackburn, G.R., and Mackerer, C.R. (1988)
Correlation of mutagenic and dermal carcinogenic activities of mineral oils with polycyclic aromatic compound content.
Fund. Appl. Toxicol. Vol 10, pp 466-476
- (26) Blackburn, G.R., Deitch, R.A., Schreiner, C.A., Mehlman, M. A. and Mackerer, C.R. (1984)
Estimation of the dermal carcinogenic activity of petroleum fractions using a modified Ames assay.
Cell Biol. and Toxicol. Vol 1, No 1, pp 67-80

Carcinogenicity**Test Substance**

Category Chemical (CAS #):	Not available																												
Test Substance (CAS #):	No CAS number available; A non-solvent refined, deasphalted, dewaxed residual paraffinic lubricant base oil																												
Test Substance Purity/Composition and Other Test Substance Comments :	<p>A non-solvent refined, deasphalted, dewaxed residual paraffinic lubricant base oil See specification information below</p> <p><u>TOTAL AND INDIVIDUAL PCA CONCENTRATIONS ON COMPLETION OF STUDY</u></p> <table border="1"> <thead> <tr> <th><u>Individual PCA</u></th> <th><u>mg/kg</u></th> </tr> </thead> <tbody> <tr> <td>Fluoranthene</td> <td>0.2</td> </tr> <tr> <td>Pyrene</td> <td>0.9</td> </tr> <tr> <td>Benz(a)anthracene</td> <td>0.3</td> </tr> <tr> <td>Chrysene/triphenylene</td> <td>2.5</td> </tr> <tr> <td>Benzo(a)fluoranthene</td> <td>1.0</td> </tr> <tr> <td>Benzo(e)pyrene</td> <td>1.6</td> </tr> <tr> <td>Benzo(a)pyrene</td> <td>0.1</td> </tr> <tr> <td>Perylene</td> <td>0.1</td> </tr> <tr> <td>Dibenz(a,j)anthracene</td> <td><0.1</td> </tr> <tr> <td>Dibenz(a,h)anthracene</td> <td><0.1</td> </tr> <tr> <td>Indeno(1,2,3-cd)pyrene</td> <td><0.1</td> </tr> <tr> <td>Benzo(ghi)perylene</td> <td><0.1</td> </tr> <tr> <td>Total PCA content (BP3 method)</td> <td>7.0% wt</td> </tr> </tbody> </table>	<u>Individual PCA</u>	<u>mg/kg</u>	Fluoranthene	0.2	Pyrene	0.9	Benz(a)anthracene	0.3	Chrysene/triphenylene	2.5	Benzo(a)fluoranthene	1.0	Benzo(e)pyrene	1.6	Benzo(a)pyrene	0.1	Perylene	0.1	Dibenz(a,j)anthracene	<0.1	Dibenz(a,h)anthracene	<0.1	Indeno(1,2,3-cd)pyrene	<0.1	Benzo(ghi)perylene	<0.1	Total PCA content (BP3 method)	7.0% wt
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Total PCA content (BP3 method)	7.0% wt																												
Category Chemical Result Type :	Measured																												

Species : Mouse
Sex : Female
Strain : CF No. 1
Route of admin. : Dermal
Exposure period : 18 months
Frequency of treatm. : Three times weekly
Doses : 0.1ml/application
Result : Negative
Control group : Yes
Year : 1991
GLP : No data
Test substance : Residual base oils (See below)

Method : 0.01 ml of undiluted test material was spread three times weekly over the shorn dorsal skin of a group of 50 female CF No.1 mice. A further two groups of 5 female mice underwent similar treatment and were killed after

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22 or 52 weeks.

The appearance and development (or regression) of superficial tissue masses was recorded weekly throughout the study, to enable calculation of the latency period of those subsequently diagnosed as being tumors.

A positive control group of 50 female mice was treated with an oil (N1) that had been shown in previous studies to be a skin carcinogen. The mice in the positive control group received the oil once a week for 22 weeks and then once every 14 days for a total of 78 weeks.

A group of 50 untreated female mice served as negative controls.

Result

: Minimal evidence of skin irritation was visible following treatment with the test materials.

No treatment-related effects were observed on clinical condition, body weight gain or mortality (NB survival rates for treated animals are not included in the report).

Changes recorded at post mortem were considered normal.

Histopathological examination of the skin of the treated mice provided no evidence of skin irritation and no tumors of epidermal origin were observed.

No cutaneous tumors were recorded in the group of untreated control mice (52% of animals survived to termination after 2 years)

The positive control group had skin reactions at the treatment site which included redness, scabbing, cracking and flaking; histopathological examination confirmed the presence of chronic inflammation (acanthosis, hyperkeratosis, ulcers, parakeratosis and scabs). In addition, skin reactions, principally at the margins of the treatment site were frequently recorded and were particularly seen during the first 22 weeks of treatment. These reactions typically included abrasions and ulceration. The severity of the lesions was such that many animals were killed on humane grounds; only 24% of animals survived to 78 weeks.

Histopathological examination of the skin revealed that over 78 weeks, 23 mice in the positive control group had 56 tumors of epidermal origin, of which 39 were benign (papillomas and keratoacanthomas) and 17 were malignant (squamous cell carcinomas and one single malignant basal cell tumor). The mean latency period was 37 weeks.

Test substance

: The test substance was described as:

"A non-solvent refined, deasphalted, dewaxed residual paraffinic lubricant base oil"

<u>Characteristic</u>	<u>Value</u>
Kinematic viscosity	
at 40 °C	1024 cSt
at 60 °C	266.6 cSt
at 100 °C	42.52 cSt
Density at 15 °C	0.9280 kg/l
Pour point	+3 °C
Flash point (COC)	315 °C
Refractive index	1.5142
Color (D1500)	8.0
Molecular weight (D2502)	660
Sulfur	1.7% wt
Aniline point	105.0 °C

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Volatiles 3 hrs at 13 °C	0.10%
Neutralization value	0.02 mg KOH/g
Viscosity gravity constant (D2140)	0.846
Refractivity intercept	1.0598
Molecular type (D2007)	
Saturates	46.3% wt
Aromatics	45.6% wt
Polars	8.0% wt
Carbon type (D2140)	
CA	15%
CN	19%
CP	66%

Total and individual PCA concentrations on completion of study

Individual PCA	mg/kg
Fluoranthene	0.2
Pyrene	0.9
Benz(a)anthracene	0.3
Chrysene/triphenylene	2.5
Benzofluoroanthenes	1.0
Benzo(e)pyrene	1.6
Benzo(a)pyrene	0.1
Perylene	0.1
Dibenz(a,j)anthracene	<0.1
Dibenz(a,h)anthracene	<0.1
Indeno(1,2,3-cd)pyrene	<0.1
Benzo(ghi)perylene	<0.1
Total PCA content (BP3 method)	7.0% wt

Reliability

: (4) not assignable

This report is a summary report and as a consequence does not provide full experimental details, but does provide sufficient information for a conclusion to be made on the skin carcinogenic potential of a non-solvent refined residual paraffinic base oil.

(103)

King, D. J. (1991)
1156, 1157 and 1158: 2-Year skin painting study.
Toxicology report 25-90-0275
BP Group Occupational Health Centre

(103)

Carcinogenicity**Test Substance**

Category Chemical (CAS #):	Not available
Test Substance (CAS #):	No CAS number available; Canthus 210; deasphalted, dewaxed residual oil
Test Substance Purity/Composition and Other Test Substance Comments :	Canthus 210 No other information
Category Chemical Result Type :	Measured

Species	: Mouse
Sex	: Male
Strain	: C3H
Route of admin.	: Dermal
Frequency of treatm.	: 3 times weekly
Doses	: 25 µl per application
Result	: Negative
Control group	: Yes
GLP	: No data
Test substance	: Canthus 210 a Deasphalted, dewaxed, residual oil
Method	: The summary states that the design of the study was similar to other conventional skin painting studies in mice. The test material was applied undiluted in 25 µl aliquots to the clipped dorsal back regions of 50 male C3H/HeJ mice, three times weekly. At each treatment period, the dorsal skin was examined for the presence of papillomas/carcinomas, mined daily for any clinical signs of ill health. Treatment continued for 24 months. A complete necropsy was conducted at the time of sacrifice. In this study, Primol 185, a medicinal grade white mineral oil was applied undiluted and served as the negative control. Heavy Clarified Oil (HCO) was applied as a 10% solution in Primol 185, and served as the positive control.
Result	: None of the animals treated with the test material or the negative control material developed skin tumors, or any other tumors considered treatment-related, over the course of the study. The positive control material, 10% HCO, responded as anticipated, producing squamous cell carcinomas in 47 of 50 treated animals.
Reliability	: (4) not assignable

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The information given is based on a summary of the study and hence it is not possible to assign reliability to the study. Nevertheless, the data provide useful information on the carcinogenic potential of residual base oils.

(87)

Exxon
REHD (MR.32DO.84)

(87)

Carcinogenicity**Test Substance**

Category Chemical (CAS #):	Not available
Test Substance (CAS #):	No CAS number available; White oil
Test Substance Purity/Composition and Other Test Substance Comments :	70 cSt white oil.
Category Chemical Result Type :	Measured

Species : Rat
Sex : Male/female
Strain : Fischer 344
Route of admin. : Oral feed
Exposure period : 2 years
Frequency of treatm. : Daily in the diet
Doses : 60, 120, 240 and 1200 mg/kg/day
Result : Negative
Control group : Yes
Method : OECD Guide-line 453 "Combined Chronic Toxicity/Carcinogenicity Studies"
Year : 2001
GLP : Yes
Test substance : White oil

Remark : This study is a study that was conducted according to OECD guidelines. It is not described in full in this summary since it is not one of the SIDS base set requirements.

Result : Survival was unaffected by exposure to the test material. There were no treatment related clinical signs, or any effects on body weight, food consumption, food conversion efficiency or ophthalmology. Furthermore, there was no treatment related effects on the hematological, serum chemistry or urinalysis parameters that were measured. At gross necropsy, there were no treatment-related gross observations and there were no treatment-related neoplastic changes.

Test substance : The test material is a 70 cSt white oil with an average molecular weight of 485.

Reliability : (1) valid without restriction

(96)

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(96) ExxonMobil (2001)
Combined chronic toxicity/carcinogenicity study of white oil
in Fischer 344 rats. Test substance 70cSt White oil.
Study performed for CONCAWE
Project No. 105970
Exxon Biomedical Sciences Inc. New Jersey July 11, 2001

Carcinogenicity**Test Substance**

Category Chemical (CAS #):	Not available
Test Substance (CAS #):	No CAS number available; 8 highly refined white oils
Test Substance Purity/Composition and Other Test Substance Comments :	Eight commercially available liquid paraffins (highly refined white oils) from eight member companies of the Japan Liquid Paraffin Industry. See specifications below No other information
Category Chemical Result Type :	Measured

Species : Rat
Sex : Male/female
Strain : Fischer 344
Route of admin. : Oral feed
Exposure period : 104 weeks
Frequency of treatm. : Continuous in the feed
Doses : 2.5 and 5% in the diet
Result : Negative
Control group : Yes
Year : 1997

Result : There were slight increases in body weights in both sexes of the 5% group (5% for males and 2.7% for females) at week 104. Food consumption was also increased in the 5% groups (11% for males and 8% for females total increase at week 104). However, no significant treatment-related differences between the control and treated groups were observed for clinical signs, mortality or hematological findings.
 In the 5% group, absolute liver and kidney weights were increased in males and absolute and relative submaxillary gland weight were reduced in females. Absolute and relative weights of heart and spleen were unaffected by treatment.
 The percentage increases/decreases in the 5% group were:

<u>Organ</u>	<u>Absolute</u>	<u>Relative</u>
Female		
Submaxillary gland	3% decrease	1.7% decrease
Male		
Liver	8.4% increase	not different

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Kidney (R)	14.9% increase	not different
Kidney (L)	9.9% increase	not different

In the 5% male group, the increased absolute organ weights were attributed to the slight increases in body weights.

A variety of tumors developed in all groups, including the control group. However, all the neoplastic lesions were histologically similar to those known to occur spontaneously in F344 rats, and no statistically significant increase in the incidence of any tumor type was found for either sex in the treated groups.

Granulomatous inflammation in the mesenteric lymph nodes, considered to be a reaction to paraffin absorption, was observed with similar incidence and severity in both sexes of the 2.5 and 5% groups.

The authors concluded that under the present experimental conditions, the high dose, about 2000-200,000 times higher than the current temporary acceptable daily intake, did not have any carcinogenic potential in F344 rats. Furthermore, the granulomatous inflammation observed in the mesenteric lymph nodes was not associated with any development of neoplastic lesions.

Test substance : The test material was composed of equal quantities of eight different commercially available liquid paraffins (highly refined white oils) obtained from eight member companies of the Japan Liquid Paraffin Industry. Each of the eight liquid paraffins complied with the requirements of the Japanese food additive and Japanese Pharmacopoeia standards. 5 of the component material had been derived from petroleum by acid treatment and the other eight had been derived by hydrotreatment.

The physical properties of a sample of the composite test material were determined by CONCAWE and were as follows:

Viscosity at 40°C	0.871
Viscosity at 100 °C	8.68
Ratio of naphthenic/paraffinic hydrocarbon	35/65
Average molecular weight	475
Carbon No. at 5% boiling point	25

Reliability : (2) valid with restrictions
Although the experimental details are not provided here, the information is nevertheless useful in establishing the lack of carcinogenicity by the oral route.

(119)

(119) Shoda, T, Toyoda, K, Uneyama, C., Takada, K. and Takahashi, M. (1997)
Lack of carcinogenicity of medium-viscosity liquid paraffin given in the diet to F344 rats.
Food and Chemical Toxicology Vol. 35, pages 1181-1190

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High Production Volume Information System (HPVIS)

Reproductive Toxicity

TEST SUBSTANCE

Category Chemical:	Select a Chemical White mineral oil (petroleum) CAS No. 8042-47-5
Test Substance:	Select a Chemical Test substance was Stock 461 (80" white oil). Its viscosity was a nominal value of 80 SUS.
Test Substance Purity/Composition and Other Test Substance Comments:	Lubricant Oil Basestocks are complex mixture of hydrocarbons rather than single compounds with identifiable purity.

Category Chemical Result Type : Measured

Unable to Measure or Estimate Justification :

METHOD

Route of Administration: Dermal

Other Route of Administration:

Type of Exposure:

Species: Rat

Other Species:

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Mammalian Strain:	Sprague-Dawley
Other Strain:	
Gender:	Male and female
Number of Animals per Dose:	20 per sex
Concentration:	100%
Dose:	0 (untreated controls), 0 (sham-exposed controls), 125, 500, and 2,000 mg/kg/day
Year Study Performed :	1985
Method/Guideline Followed:	Study was similar to OECD Guideline 415 (One-Generation Reproduction Toxicity Study). Differences included the use of 2,000 mg/kg rather than the limit dose of 1,000 mg/kg and administration of doses 5 times per week during much of the study rather than 7 times per week.
GLP:	Study was conducted in accordance with EPA Good Laboratory Practices.
Exposure Period:	Approximately 10 weeks pre mating, 3 weeks for mating period, 3 weeks gestation, and 3 weeks postpartum. Dams were sacrificed on day 21 of lactation.
Frequency of Treatment:	Females: 5 days/wk during pre mating and mating Daily on gestation days 0-20 5 days/wk during postpartum period Males were split into two subgroups within each dose group. Half of the males were dosed 5 days/wk during pre mating and mating. These males were sacrificed after mating. Half of the males were dosed 5 days/wk during pre mating, mating, and post-mating until sacrifice within 2 weeks of the last sacrifice of pups (i.e., during postpartum weeks 5 and 6).
Post-Exposure Period:	None
Method/Guideline and Test Condition Remarks:	Stock 461 was applied dermally with a 1 cc syringe to the clipped intact dorsal skin of the rats. The application sites were not covered; therefore rats were fitted with Elizabethan collars to minimize ingestion of the test substance.

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During the mating period, the test material remained on the animals for a minimum of 4 hours. Excess material was then removed with a gauze pad before cohabitation to minimize ingestion from preening during cohabitation. Untreated controls were not clipped to remove hair or collared. Sham-exposed controls were clipped, collared, and received mock dosing with a syringe, but not test material was applied.

For maternal females, body weights were measured weekly during premating and at intervals during gestation and lactation. Food consumption was measured at intervals during premating and gestation. Females that did not deliver were sacrificed on GD 25 and necropsied. Females that delivered were sacrificed on postpartum day 21 and necropsied. At necropsy, ovaries and uterus were examined grossly, weighed, and preserved. The number of implantations and any remarkable findings were recorded. In addition, the estrus cycle was followed 5 days/wk in 5 females in the untreated controls, sham-exposed controls, and rats dosed with 2,000 mg/kg for 2 weeks prior to mating and during mating until breeding activity began.

All offspring were observed individually during the postpartum period until sacrifice for body weight, behavior, appearance. All viable neonates were examined as early as possible for sex and external anomalies. Litters of sufficient size were culled to 8 pups on postpartum day 4 (4/sex if possible). The number of open eyelids for each pup was recorded on postpartum day 10 and continued until both eyelids were open. All pups were tested for surface righting reflex on postpartum day 14. Pups were weaned on postpartum days 21 and then sacrificed and necropsied with gross observations on postpartum day 28.

Data from the gestation and postpartum phases were analyzed with ANOVA followed by group comparisons using Fisher's Exact or Dunnett's Test.

Pre-Mating Exposure / Males : 10 weeks

Pre-Mating Exposure / Females: 10 weeks

TEST RESULTS

Concentration (LOAEL/LOAEC/NOAEL/NOAEC)

Type	Population:	Value Description:	Value or Lower Concentration:	Upper Concentration:	Units:
NOAEL	Pregnant females	=	2,000		Mg/kg
NOAEL	offspring	=	2,000		Mg/kg

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<p>Results:</p>	<p>The estrus cycle was not affected by treatment in the limited number of animals examined. The fertility index among those females was 100% in the sham-exposed controls and 2,000 mg/kg/day groups and 80% in the untreated controls due to one female with an abnormal estrus cycle.</p> <p>During gestation, erythema, scabs, and flaking were observed on the skin of nearly all animals treated with Stock 461. Similar findings were reported during lactation. Body weight gain during the gestation and postpartum periods appeared normal. Mean body weight of females in the 2,000 mg/kg/day group were significantly lower than the untreated control during the first half of gestation, but were similar to mean weights for the sham-exposed controls.</p> <p>No effects of treatment with Stock 461 were noted at necropsies of dams. No effects were seen in dams on the percentage of pregnant females, duration of gestation, or number of implantation sites per dam. No adverse effects were noted among the litters for Liveborn Index, Day 4 Survival index, or Day 21 Survival Index. Mean pup weight was not affected by treatment during postpartum days 0 to 28. Eyelid dysjunction and surface righting reflex were not affected by treatment. Observations of offspring at birth and at necropsy were not affected by treatment.</p>
<p>Results Remarks:</p>	
<p>Conclusion:</p>	<p>The study director concluded that dermal application of Stock 461 at doses up to 2,000 mg/kg/day beginning 10 weeks before mating did not have any adverse effects on reproductive performance of female rats or on the <i>in utero</i> and postnatal survival or development of offspring.</p> <p>Note that although histopathology was not available in this study with Stock 461, no treatment-related effects were seen in testes or ovaries during 13-week dermal studies with other LOBs at comparable doses (API, 2010).</p>
<p>RELIABILITY/DATA QUALITY</p>	
<p>Reliability:</p>	<p>2 – Reliable with restrictions</p>
<p>Reliability Remarks:</p>	<p>Study was well designed and conducted. However, the testing laboratory was closed before microscopic evaluation of tissues was performed and a pathology report was not prepared on histopathology, limiting the utility of the study.</p>
<p>Key Study Sponsor Indicator:</p>	<p>Stock 461 rat reproduction study</p>

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REFERENCE

Reference:

American Petroleum Institute (API). 2010. Summary of Mobil Study 40921-A (Stock 461 rat reproduction study) and Mobil 40921-B (Stock 461 rat subchronic study). API, Washington, DC. Dated December 2, 2010.

Mobil. 1987. Stock 461 rat reproduction study. Interim (biophase) report on Stock 461 rat reproduction study. Study number 40921A. Mobil Environmental and Health Science Laboratory, Princeton, NJ.

Reproductive Toxicity

Test Substance

Category Chemical (CAS #):	64742-54-7
Test Substance (CAS #):	64742-54-7; hydrotreated heavy paraffinic oil; Chevron 100 neutral oil
Test Substance Purity/Composition and Other Test Substance Comments :	Chevron 100 neutral (refined) No other information
Category Chemical Result Type :	Measured

Type : One generation study
Species : Rat
Sex : Male/female
Strain : Sprague-Dawley
Route of admin. : Gavage
Frequency of treatm. : Daily
Doses : 1.15 ml/kg
Control group : No
Method : OECD Guideline 421, Reproductive/Developmental Toxicity screening test
Year : 1995
GLP : Yes
Test substance : Chevron 100 neutral (refined) CAS 64742-54-7

Method : The method used was as described in OECD guideline 421.

The base oil was administered by gavage at a dose of 1.15 ml/kg (bw) to a group of 12 male and 12 female Sprague Dawley rats. Rats designated F0 animals were dosed for a minimum of 14 days prior to mating. Dosing was continued after mating until a total dosing period of 30 days had elapsed for males and until day 4 of lactation for females (39 days). The animals were observed twice daily for appearance, behavior, morbidity and mortality. Males and females were also observed during dosing and for one hour thereafter.

Male F0 body weights were recorded weekly. Female F0 body weights were also recorded weekly until evidence of mating was observed and then on gestation days 0, 7, 14 and 20 and on lactation days 1 and 4. Food consumption was also recorded for F0 both sexes.

Animals were paired on a 1:1 basis. Positive evidence of mating was confirmed either by the presence of sperm in a vaginal smear or a vaginal plug. The day when evidence of mating was identified was termed Day 0

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of gestation.

The following Fertility indices were calculated:

- Female mating index
- Male mating index
- Female fertility index
- Male fertility index

All females were allowed to deliver their young naturally and rear them to post-natal day 4. Females were observed twice daily during the period of expected parturition for initiation and completion of parturition and for signs of dystocia. After parturition, litters were sexed and examined for evidence of gross malformations, numbers of stillborn and live pups.

Litters were examined daily and each pup received a detailed physical examination on days 1 and 4 of lactation. Any abnormalities were recorded.

The live litter size and viability index were calculated.

All surviving pups were necropsied on post-natal day 4.

A complete gross examination was made on all animals at necropsy.

Selected organs of parental animals were weighed and a wide range of tissues was fixed for subsequent histopathological examination.

Result : Only the results for the base oil control group are reported below.

There were no clinical findings and growth rates and food consumption values were normal.

Fertility indices and mating indices for males and females were both 100%.

At necropsy, there were no consistent findings and the animals were considered to be normal.

Organ weights and histopathology was considered normal.

Reliability : (2) valid with restrictions

The study was on an oil additive in base oil at two concentrations. The base oil alone was used as the control. Therefore, no control was available with which to compare the study control group. However, since all the recorded values were within normal limits, it could be concluded that the base oil was without effect.

(128) WIL Research Laboratories Inc. (1995)
An oral reproduction/developmental toxicity screening study
of **** in finished oil in rats.
Laboratory Study No. WIL-187007

(128)

Reproductive Toxicity

Test Substance

Category Chemical (CAS #):	8012-95-1
Test Substance (CAS #):	8012-95-1; White oil
Test Substance Purity/Composition and Other Test Substance Comments :	White oil No other information available
Category Chemical Result Type :	Measured

Type : One generation study
Species : Rat
Sex : Male/female
Strain : Sprague-Dawley
Route of admin. : Gavage
Exposure period : 13 weeks prior to mating
Frequency of treatm. : 5 times weekly
Premating exposure period
 Male : 13 weeks
 Female : 13 weeks
Duration of test : One generation after 13 weeks dosing
No. of generation studies : 1
Doses : 5 ml/kg
Control group : No
Year : 1987
GLP : No data
Test substance : White oil CAS 8012-95-1

Method : 72 female and 36 male Sprague-Dawley rats were given white oil at a dose of 5 ml/kg, 5 days a week for 13 weeks. After this time each of the males was housed with 2 females for 10 consecutive nights, or until mating was confirmed by the appearance of a copulatory plug or by the presence of sperm in a vaginal rinse.
 The mated females were maintained without further dosing through gestation and lactation to post-partum day 21.
 Detailed maternal physical examinations and body weight measurements were made on days 0, 7, 14 and 21 of gestation and on days 0, 4, 14 and 21 of lactation.
 All dams and surviving litters were sacrificed and grossly examined on day

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Remark : 21 of lactation. Each of the offspring was examined for external malformations. All pups were then sacrificed, necropsied and subjected to visceral organ and brain examination. Pups which died spontaneously were also necropsied unless this was precluded by cannibalism or aut

: White oil was used as solvent control in a study to determine the effects of two EDS coal liquids in a 13 week subchronic a single generation reproduction study. There were three dose groups and a control group for each test material in this study. The information in this robust summary relates only to the white oil control groups (one for each of the test materials) and NOT to the groups exposed to EDS coal liquids.

Result : The CAS# for the material that was used in this study is not included in the Lubricating Base Stocks category. However, because white oils are so highly purified, toxicologically and compositionally they are all very similar. Therefore, the Testing Group thinks the results on CAS # 8012-95-1 are applicable to the highly refined base oils that are included in this category.

: The data for the two control groups are summarized below.

<u>Parameter</u>	<u>Control 1</u>	<u>Control 2</u>
Impregnation frequency	80.8%	80.9
Gestation	22.6 days	22.6
Pups delivered	11.7	11.1
Live births	11.2	10.7
Survival at day 4	10.5	9.6
Survival at day 14	10.2	9.3
Survival at day 21	10.1	9.3
Offspring body weights		
Day 0 lactation	6.7	6.9
Day 4 lactation	9.3	9.9
Day 14 lactation	26.9	27.1
Day 21 lactation	43.2	46.7

No unusual behavior was reported during the gestation period for either of the control groups. The general condition of offspring and dams was good through weaning.

Gross observations of pups and dams were generally unremarkable. In one base oil group, 3 malformed pups were found in 2 litters. Two of the malformed pups had syndactyly and renal agenesis and one of these also exhibited agnathia. The third pup had a small eye.

In the other control group, four malformed pups were found in 4 litters. Two of the pups had tail abnormalities, one had a depression in the sternum and the fourth had a short snout.

The authors comment that a similar spectrum of malformations in Sprague-Dawley rats from the same supplier has been reported elsewhere. The authors also comment that this spectrum of malformations can occur spontaneously in the Sprague-Dawley rat and are not regarded as treatment-related.

Test substance : The test substance is not listed in the US HPV program. Nevertheless, it is a white oil and the results are directly applicable to other

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Reliability

highly refined white oils.
: (2) valid with restrictions
Not all the raw data are presented in this publication. However, the data are useful in determining that white oils do not cause effects on reproduction after prior exposure for 13 weeks.

(105)

(105)
McKee, R. H., Plutnick, R. T. and Traul, K. A. (1987)
Assessment of the potential reproductive and subchronic
toxicity of EDS coal liquids in Sprague-Dawley rats.
Toxicology Vol 46, pp 267-280

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High Production Volume Information System (HPVIS)

DEVELOPMENTAL TOXICITY/TERATOGENICITY

TEST SUBSTANCE

Category Chemical:	8042-47-5
Test Substance:	8042-47-5 ; Stock 461; White mineral oil, petroleum (80")
Test Substance Purity/Composition and Other Test Substance Comments:	Stock 461 (CRU 85018) Witco Chemical Co. Viscosity was a nominal value of 80 SUS. No other information
Category Chemical Result Type :	Measured
Unable to Measure or Estimate Justification :	
METHOD	
Route of Administration:	Dermal (non occluded), inhalation, and oral gavage
Other Route of Administration:	
Type of Exposure:	Teratology
Species:	Rat
Other Species:	None
Mammalian Strain:	Sprague-Dawley
Other Strain:	None
Gender:	Female

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Number of Animals per Dose:	20
Concentration:	100%
Dose:	0 (sham-treated control groups for each route), 2,000 mg/kg/day dermally, 5,000 mg/kg/day orally, and 1,000 mg/m ³ aerosol for 6 hr/day by inhalation
Year Study Performed :	1985
Method/Guideline Followed:	Other; similar to guideline study, but dosing period is only gestation days 6-19
GLP:	Study was conducted in accordance with EPA Good Laboratory Practices.
Exposure Period:	Gestation days 6 – 19
Frequency of Treatment:	Daily
Post-Exposure Period:	None
Method/Guideline and Test Condition Remarks:	<p>Prior to the initiation of dosing with the test material, females were placed with males. Once mating occurred, the individual females were randomly assigned to a treatment group and dosing began for that animal. Doses for each route were considered the maximal practical doses that could be used for that route.</p> <p>For dermal dosing, Stock 461 was applied daily to the clipped, intact dorsal skin of the rats at 2000 mg/kg/day. The test substance was spread evenly on the skin with the tip of the syringe. and the sites were left uncovered. Rats were fitted with Elizabethan collars to minimize ingestion. Control animals were treated similarly, but without dosing of test material.</p> <p>For inhalation exposures, rats were exposed for 6 hours daily on GD 6-19 to 1,000 mg/m³ of aerosolized Stock 461. Exposures were whole-body. Mass median aerodynamic diameter was 1.2 µm with a geometric standard deviation of 1.8. The control group received sham exposures.</p> <p>For oral dosing, 5,000 mg/kg was given by gavage daily by use of a 3 mL syringe fitted with a 16-gauge gavage needle. Control animals were gavaged with tap water.</p> <p>Each female was observed daily for clinical signs. Body weights were measured on GD 0, 6, 8, 10, 13, 16, 18, and 20. Individual food consumption was measured for 7 successive intervals during gestation. Each female was sacrificed on GD 20 and necropsied. Aortic blood was sampled for analysis of alanine aminotransferase, albumin, alkaline phosphatase, aspartate aminotransferase, bilirubin, calcium, chloride, cholesterol, creatinine, globulin, glucose, iron, inorganic phosphorus, lactate dehydrogenase, potassium, sodium, total protein, triglycerides, urea nitrogen, and uric acid. Thoracic and abdominal organs were examined grossly. Ovaries and uterus were excised and examined grossly. The number of corpora lutea per ovary and the weight of the gravid uterus were recorded. In the uterus, the number and location of implantations, early and late resorptions, and live and dead fetuses were recorded.</p> <p>Each fetus was gendered, weighed and grossly examined for anomalies, malformations and variations.</p>

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The following definitions and terminology were used in describing fetal findings:

- 1) Anomaly: Any deviation (malformation or variation) from "normal."
- 2) Malformation: A permanent structural deviation which generally is incompatible with, or severely detrimental to, normal postnatal survival or development. Absence structures which should have been present, as well as deviations in tail development, are also classified as malformations.
- 3) Variation: A variation is a divergence beyond the usual range of structural constitution. It has an indeterminate effect on health and generally has no effect on survival.

Approximately half of the fetuses were used for examination of soft tissues (viscera) using a modification of Wilson's technique. The other half were differentially stained for cartilage and bone, cleared, and examined for skeletal abnormalities.

Statistical analysis: Data from the maternal biophase, caesarean section, and fetal examinations were evaluated by ANOVA followed by group comparisons using Fisher's Exact or Dunnett's Test.

TEST RESULTS

Concentration (LOAEL/LOAEC/NOAEL/NOAEC)*

Type	Population:	Value Description:	Value or Lower Concentration:	Upper Concentration:	Units:
NOAEL (dermal)	Maternal- Rat	=	2000		mg/kg/day
NOAEL (dermal)	Offspring (F1) - Rat	=	2000		mg/kg/day
NOAEL (oral)	Maternal- Rat	=	5,000		mg/kg/day
NOAEL (oral)	Offspring (F1) - Rat	=	5,000		mg/kg/day
NOAEC (inhalation)	Maternal- Rat	=	1,000		mg/m ³ /6 hr per day
NOAEC (inhalation)	Offspring (F1) - Rat	=	1,000		mg/m ³ /6 hr per day

*Determined by reviewer

Results Remarks:

Red nasal exudate and chromodacryonhea were observed in all treatment groups, but more commonly in the dermally exposed animals. These observations are common in animals that are collared. Alopecia was observed in all of the experimental groups.

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Erythema and flaking of the treated skin was seen in all but one female dosed dermally. Perianal staining was observed in all females treated orally and appeared to result from a clear oily anal discharge within a few hours of dosing.

The mean body weight of the pregnant females from all of the groups increased throughout the study, following what would be regarded as a normal curve of weight gain. The dermal groups consumed more food ($p < 0.05$) than either of the other groups during the treatment period (gestation days 6-19). There were no remarkable intragroup differences in daily food consumption.

Due to their low incidence or their co-appearance in control groups, necropsy observations were not considered to be related to exposures to the test material or to the mode of administration. The overall incidence of pregnancy for the study was 94% (115/122). At least one resorption per litter was observed in 55% of Stock 461 dermal litters, 57% of dermal control litters, 55% of Stock 461 inhalation litters, 53% of inhalation control litters, 68% of Stock 461 oral gavage litters, and 56% oral gavage control litters. Only one dam (dermal control) completely resorbed the entire litter. None of the parameters evaluated appeared to be affected by the mode of administration and/or exposure to Stock 461.

Neither fetal body weights nor crown-rump lengths were affected by the mode of administration or by exposure to Stock 461.

Due to their low incidence or their occurrence in control group fetuses, external fetal abnormalities, or fetal skeletal/visceral malformations observed were not considered to be related to the test material or to the route of administration.

Conclusion:

Determined by the reviewer:

The maternal NOAEL for dermal exposure to Stock 141 during GD 6-19 was determined to be 2000 mg/kg/day (LOAEL= not identified >2000 mg/kg/day)

The maternal NOAEL for oral exposure to Stock 141 during GD 6-19 was determined to be 5000 mg/kg/day (LOAEL= not identified >5000 mg/kg/day)

The maternal NOAEC for inhalation exposure to Stock 141 during GD 6-19 was determined to be 1,000 mg/m³ for 6 hrs/day (LOAEC= not identified >1,000 mg/m³ for 6 hrs/day)

The developmental NOAEL for dermal exposure to Stock 141 during GD 6-19 was determined to be 2000 mg/kg/day (LOAEL= not identified >2000 mg/kg/day)

The developmental NOAEL for oral exposure to Stock 141 during GD 6-19 was determined to be 5000 mg/kg/day (LOAEL= not identified >5000 mg/kg/day)

The developmental NOAEC for inhalation exposure to Stock 141 during GD 6-19 was determined to be 1,000 mg/m³ for 6 hrs/day (LOAEC= not identified >1,000 mg/m³ for 6 hrs/day)

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There were no effects observed at the highest doses tested and there was no evidence of abnormal development observed during external, skeletal, and visceral evaluations of rat fetuses from pregnant dams exposed to Stock 141.

There was slight dermal irritation in treated dams at the site of dermal dosing and an oily anal discharge in animals treated orally.

RELIABILITY/DATA QUALITY

Reliability: 1 – Reliable without restrictions

Reliability Remarks: Similar to guideline study but difference in exposure period; sufficient experimental detail

Key Study Sponsor Indicator: Key

REFERENCE

Reference: Stock 461 rat teratology study. Final report on study 40922. Mobil Environmental and Health Science Laboratory, Princeton, NJ. 1987.

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High Production Volume Information System (HPVIS)

DEVELOPMENTAL TOXICITY/TERATOGENICITY

TEST SUBSTANCE

Category Chemical:	64742-65-0
Test Substance:	64742-65-0; Stock 141; Distillates, petroleum, solvent-dewaxed heavy paraffinic (CRU 84120) Its viscosity was ~102 SUS at 100°F and 40 SUS at 210°F
Test Substance Purity/Composition and Other Test Substance Comments:	Stock 141 (CRU No. 84120) No other information
Category Chemical Result Type :	Measured
Unable to Measure or Estimate Justification :	
METHOD	
Route of Administration:	Dermal, non-occluded
Other Route of Administration:	
Type of Exposure:	Developmental toxicity screen
Species:	Rat
Other Species:	Not applicable
Mammalian Strain:	Sprague-Dawley (Charles River, Kingston, NY)
Other Strain:	Not applicable
Gender:	Females, presumed pregnant (non treated males used for mating)

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Number of Animals per Dose:	15 presumed-pregnant females at and 2000 mg/kg/day 10 presumed pregnant females at 125 and 500 mg/kg/day
Concentration:	
Dose:	0 (sham-treated), 125, 500 and 2000 mg/kg/day
Year Study Performed :	1986
Method/Guideline Followed:	Similar to OECD 414 (Prenatal Developmental Toxicity Study). Main difference was that fewer females were used (10/group versus 20), and high dose was twice as high as the OECD limit dose
GLP:	No information
Exposure Period:	GD 0-19
Frequency of Treatment:	Once per day
Post-Exposure Period:	None
Method/Guideline and Test Condition Remarks:	<p>The study was designed to obtain data on the influence of Stock 141 on parameters of reproductive performance during gestation (implantation, litter size) and viability and development of the embryo/fetus. The study was also designed to include clinical chemistry analyses of maternal sera, and residue analyses of Stock141 in maternal blood, placentae and fetuses.</p> <p>Prior to the initiation of dosing with the test material, females were placed with untreated males (approximate 1:1 ratio). Once mating occurred and confirmed by detection of a vaginal plug (<u>in situ</u> or expelled), the individual, presumed pregnant females were randomly assigned to eight treatment groups and dosing began for that animal. The treatment groups and time exposure periods were as follows, where designation as GD 0 followed detection of a vaginal plug, and spermatozoa in the vaginal lavage fluid:</p> <ol style="list-style-type: none"> 3. Sham control (0 mg/kg/day) – GD 0-19 – 10 animals 4. Stock 141 125 mg/kg/day – GD 0-19 – 15 animals 5. Stock 141 500 mg/kg/day – GD 0-19 – 15 animals 6. Stock 141 2000 mg/kg/day – GD 0-19 – 10 animals 7. Radio-labeled Stock 141 2000 mg/kg/day – GD 1-18 – 5 animals (residue study group) <p>The exposure levels were based on results of a 13 week study previously conducted on the same material.</p> <p><u>Developmental study (Groups 1-4):</u> The test material was administered to groups 2-4 on GD 0-19. Hair was clipped from the dorsal trunk of each animal on GD 0, and once weekly during the study. Each treatment day, animals were dosed by even application of the test material to their shaved backs, using the tip of a syringe. The test material dose, calculated from each rat's most</p>

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recent body weight, was measured by weight. Rats were fitted with Elizabethan collars to minimize ingestion of test material. Controls were handled in the same manner, minus application of the test material. Control animals were clipped and collared and the intact dorsal skin of each rat was stroked with the tip of a syringe, but no test material was applied.

Each rat was observed at least once a day throughout gestation until sacrifice for 1) changes in appearance, behavior, and excretory function, and 2) signs of ill-health, mortality or abortion. All unusual findings were noted.

Individual body weights were recorded on days 0, 3, 6, 10, 13, 16, and 20 of gestation. Individual food consumption was measured during the study was calculated for GD intervals 0-3, 3-6, 6-10, 10-13, 13-16, and 16-20.

Each female was sacrificed by overexposure to ether on day 20 of its presumed gestation. The thoracic and abdominal cavities were exposed and all organs were examined grossly for evidence of pathosis. The ovaries and uterus of each rat were excised and examined grossly. The number of corpora lutea per ovary and the weight of the gravid uterus were recorded. The ovaries in nonpregnant females were grossly examined and then discarded. In the uterus, the number and location of implantations, early and late resorptions, and live and dead fetuses were recorded. An "early resorption" was defined as a reabsorbed dead conceptus in which it was not grossly evident that organogenesis had occurred; a "late resorption" was defined similarly but as one in which it was evident that organogenesis had occurred. A "live fetus" was defined as a fetus which responded to a stimulus, such as touch; a "dead fetus" did not respond to stimuli, nor did it demonstrate the autolysis characteristic of late resorptions. The uterus of each female that appeared non-gravid was pressed between two glass slides and examined grossly for evidence of implantation.

Blood samples were collected at the time of sacrifice from the aorta of each rat and serum was analyzed for alanine aminotransferase, albumin, alkaline phosphatase, aspartate aminotransferase, bilirubin, calcium, chloride, cholesterol, creatinine, globulin, glucose, lactate dehydrogenase, iron, inorganic phosphorus, potassium, sodium, sorbitol dehydrogenase, total protein, triglycerides, urea nitrogen, and uric acid. The globulin and albumin/globulin ratios were calculated.

Each fetus was gendered, weighed and grossly examined for anomalies, malformations and variations.

The following definitions and terminology were used in describing fetal findings:

- 4) Anomaly: Any deviation (malformation or variation) from "normal."
- 5) Malformation: A permanent structural deviation which generally is incompatible with, or severely detrimental to, normal postnatal survival or development. Absence structures which should have been present, as well as deviations in tail development, are also classified as malformations.
- 6) Variation: A variation is a divergence beyond the usual range of structural constitution. It has an indeterminate effect on health and generally has no effect on survival.

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After gross evaluation, fetuses in each litter were equally distributed into two groups, and preparation begun for either soft tissue or skeletal evaluations. Approximately half of the fetuses were randomly assigned for examination of soft tissues (visceral) and were fixed in Bouin's solution, using a modification of the Wilson's technique with sectioning by razor blade. The other half were fixed in 95% ethanol, macerated in potassium hydroxide, differentially stained for cartilage and bone, cleared in glycerin and examined for skeletal anomalies.

Residue Study (Group 5)

Female rats were clipped, collared and dosed as above except that Stock 141 was applied on gestation days 0-17., was administered on day 18 of gestation. From gestation day 0 through the morning of gestation day 17, the rats were housed in stainless steel cages with wire fronts and bottoms. Unlabelled Stock 141 was applied at a dose of 2000 mg/kg/day during this period. On gestation day 18, the animals were dosed with Stock 141, fortified with C-14 octosane (2000 mg/kg). C-14 octosane was chosen as a radioactive surrogate of Stock 141. since its physicochemical properties are similar to those of the majority of chemical components in Stock 141. From GD 18 to GD 20, the rats were housed in metabolism cages.

On GD 20, 48 hrs after the administration of the radio-fortified Stock 141, animals were sacrificed by overexposure to ether and the following samples were collected for residue analyses: maternal blood, placentae, and fetuses. Placental and fetal samples were homogenized before combustion and blood samples were combusted directly. C-14 and H-3 radioactivity present originally in combusted samples were determined. All samples were counted in duplicate or triplicate. Residual concentrations of Stock 141 in blood, placentae, and fetuses were obtained from the calculation of microgram equivalents of the test material in per gram of sample.

Statistical analysis:

Data from the maternal biophase, caesarean section, and gross fetal examinations were evaluated by ANOVA, followed by group comparisons using Fisher's Exact or Dunnett's Test. Data from skeletal and visceral examination were evaluated by ANOVA followed by group comparisons using Fisher's Exact Test. Statistical analyses of clinical chemistry data were performed separately on individual serum components using SAS procedures. First the F-test was employed to do an analysis of variance on the serum data obtained from the control and exposed groups. Next the Student-Newman-Keul's multiple comparison test was employed to identify the specific group subsets within the serum data sets identified as having nonrandom variance. Differences between control and treated groups were considered statistically significant only if the probability of the differences being due to chance was less than 5% ($p < 0.05$).

TEST RESULTS

Concentration (LOAEL/LOAEC/NOAEL/NOAEC)*

Type	Population:	Value Description:	Value or Lower	Upper	Units:
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			Concentration:	Concentration:	
NOAEL – Dermal	Maternal	=	2000		mg/kg/day
LOAEL- Dermal	Maternal		Not identified >2000		mg/kg/day
NOAEL - Dermal	Offspring (F1)	=	2000		mg/kg/day
LOAEL - Dermal	Offspring (F1)		Not identified >2000		mg/kg/day

***Determined by reviewer**

Results Remarks:

The animals used in the study were approximately 8 weeks old at receipt and approximately 11 weeks old at exposure initiation.

The red nasal exudate, chromodacryonhea, and lacrimations that were observed in control and Stock 141-exposed groups are common in animals that are collared. Also, neck lesions were observed in control and Stock 141-exposed groups, in spite of the protective soft rubber tubing that lines the inner surface of the cardboard collar. Scratches were observed on the backs of many animals at the time of the first clipping; in all but one instance, these scratches probably occurred during mating activity. Alopecia was observed in the control group as well as in all of the Stock 141-exposed groups. Due to its appearance in the control group, this finding is not considered to be test material-related. One animal from the mid-dose group developed scabs on its tail. This finding has been observed in other studies conducted at this laboratory. On the last day of study, one animal in the high-dose group had a decreased amount of stool. It was observed that the water valve in this animal's cage was clogged; because of this, the animal ate very little food (35 grams for this animal compared to 122 grams for the group mean) which resulted in a decreased amount of stool. Body weight and food consumption data for this animal are excluded from data calculations for gestation day 20.

Signs of dermal irritation were observed in all Stock 141-exposed groups. Erythema and flaking of skin at the site of administration were observed in all of the groups exposed to Stock 141. One isolated case of dermal edema was observed in the mid-dose group.

The mean body weight of the pregnant females from all of the groups increased throughout the study, following what would be regarded as a normal curve of weight gain. No statistically significant differences in mean body weight gain or in mean carcass weight were observed. The mean amounts of food consumed during gestation by each of the experimental groups were similar for all intervals during which food consumption measurements were made.

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Summary of Selected Maternal Weight Parameters

Dose (mg/kg/day)	0	125	500	2000
Body wt –final (gr)	396	381	379	375
GD 0-3 wt gain (gr)	17	15	13	14
GD 3-6 wt gain (gr)	13	11	11	10
GD 6-10 wt gain (gr)	20	20	17	20
GD 10-13 wt gain (gr)	17	17	19	17
GD 13-16 wt gain (gr)	24	22	23	23
GD 16-20 wt gain (gr)	66	62	64	58
GD 0-20 wt gain (gr)	156	147	146	141
Gravid uterus (gr)	79.8	79.3	80.4	75.3
Carcass (gr)	315.8	301.9	298.3	299.1
Net wt change from day 0 (e)	76.5	67.7	65.9	64.5

*residue group – data not collected

- a) Statistically different from control (p<0.05)
- b) Statistically different from control (p<0.01)
- c) = Carcass weight minus day 0 body wt.

At the time of necropsy, no findings attributable to exposure to the test material were observed.

Except for the number of dams per experimental group with resorptions, no statistically significant differences were observed for any of the reproductive parameters evaluated. Although fewer pregnant dams from the stock 141-exposed groups had at least one resorption, the overall percentages of resorptions/litter were comparable.

Summary of Mean Selected Reproduction Data

Dose (mg/kg/day)	0	125	500	2000
Implantation sites – total	241	157	156	207
Implantation sites – mean	16.1	15.7	15.6	14.8
Preimplantation loss (%)	6.8	8.1	7.9	8.1
Viable fetuses	225	151	148	192
Litter size (e)	15.0	15.1	14.8	13.7
Viable male fetuses (%)	52	45	57	53

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Resorptions (mean)	1.1	0.8	0.8	1.1
Resorptions (mean %)	6.7	4.0	5.1	7.7
Dams with resorptions (%)	97	40a	50	57

- a) Statistically different from control (p<0.05)
b) Statistically different from control (p<0.01)
c) Number of viable fetuses/number of litters evaluated.

Statistically significant differences between the data from control and treated rats were not observed for any serum components except triglycerides, and then only at the 2000 mg/kg dose level. When historical reference values are taken into consideration, the dose-response curve for serum triglycerides falls within the 95% normal range as defined by the historical control data (mean \pm two standard deviations).

Neither fetal body weight or crown-rump length parameter was affected by exposure to Stock 141.

No anomalies attributable to exposure to the test material were observed at the time of external examination. The only incidental observation noted in fetuses was bruising. This finding was observed in 1 fetus from one control litter, 2 fetuses from two 125 mg/kg/day dose litters, 2 fetuses from two 500 mg/kg/day litters, and 4 fetuses from two 2000 mg/kg/day litters. Due to its low incidence and its occurrence in control group fetuses, this observation is not considered to be test material-related. Bruising of fetuses has been observed in other developmental toxicity studies conducted at this facility. It can result from normal handling procedures.

No malformations or variations attributable to exposure to the test material were observed at the time of skeletal or visceral examination.

Fetal Endpoints

Dose (mg/kg/day)	0	125	500	2000
Fetal weights (gr)	3.5	3.5	3.5	3.6
Crown-rump length (mm)	33.1	33.3	33.6	33.9

- a) Statistically different from control (p<0.05)
b) Statistically different from control (p<0.01)

Residue Analyses

Less than 0.2% of the radioactivity in the Stock 141 dose was found in the collected blood, placentae, or fetuses (0.18, 0.07, and 0.17 percent, respectively). The C-14 concentrations in these samples are approximately 2-4 times greater than the method limits of detection. (16-20 ppm of Stock 141). The results clearly show that Stock 141 components and their metabolites in the maternal blood passed through the placental barrier to the fetuses. The exposure to the fetus was limited since radioactivity was lower in the fetuses than in the maternal blood. These data

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suggest that Stock 141 components and their metabolites do not bioaccumulate in fetuses.

Conclusion:

Determined by the reviewer:

The maternal NOAEL for dermal exposure to Stock 141 during GD 0-19 was determined to be 2000 mg/kg/day (LOAEL= not identified >2000 mg/kg/day)

The developmental NOAEL for dermal exposure to Stock 141 during GD 0-19 was determined to be 2000 mg/kg/day (LOAEL = not identified; >2000 mg/kg/day. There were no effects observed at the highest dose tested.)

No evidence of abnormal development was observed during external, skeletal, and visceral evaluations of rat fetuses from pregnant dams exposed to Stock 141.

RELIABILITY/DATA QUALITY

Reliability:

Valid Without Restrictions (KS=1)

Reliability Remarks:

Comparable to guideline study

Key Study Sponsor Indicator:

Key

REFERENCE

Reference:

Developmental Toxicity Screen in Rats Exposed Dermally to Stock 141. 1987. Mobil Environmental and Health Sciences Laboratory Report 51841.

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High Production Volume Information System (HPVIS)

DEVELOPMENTAL TOXICITY/TERATOGENICITY

TEST SUBSTANCE

Category Chemical:	64742-65-0																																		
Test Substance:	64742-65-0; Solvent-dewaxed heavy paraffinic distillate (SDHP)																																		
Test Substance Purity/Composition and Other Test Substance Comments:	<p>Solvent-dewaxed heavy paraffinic distillate (Site #23, Sample #7); Batch no. TA-125503/ CRU Nos. 30961 and 60901.</p> <p>PAC Content – report no. PTI 2009-0303 (API 2009); PTI 2009-0602 (API, 2009)</p> <p>PAC 2:</p> <table border="1"> <thead> <tr> <th>Sample #</th> <th>DMSO wt.%¹</th> <th>1-ARC (%)²</th> <th>2-ARC (%)</th> <th>3-ARC (%)</th> <th>4-ARC (%)</th> <th>5-ARC (%)</th> <th>6-ARC (%)</th> <th>7-ARC (%)</th> </tr> </thead> <tbody> <tr> <td>30961</td> <td>0.0</td> <td>0.0</td> <td>0.0</td> <td>0.0</td> <td>0.0</td> <td>0.0</td> <td>0.0</td> <td>0.0</td> </tr> <tr> <td>60901</td> <td>0.0</td> <td>0.0</td> <td>0.0</td> <td>0.0</td> <td>0.0</td> <td>0.0</td> <td>0.0</td> <td>0.0</td> </tr> </tbody> </table> <p>1) Percent of DMSO-extractable materials (mostly PACs), determined by the PAC 2 method as described in API (2008).</p> <p>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.</p>								Sample #	DMSO wt.% ¹	1-ARC (%) ²	2-ARC (%)	3-ARC (%)	4-ARC (%)	5-ARC (%)	6-ARC (%)	7-ARC (%)	30961	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	60901	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Sample #	DMSO wt.% ¹	1-ARC (%) ²	2-ARC (%)	3-ARC (%)	4-ARC (%)	5-ARC (%)	6-ARC (%)	7-ARC (%)																											
30961	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0																											
60901	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0																											
Category Chemical Result Type :	Measured																																		
Unable to Measure or Estimate Justification :																																			
METHOD																																			
Route of Administration:	Dermal, non-occluded																																		
Other Route of Administration:																																			
Type of Exposure:	Developmental toxicity screen																																		

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Species:	Rat
Other Species:	None
Mammalian Strain:	Sprague-Dawley (Charles River Laboratories, Inc., Raleigh, NC)
Other Strain:	Not applicable
Gender:	Females, presumed pregnant (non treated males used for mating)
Number of Animals per Dose:	20
Concentration:	100%
Dose:	0 (sham-treated control group), 1000 mg/kg/day
Year Study Performed :	2009
Method/Guideline Followed:	USEPA Health Effects Test Guidelines OPPTS 870.3700; OECD 414 -limit study
GLP:	Yes
Exposure Period:	Gestation days (GD) 0-19
Frequency of Treatment:	Daily
Post-Exposure Period:	None
Method/Guideline and Test Condition Remarks:	<p>The objective of the study was to determine the potential for the test material (SDHP) to induce developmental toxicity after maternal exposure during the critical period of organogenesis; to characterize maternal toxicity at the exposure levels tested; and to determine a no-observed-adverse-effect level (NOAEL) for maternal and developmental toxicity.</p> <p>Prior to the initiation of dosing with the test material, females were placed with untreated males (approximate 1:1 ratio). Positive evidence of mating was confirmed by the presence of a vaginal copulatory plug or the presence of sperm in a vaginal lavage and verified by a second biologist. Each mating pair was examined daily. The day on which evidence of mating was identified was termed gestation day 0 and the animals were separated and assigned randomly assigned to two treatment groups and dosing began for that animal. The treatment groups and time exposure periods were as follows, where designation as GD 0 followed positive evidence of mating:</p> <ol style="list-style-type: none">8. Sham control (0 mg/kg/day) – GD 0-19 – 25 animals9. SDHP 1000 mg/kg/day – GD 0-19 – 25 animals <p>The test substance was applied evenly over the clipped, unabrased area of skin and distributed using a stainless steel microspatula (to ensure contact with the skin) once daily during gestation days 0-19. No substance was applied</p>

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to the skin of females in the sham (control) group. Individual dosages were based on the most recently recorded body weights to provide the correct mg/kg/day dose. The dosage volume for the test substance-treated group was 1.14 mL/kg. Rats were fitted with Elizabethan collars to minimize ingestion. Control animals were treated similarly, but without dosing of test material. Approximately 1 week prior to randomization, the animals were acclimated to wearing Elizabethan collars.

All rats were observed twice daily, once in the morning and once in the afternoon, for moribundity and mortality. Individual clinical observations were recorded from gestation days 0 through 20 (prior to dose administration during the treatment period). Animals were also observed for signs of toxicity at the time of dose administration and approximately 1-2 hours following dose administration. The absence or presence of findings was recorded for individual animals.

The application site was scored daily (prior to dose administration during the treatment period) for erythema and edema in accordance with a 4-step grading system (Draize). Other remarkable dermal findings, if present, were recorded.

Individual maternal body weights were recorded on gestation days 0, 3, 6, 9, 12, 15, 18, and 20. Group mean body weights were calculated for each of these days. Mean body weight changes were calculated for each corresponding interval and also for gestation days 0-20. Collars were removed prior to collection of body weights. Gravid uterine weight was collected and net body weight (the gestation day 20 body weight exclusive of the weight of the uterus and contents) and net body weight change (the gestation day 0-20 body weight change exclusive of the weight of the uterus and contents) were calculated and presented for each gravid female at the scheduled laparohysterectomy. Laparohysterectomies and macroscopic examinations were performed blind to treatment group. All females were euthanized on gestation day 20 by carbon dioxide inhalation. The thoracic, abdominal, and pelvic cavities were opened by a ventral mid-line incision, and the contents were examined. In all instances, the postmortem findings were correlated with the antemortem comments, and any abnormalities were recorded. The uterus and ovaries were then exposed and excised. The number of corpora lutea on each ovary was recorded. The trimmed uterus was weighed and opened, and the number and location of all fetuses, early and late resorptions, and the total number of implantation sites were recorded. The placentae were also examined. The individual uterine distribution of implantation sites was documented. All implantation sites, including resorptions, were numbered in consecutive order beginning with the left distal to the left proximal uterine horn, noting the position of the cervix, and continuing from the right proximal to the right distal uterine horn.

Samples of dorsal skin were collected from the application site and adjacent untreated area of the test substance-treated females and placed in 10% neutral-buffered formalin for histopathological evaluation. For the sham (control) group, samples of dorsal skin from the shaved and unshaved areas were collected and placed in 10% neutral-buffered formalin; only the samples from the shaved areas were examined microscopically. The carcass of each female was

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then discarded.

At the scheduled necropsy, the adrenal glands and thymus were weighed from all animals, respectively. Paired organs were weighed together.

Fetal examinations were performed blind to treatment group. Each viable fetus was examined externally, individually sexed, weighed, euthanized by hypothermia followed by an intrathoracic injection of sodium pentobarbital (if necessary), and tagged for identification. Fetal tags contained the WIL study number, the female number, and the fetus number. The detailed external examination of each fetus included, but was not limited to, an examination of the eyes, palate, and external orifices, and each finding was recorded. Crown-rump measurements and degrees of autolysis were recorded for late resorptions, a gross external examination was performed (if possible), and the tissues were discarded.

Each viable fetus was subjected to a visceral examination to include the heart and major blood vessels. The sex of each fetus was confirmed by internal examination. Fetal kidneys were examined and graded for renal papillae development. Heads from approximately one-half of the fetuses in each litter were placed in Bouin's fixative for subsequent soft-tissue examination by the Wilson sectioning technique. The heads from the remaining one-half of the fetuses were examined by a mid-coronal slice. All carcasses were eviscerated and fixed in 100% ethyl alcohol. Following fixation in alcohol, each fetus was macerated in potassium hydroxide and stained with Alizarin Red S and Alcian Blue. External, visceral, and skeletal findings were recorded as developmental variations (alterations in anatomic structure that are considered to have no significant biological effect on animal health or body conformity and/or occur at high incidence, representing slight deviations from normal) or malformations (those structural anomalies that alter general body conformity, disrupt or interfere with normal body function, or may be incompatible with life).

The fetal developmental findings were summarized by: 1) presenting the incidence of a given finding both as the number of fetuses and the number of litters available for examination in the group; and 2) considering the litter as the basic unit for comparison and calculating the number of affected fetuses in a litter on a proportional basis.

Statistical analyses: All statistical tests were performed using appropriate computing devices or programs. Analyses were conducted using two-tailed tests (except as noted otherwise) for minimum significance levels of 1% and 5%, comparing the test substance-treated group to the sham (control) group. Each mean was presented with the standard deviation (S.D.), standard error (S.E.), and the number of animals (N) used to calculate the mean. Data obtained from nonpregnant animals were excluded from statistical analyses. Due to the different rounding conventions inherent in the types of software used, the means, standard deviations, and standard errors on the summary and individual tables may differ by ± 1 in the last significant figure. Where applicable, the litter was used as the experimental unit. Mean maternal body weights (absolute and net), body weight changes (absolute and net), and food consumption, gravid

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uterine weights, organ weights, numbers of corpora lutea, implantation sites, and viable fetuses, and fetal body weights (separately by sex and combined) were subjected to a two sample t-test (Snedecor and Cochran, 1980) to determine intergroup differences between the sham (control) and test substance-treated group. Mean litter proportions (percent per litter) of prenatal data (viable and nonviable fetuses, early and late resorptions, total resorptions, pre- and postimplantation loss, and fetal sex distribution), total fetal malformations and developmental variations (external, visceral, skeletal, and combined) and each particular external, visceral, and skeletal malformation or variation were subjected to Dunn's test to determine intergroup differences between the sham (control) and test substance-treated group.

TEST RESULTS

Concentration (LOAEL/LOAEC/NOAEL/NOAEC)*

Type	Population:	Value Description:	Value or Lower Concentration:	Upper Concentration:	Units:
NOAEL (dermal)	Maternal- Rat	=	1000		mg/kg/day
NOAEL (dermal)	Offspring (F1) - Rat	=	1000		mg/kg/day

*LOAELs not identified since no adverse effects observed at highest dose tested

Results Remarks:

All females in the sham (control) and test substance-treated groups survived to the scheduled necropsy on gestation day 20. No test substance-related clinical findings were noted at the daily examinations, at the time of dose administration, or 1-2 hours following dose administration in the 1000 mg/kg/day group. A clinical finding of unkempt appearance was noted in all females in the 1000 mg/kg group during gestation days 2-20. This finding was attributed to the impaired grooming behavior of the females following the placement of Elizabethan collars to prevent ingestion of the test substance and distribution of the test substance, a lubricant, to the body surface following application. Other clinical findings noted in the 1000 mg/kg/day group, including hair loss on various body surfaces and yellow, clear, and/or red material on various body surfaces, occurred infrequently or at similar frequencies in the sham (control) group.

No dermal findings were noted for females in the test substance-treated group.

Mean maternal body weight, body weight gain, net body weight, net body weight gain, and gravid uterine weight in the 1000 mg/kg/day group were unaffected by test substance administration. Differences from the sham (control)

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group were slight and not statistically significant. Maternal food consumption, evaluated as g/animal/day and g/kg/day, in the 1000 mg/kg/day group was unaffected by test substance administration. Significantly ($p < 0.05$ or < 0.01) higher food consumption values were noted in the 1000 mg/kg/day group compared to the sham (control) group during gestation days 15-20 for the g/animal/day values and during gestation days 6-20 and 0-20 for the g/kg/day values. There were no corresponding effects on mean body weight or body weight gain during these intervals and the magnitude of change was slight (3-4 g/animal/day), therefore, the effects on mean food consumption noted in the 1000 mg/kg/day group were not considered to be test substance-related.

At the scheduled necropsy on gestation day 20, no test substance-related internal findings were observed for females in the 1000 mg/kg/day group. Macroscopic findings observed in the test substance-treated group were limited to yellow matting of the skin which was due to the physical nature of the test substance and not considered adverse. All females were gravid with the exception of 1 female each in the sham (control) and 1000 mg/kg/day groups.

A test substance-related finding of minimal, multifocal mononuclear infiltrate was observed in the superficial dermis of the 1000 mg/kg/day group rats. The infiltrate was composed of lymphocytes with occasional macrophages and partially degranulated mast cells. In 2 females, there were very low numbers of neutrophils observed focally in the dermal capillaries or associated with the mononuclear infiltrate in the dermis. The mononuclear infiltrate was also observed in the untreated application site of 3 females in the 1000 mg/kg/day group, but the incidence in the treated application site was much higher, indicating a test substance-related effect. The infiltrate was minimal and was considered a non-adverse finding.

A significant increase ($p < 0.05$) in the mean absolute weight of the adrenal glands was observed in the 1000 mg/kg/day group compared to the sham (control) group value (14.5%). The mean absolute weight of the thymus was lower (12.5%) than the sham (control) group mean; the difference was not statistically significant. These organ weight changes were considered to be test substance-related. The adrenal weight change in the treated animals may be a sign of stress in the animals due to the presence of the liquid that sham (control) animals did not experience. In a parallel subchronic study on the same material, the residual presence of the test substance was significant enough to warrant protocol amendments to include daily pat-downs and weekly baths to remove excess test material on the animals and in the cages. The effects noted in the current study are consistent with other cited reports in which chronic stress is associated with adrenal enlargement. Due to the small magnitude of change from the sham (control) group and the absence of signs of maternal toxicity, the organ weight changes were considered to be non-adverse.

Intrauterine growth and survival were unaffected by test substance administration. Parameters evaluated included postimplantation loss, live litter size, mean fetal body weights, and fetal sex ratios. Mean numbers of corpora lutea and implantation sites and the mean litter proportions of preimplantation loss were similar across both groups.

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Differences from the sham (control) group were slight and not statistically significant.

The numbers of fetuses (litters) available for morphological evaluation were 346(24) and 346(24) in the sham (control) and 1000 mg/kg/day groups, respectively. Malformations were observed in 2(2) and 2(2) fetuses (litters) in these same respective dose groups and were considered spontaneous in origin. External malformations were noted in 2(2) and 1(1) fetuses (litters) in the sham (control) and 1000 mg/kg/day groups, respectively. Unilateral microphthalmia was noted in fetus no. 56158-13 in the sham (control) group and fetus no. 56152-05 in the 1000 mg/kg/day group; the sham (control) group fetus had a skeletal confirmation of orbit smaller than normal. Because this finding was also noted in the sham (control) group it was not considered to be test substance-related. In addition, one fetus in the sham (control) group was noted with vertebral agenesis (curly tail). All vertebrae posterior to sacral vertebra no. 3 were absent in this fetus at the skeletal examination. No external developmental variations were noted for any fetuses in this study.

No test substance-related visceral malformations were noted for any fetuses in this study. A visceral finding of situs inversus (trachea, esophagus, lungs, liver, stomach, spleen, pancreas, kidneys, adrenal glands, and intestine laterally transposed) was noted for one fetus in the 1000 mg/kg/day group. This finding was not considered to be test substance-related because it occurred in a single fetus, the mean litter proportion (0.3% per litter) was not statistically significant from the concurrent sham (control) group, and the value was within the WIL developmental historical control range (0.0-0.4% per litter) for this finding.

Soft tissue developmental variations noted in the 1000 mg/kg/day group included hemorrhagic ring around the iris for two fetuses and distended ureters for another. These developmental variations occurred in a single fetus or litter, the mean litter proportions of these findings were not statistically significant from the sham (control) group, and/or were within the WIL developmental historical control data ranges. Therefore, these developmental variations were not considered test substance-related. A dark red area on the left adrenal gland was observed in one fetus in the sham (control) group. This finding was not classified as either a malformation or developmental variation and was not included in any tabulation.

No skeletal malformations were noted in the 1000 mg/kg/day group. Skeletal developmental variations observed in the 1000 mg/kg/day group, including, unossified sternebra(e) nos. 5 and/or 6 and/or nos. 1, 2, 3, and or 4; ossified cervical centrum no. 1; sternebra(e) malaligned (slight or moderate); 14th rudimentary rib(s); 7th cervical rib(s); reduced ossification of the 13th rib(s), skull, and/or vertebral arches; and bent rib(s), were noted in single fetuses, were noted similarly in the concurrent sham (control) group, and/or the mean litter proportions were within the range of the WIL developmental historical control data. Additionally, there were no statistically significant differences from the concurrent sham (control) group. Therefore, these skeletal developmental variations were not considered test substance-related.

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Due to their low incidence or their occurrence in control group fetuses, external fetal abnormalities, or fetal skeletal/visceral malformations observed were not considered to be related to the test material or to the route of administration.

Conclusion:

The maternal NOAEL for dermal exposure to SDHP during GD 0-19 was determined to be 1000 mg/kg/day (LOAEL= not identified >1000 mg/kg/day)

The developmental NOAEL for dermal exposure to SDHP during GD 0-19 was determined to be 1000 mg/kg/day (LOAEL= not identified >1000 mg/kg/day)

There were no adverse effects observed (as determined by the authors) at the highest doses tested and there was no evidence of abnormal development observed during external, skeletal, and visceral evaluations of rat fetuses from pregnant dams exposed to SDHP

RELIABILITY/DATA QUALITY

Reliability: 1 – Reliable without restrictions

Reliability Remarks: Guideline study

Key Study Sponsor Indicator: Key

REFERENCE

Reference: API, 2009. A dermal prenatal developmental toxicity study of solvent dewaxed heavy paraffinic distillates (petroleum) (CAS # 6474265-0) in rats. WIL Research Laboratories, WIL-402008.

API. 2009. Characterization and quantitation of polynuclear aromatic compounds (PAC) in three HPV solvent-dewaxed heavy paraffinic distillates by PRR (Mobil-Method 2) PAC. Port Royal Research, PTI 2009-0303.

API. 2009. Characterization and quantitation of polynuclear aromatic compounds (PAC) in three HPV solvent-dewaxed heavy paraffinic distillates by PRR (Mobil-Method 2) PAC. Port Royal Research, PTI 2009-0602.

Developmental Toxicity/Teratogenicity**Test Substance**

Category Chemical (CAS #):	Not available
Test Substance (CAS #):	No CAS number identified; white mineral oil USP
Test Substance Purity/Composition and Other Test Substance Comments :	White mineral oil USP No other information
Category Chemical Result Type :	Measured

Type : Reproduction/developmental study
Species : Rat
Sex : Male/female
Strain : Sprague-Dawley
Route of admin. : Dermal
Exposure period : 14 days pre mating to day 20 of gestation
Frequency of treatm. : Daily
Premating exposure period
 Male : 14 days
 Female : 14 days
Doses : 1 ml/kg
Control group : Yes
Method : OECD Guide-line 421
Year : 1997
GLP : No data
Test substance : Mineral oil USP

Method : The study was performed in accordance with OECD guideline 421 with the addition that males were treated for 8 weeks to improve observation of effects on the reproductive system. Also females were weighed 7 times during gestation rather than 4, and at necropsy, 7 organs in addition to the reproductive organs were weighed.

Ten approximately eight week old male Sprague Dawley rats (275-285g) and 10 females of the same age (183-187g) were treated dermally with kerosene at concentrations of 20, 40 or 60% (v/v) in mineral oil in a dosing volume of 1 ml/kg. These doses were selected on the basis of the results of a preliminary 2-week range finding study. In addition There were two control groups: the vehicle control was given mineral oil only at a rate of 1 ml/kg/day and in the sham-treated group the

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animals had been fitted with collars and were stroked with the tip of a syringe, but no material was applied.

Test material or mineral oil was applied daily to the shorn skin of the animals 7 days/week from 14 days pre-mating, during 14 days mating and through 20 days of gestation. Collars were fitted to the animals during the dosing period to prevent ingestion of applied materials. After the final dose, the collars were removed and residual test material was wiped from the skin. Males continued treatment through gestation until final female sacrifice on days 4-6 of lactation.

During the mating period the test material remained on the animal's backs for 6 hours. Prior to pairing, the test material was removed by wiping. Rats were mated overnight on a 1:1 ratio and were separated the following morning. Collars were then applied prior to the next dose being applied. Females were monitored for evidence that mating had taken place. Pregnancy was determined by the presence of a vaginal plug or sperm in a vaginal lavage sample. If observed, the female was considered to be at day 0 of gestation. Any female that did not show evidence of mating was placed with the same male the following evening. Any female that did not show evidence of mating at the end of a 2 week mating period was presumed pregnant (gestation day 0 = last day of cohabitation).

Animals were checked twice daily for morbidity and mortality during weekdays but only once daily at weekends. Animals were also observed immediately prior to dosing and after the last animal had been dosed for appearance, behavior and motor activity, respiratory function, central nervous system function, excretory function and biological discharges. Effects of test material on the skin were assessed and scored weekly, using Draize scales for erythema and edema and for chronic deterioration. Males were weighed on the first day of dosing, then weekly and on the day of sacrifice. Females were also weighed on the first day of dosing, then weekly until mating was confirmed and thereafter on gestation days 0, 3, 6, 10, 13, 16 and 20 and on post partum days 0 and 4. Food consumption was also monitored on a similar schedule except through the mating period.

Each presumed-pregnant female was observed daily from gestation day 20 for parturition; evidence of dystocia was noted. The day of delivery was designated postpartum day 0. Maternal behavior and appearance were monitored daily until sacrifice.

Each litter was examined as soon as possible after birth to establish the number and sex of pups, stillbirths, live births and the presence of gross abnormalities. Pups were examined daily for presence of milk in their stomachs. Any pup found dead was examined externally and unusual findings were recorded. The body weight of each viable offspring was individually measured and recorded on post partum days 1 and 4.

Adult females that did not deliver were sacrificed on day 25 of gestation. Dams that delivered and maintained their litters until post partum day 4 were sacrificed with their offspring on post partum days 4-6. All males were sacrificed after the females had been killed. All animals were examined macroscopically for structural anomalies and

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pathological changes, with emphasis on the reproductive organs. The numbers of implantation sites and corpora lutea of each adult female was recorded. No tissues from offspring were retained.

The liver, kidneys, adrenals, thymus, spleen, brain and heart of all parental animals were weighed. In addition the testes and epididymides of parental males were weighed.

Skin from treated sites, ovaries and testes and epididymides were prepared for histological examination. Pathological evaluation was performed on reproductive organs from all males and pregnant females in both control groups and the high dose group and on treated skin from all groups.

Statistical evaluation

Quantitative data (body weight and food consumption) were analyzed by parametric methods: analysis of variance (ANOVA) and associated F-test, followed by Dunnett's test for multiple comparisons, provided there was statistical significance in the ANOVA. Maternal reproductive data were evaluated by ANOVA followed by group comparisons using Fisher's exact test. Differences between control and treatment groups were considered statistically significant only if the probability of the differences being due to chance was less than 5% ($P < 0.05$).

Remark : This is a study of the effects of kerosine and two control groups were used:
1 Sham-treated control
2 Mineral oil applied at 1 ml/kg/day

Only the results relating to mineral oil are presented in this robust summary.

Result : Only the results of the untreated control group and the group given mineral oils are summarized below.

No animals died or were prematurely sacrificed and no clinical signs of toxicity were observed.

Skin irritation among males varied from slight to moderate with increasing dose and was most severe in the high dose group. Mild to moderate skin irritation was observed in females at the highest concentration.

At terminal sacrifice, no findings were reported except for those on the skin. Microscopic changes were found in the skin of vehicle control and all kerosine-treated groups in the males. In females changes were only observed in the high dose group animals. The skin findings (macroscopic and microscopic) are shown in the following table.

Parameter	Control	Mineral oil
Males		
No animals	10	10
Max. skin irritation score, Week of max severity	-	2
Mean (SD)	0	1.3 (1.2)
Min/max score	0	0/3
Gross necropsy observations		
Crust/scab	1	0
Scaly/dry/flaky	0	0

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Histopathological observations		
Acanthosis/hyperkeratosis	2	5
Hyperplasia, sebaceous glands	3	5
Inflammation, dermal	2	1
Necrosis, epidermal, focal	1	0
Females		
No animals	10	6
Max. skin irritation score, sum of means		
Week of max severity	6	7
Mean (SD)	0.2(0.6)	0.7(1.0)
Min/max score	0/2	0/2

Gross necropsy observations		
Crust/scab	0	1
Scaly/dry/flaky	0	0

Histopathological observations		
Acanthosis/hyperkeratosis	3	2
Hyperplasia, sebaceous glands	1	0
Inflammation, dermal	0	1
Necrosis, epidermal, focal	0	0

Body weights were unaffected by treatment.

Reproductive/fertility data are shown in the following table

Parameter	Controls	
	Sham-treated	Mineral Oil
No animals	10	10
Fertility index	100%	90%
Litter with liveborn pups	10	9
Corpora lutea		
Number	169	151
Mean (SD)	16.9 (1.9)	16.8 (2.4)
Implantation sites		
Number	163	149
Mean (SD)	16.3 (1.9)	16.6 (2.4)
Pups delivered		
Total	152	131
Mean (SD)	15.2 (2.0)	14.6 (2.7)
Liveborn	152	130
Livebirth index	100%	99%
Pups dying		
day 0	3	0
days 1-4	2	4
Pups surviving		
4 days	147	126
Viability index	97	97
Pup weight/litter (g)		
day 1 mean	6.9	6.8
day 4 mean	9.9	9.6

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Reliability : No test-material-related microscopic changes were observed in the testes or epididymides of adult male rats or in the ovaries of adult female rats.
(1) valid without restriction (113)

(113) Schreiner, C., Bui, Q., Breglia, R., Burnett, D., Koschier, F., Podhasky, P., Lapadula, L., White, R., Feuston, M., Krueger, A. and Rodriguez, S. (1997)
Toxicity evaluation of petroleum blending streams: reproductive and developmental effects of hydrodesulfurized kerosine
J. Tox. and Env. Health Vol 52, pp 211-229

Developmental Toxicity/Teratogenicity**Test Substance**

Category Chemical (CAS #):	8012-95-1
Test Substance (CAS #):	8012-95-1; White oil
Test Substance Purity/Composition and Other Test Substance Comments :	White oil No other information
Category Chemical Result Type :	Measured

Species : Rat
Sex : Female
Strain : Sprague-Dawley
Route of admin. : Gavage
Exposure period : Days 6 through 19 of gestation
Frequency of treatm. : Daily
Year : 1987
GLP : No data
Test substance : White oil CAS 8012-95-1

Method : Two groups of animals (50 and 25) were administered white oil by gavage at a dose of 5 ml/kg, every day during gestation days 6 to 19 inclusive. Food and water were available continuously. Animals were examined for viability and clinical effects twice daily. Body weights were recorded on days 0, 6, 10 and 20 of gestation. On day 20 of gestation, all animals were euthanized with methoxyfluorane and examined for gross changes. Each gravid uterus was removed and weighed. The number, location and viability of each fetus and the number of implant sites were recorded. Fetuses were removed, weighed and the crown-rump lengths measured. All live and dead fetuses that had not been resorbed were examined for external malformations. Approximately half of the fetuses from each litter were decapitated and the heads preserved for subsequent examination for abnormalities. The viscera were also examined for malformations under low power magnification. The remaining fetuses were stained with Alizarin red and subsequently examined for skeletal abnormalities. No organs, other than the uteri were weighed and no organs were examined histologically in this study.

Remark : White oil was used as the solvent control in two separate studies, one for each of two test materials. This summary only reports on the outcome of the animals in ps.

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Result

The CAS# for the material that was used in this study is not included in the Lubricating Base Stocks category. However, because white oils are so highly purified, toxicologically and compositionally they are all very similar. Therefore, the Testing Group thinks the results on CAS # 8012-95-1 are applicable to the highly refined base oils that are included in this category.

: One animal died in the control group containing 50 animals and this was attributable to misdosing.

Increases in body weight during the study were considered summarized in the table below.

Day of gestation	Group 1 (25 rats)	Group 2 (50 rats)
Body weights (g)		
0	207.2	225.4
6	227.5	248
10	235.9	259.3
15	260	284.3
20	329.1	351.9
Uterine wt	67.2	70.7
Number of litters	25	49
Implants/litter	11.3	12.0
Resorptions/litter	0.06	0.47
<u>Males</u>		
No./litter	5.12	5.96
Crown-rump length (mm)	3.66	3.6
Wt. of fetuses	4.26	4.23
<u>Females</u>		
No./litter	5.6	5.61
Crown-rump length (mm)	3.61	3.52
Wt. of fetuses	4.02	4.07

In the control group containing 50 animals, 3 malformed fetuses were found in 3 litters; one had an extra lumbar vertebra, one had a discrete area of ossification in the area of the junction of the frontal and nasal bones, one had moderately dilated lateral ventricles of the brain.

3 malformed fetuses were also found in 3 litters of the other control group. These were, a vertebral arterial canal of a cervical process fully ossified in 2 fetuses and angulated ribs in a third fetus.

Reliability

The authors considered these malformations to be minor and that the findings were within the normal ranges for the strain of rat.

: (2) valid with restrictions

Although there were no untreated animals for comparison, the results were nevertheless, considered to be within normal limits. Consequently, the study is useful in providing evidence of the lack of developmental effects for white oil.

(104)

(104)

McKee, R. H., Pasternak, S. J. and Traul, K. A. (1987)
Developmental toxicity of EDS recycle solvent and fuel oil.
Toxicology Vol 46, pp 205-215

ADDITIONAL REMARKS

Type : CORRELATION OF TOXICITY WITH CHEMICAL COMPONENTS OF REFINERY STREAMS

Remark : Heavy vacuum gas oil is used as a starting material for base oil production. As such, it can be considered a "worst case" example of the unrefined/mildly refined base oil subcategory. Studies on this material are summarized below.

Type : 90-day study on Heavy vacuum gas oil

Method : Undiluted heavy vacuum gas oil was applied at doses of 0, 30, 125, 500 and 2000 mg/kg/day to the shorn skin of groups of ten male and ten female Sprague Dawley rats. The males weighed between 220 and 230 g and the females weighed between 160 and 170 g at the start of the study. The material was applied 5 days each week for 13 weeks. Collars were fitted to the animals to prevent oral ingestion. Body weights were recorded weekly throughout the study and clinical observations were made daily. Skin irritation was assessed weekly. At 5 and 13 weeks, blood samples were taken for measurement of the following hematological and clinical chemical parameters:

Hematology

Red blood cell count	Hemoglobin
Hematocrit	White blood cell count
Differential WBC count	MCV, MCH & MCHC caclulated

Clinical chemistry

Glucose	Urea nitrogen
Uric acid	Total protein
Albumin	Globulin (calculated)
Albumin/Globulin ratio	Calcium
Alkaline phosphatase	Alanine aminotransferase
Aspartate aminotransferase	Lactate dehydrogenase
Sorbitol dehydrogenase	Creatinine
Cholesterol	Triglycerides
Total Bilirubin	Calcium
Phosphorus	Sodium
Potassium	Chloride

At the end of the study (13 weeks) all surviving animals were sacrificed and a gross necropsy examination was performed. The following organs were weighed:

Adrenals	Kidneys	Spleen
Brain	Liver	Testes
Epididymes	Ovaries	Thymus
Heart	Prostate	Uterus

The following tissues in the high dose group animals were examined

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microscopically:
Adrenals (both) Ovaries (both)
Bone & marrow (sternum) Pancreas (head)
Brain (3 sections) Salivary gland (submaxillary)
Eye & optic nerve Skin (treated, 2 sections)
Heart
Colon Duodenum
Stomach Kidneys (both)
Testes (both) Liver (2 lobes)
Thymus (both lobes) Lung (left lobe)
Thyroid (both lobes) Muscle (skeletal, thigh)
Urinary bladder Peripheral nerve (sciatic)
Gross lesions

Result

Histopathological examination was only undertaken on thymus, spleen and sternum for the 500 mg/kg/day animals and thymus only for the 125 mg/kg/day animals.

: Two males and one female in the high dose group died during the study. The male deaths were considered to be compound related but the female death was considered incidental. Growth rates of males and females in the highest dose group were reduced compared to controls. At 13 weeks the males weighed 20% less and the females 15% less than controls. At 2000 mg/kg/day males and females had reduced erythrocytes and reduced platelets at 5 and 13 weeks. Similar effects were also found in the 500 mg/kg/day females.

Clinical chemical changes in males and females at 2000 mg/kg/day consisted of:

- twofold increase in sorbitol dehydrogenase
- twofold increase in cholesterol
- 50% reduction in uric acid

In addition in females at 500 mg/kg/day, glucose was reduced and in the 500 mg/kg males cholesterol was increased.

At gross necropsy, relative thymus weights were reduced in the 500 (by 25%) and 2000 mg/kg/day (by 50%) animals of both sexes. Relative liver weights were also increased at 500 and 2000 mg/kg/day for both sexes.

Histological examination revealed decreased erythropoiesis and fibrosis of the bone marrow in the 2000 mg/kg/day males.

There was a reduction in thymic lymphocytes in the 2000 mg/kg/day groups (marked for males and moderate for females) and a slight reduction in the 500 mg/kg/day groups for both sexes.

No effects were found on either sperm morphology or in the results of the urinalysis.

Test substance

The NOEL for both males and females was found to be 125 mg/kg/day.

: The sample of Heavy vacuum gas oil was produced by the vacuum distillation of crude oil. It was a dark amber liquid with a boiling range of approximately 657 to 1038 °F. The sample originated from the Beaumont crude unit B (CRU #85244) and contained:

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Reliability : 54% paraffins
35% polycyclic aromatic hydrocarbons
2% nitrogen-containing polycyclic aromatic hydrocarbons
9% residuals.
(2) valid with restrictions
The report evaluated was incomplete but nevertheless was sufficient to identify the relevant effects of exposure to the test material. (106)

(106) Mobil (1988)
Thirteen-week dermal administration of heavy vacuum gas oil to rats.
Study No. 61590
Mobil Environmental and Health Science Laboratory

Type : DEVELOPMENTAL TOXICITY SCREEN ON HEAVY VACUUM GAS OIL

Method : Groups of 10 presumed-pregnant rats (approximately 9-10 weeks old) were distributed into the following groups:

<u>Group</u>	<u>Dose level</u> (mg/kg/day)	<u>Gestation days of</u> <u>administration</u>
1	0 (remote control)	0-19
2	0 (proximate control)	0-19
3	30	0-19
4	125	0-19
5	500	0-19
6	1000	0-19
7*	500 (bioavailability)	10-12

* Group size was 5 at start but increased to 8 after study initiation.

The test material was applied daily to the shorn dorsal skin at the dose levels shown above and for the duration indicated. The rats were fitted with collars to prevent oral ingestion of the applied material. Since it was believed that inhalation of test material could be a confounding factor a second group of controls (remote controls) were housed in an area in which they could not inhale gasoil that had been applied to other animals.

Observations were made daily for clinical signs and body weights and food consumption were recorded regularly throughout the study.

Each female was sacrificed on day 20 of presumed gestation and the thoracic and abdominal cavities were examined grossly. The thymus and liver were removed from each animal and weighed and then preserved in formalin but not examined further.

The uterus and ovaries were removed and examined grossly. The number of corpora lutea per ovary for each rat was recorded. The ovaries of non-pregnant females were examined and then discarded. Uterus weights were also determined.

The uterine contents of each pregnant rat were exposed and a record

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made of the number and location of all implantations.
At necropsy, blood samples were taken from all the animals and a range of clinical chemical measurements were made of the following:

Alanine aminotransferase (ALT)	Glucose
Albumin	Iron
Albumin/globulin ratio	Phosphorus, inorganic
Alkaline phosphatase (ALP)	Potassium
Bilirubin, total	Sodium
Calcium	Sorbitol dehydrogenase (SDH).
Chloride	Total protein
Cholesterol	Triglycerides
Creatinine	Urea nitrogen
Globulin	Uric acid.

Fetuses were examined and half were preserved in Bouin's solution for examination of soft tissue abnormalities, the remainder were being differentially stained for subsequent skeletal examination.

Statistical analysis

Maternal biophase and cesarean section data and fetal data were evaluated statistically by analysis of variance followed by group comparisons using Fisher's Exact or Dunnett's Test.

Fetal skeletal and visceral data were evaluated statistically by ANOVA followed by group comparisons using Fisher's Exact test.

Thymus and liver weights were evaluated statistically using Student-Newman-Keul's test.

Statistical analyses of clinical chemistry data were performed separately on individual serum components using SAS procedures. First the F-test was employed to do an analysis of variance on the serum data obtained from control and exposed groups. Next, the Student-Newman-Keul's multiple comparison test was employed to identify the specific group subsets within the serum data sets identified as having nonrandom variance.

In general, for all statistical tests, differences between control and treated groups were considered statistically significant if the probability of the difference being due to chance was less than 5% ($P < 0.05$).

Result

: Parental animals.

There were no clinical signs attributable to exposure to HVGO other than in the highest dose group in which 2 rats had a red vaginal discharge, one animal was pale in color and six had decreased stool. The latter observation was probably associated with smaller food consumption in this group. Although food consumption was generally also less than controls in the 500 mg/kg/day group there was no associated body weight decrease. At doses in excess of 125 mg/kg/day there was a decrease in mean body weights which reflected the decreased litter sizes for this group. The only dose-related finding at gross necropsy was a pale appearance of lungs in a few animals. 4 animals were affected at the highest dose and only one in the 500 mg/kg/day group.

Mean thymus weights of animals in the highest dose group were approximately half those of the control groups.

Although absolute liver weights were unaffected by exposure to HVGO, mean relative liver weights were increased (approximately 15%) in groups exposed to doses greater than 125 mg/kg/day.

Observations of Dams at Caesarean section.

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Parameters with treatment-related effects are shown below.

	Dose group (mg/kg/day)					
	0(R)	0(P)	30	125	500	1000
Pregnant females	9	10	10	8	10	9
Dams with viable fetuses	9	10	10	8	10	6
Dams with all resorptions	0	0	0	0	0	3
Mean litter size of viable fetuses	13.9	14	13.8	14.4	10	5.8
Resorptions						
Mean	1.1	0.6	1.1	1.1	5.6	9.9
% Dams with resorptions	56	50	70	63	100	100

Parameters unaffected were:

- No. premature births
- Female mortality
- No. corpora lutea
- No. implantation sites
- Pre-implantation losses
- Viable male fetuses
- Viable female fetuses
- No. dead fetuses

Fetal evaluations

fetal body weights were significantly reduced in fetuses exposed in utero to HVGO at doses in excess of 125 mg/kg/day.

Although there were differences between control and treated crown-rump lengths they were not statistically significant.

At the time of external examination, malformations were observed in one fetus in the 1000 mg/kg/day group. The fetus was edematous and pale in color. Both hindpaws were ceded in size with a spect of each of the digits. Malformations of the vertebral column were restricted to the 500 mg/kg/day group.

Although a variety of skeletal malformations were observed in treated and control groups the degree of aberrant development in control fetuses was not as severe as in the HVGO-exposed groups.

Visceral malformations were restricted to two fetuses in the 500 mg/kg/day group. One fetus had microphthalmia and the other fetus had a diaphragmatic hernia which displaced the heart from the left to right hand side.

The authors concluded that the maternal NOAEL was 125 mg/kg/day and that the fetal NOAEL was also 125 mg/kg/day

Test substance

: The sample of Heavy vacuum gas oil (CAS 64741-57-7) was produced by the vacuum distillation of crude oil.
It was a dark amber liquid with a boiling range of approximately 657 to 1038 °F and density 0.93 g/ml.
The sample (CRU #85244) originated from the Beaumont crude unit B and

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contained:

54% paraffins
35% polycyclic aromatic hydrocarbons
2% nitrogen-containing polycyclic aromatic hydrocarbons
9% residuals

Reliability

: (2) valid with restrictions

The report evaluated was incomplete but nevertheless was sufficient to identify the relevant effects of exposure to the test material.

(107)

(107)

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ATTACHMENT 1: Physico-chemical properties for selected lubricating oil basestocks

Base oil description	Kinematic viscosity *		Flash Point (°C)	Pour Point (°C)	Density (kg/l)	Average Molecular Weight
	at 40 ⁰ C (mm ² !s)	at 100 ⁰ C (mm ² !s)				
	ASTM D445	ASTM D445	ASTM D93	ASTM D97	ISO 12185	ASTM D2502
Distillate oils						
Solvent-dewaxed, light paraffinic (64742-56-9)	8.4	2.4	157	-18	0.85	280
Solvent-dewaxed, heavy paraffinic (64742-65-0)	25.1	4.8	204	-12	0.86	390
Hydrotreated, light paraffinic (64742-55-8)	17.0	3.7	190	-18	0.86	360
Hydrotreated, heavy paraffinic (64742-54-7)	73.9	9.1	232	-9	0.88	500
Hydrotreated, light naphthenic (64742-53-6)	8.5	2.2	145	-60	0.87	290
Hydrotreated, heavy naphthenic (64742-52-5)	145	10.5	220	-24	0.91	440
White mineral oil (8042-47-5)	27.3	5.0	217	-15	0.86	400
Residual oils						
Solvent-dewaxed (64742-62-7)	1300	50	285	-6	0.95	700

· Kinematic viscosity is often expressed in Centistokes (cSt). It should be noted that 1 cSt = 1mm²/second.

ATTACHMENT 2: Summary of repeated dermal studies with base oils

Material	Duration	Dose (mg/kg)	Effects on skin	Systemic effects	API Report No.
Paraffinic distillates					
Unrefined API 84-01	28 days 3 doses per week	2000	Moderate irritation Proliferative changes	Marginal body weight decrease	33-31642
		1000	Slight irritation	None observed	
		200	Minimal irritation	None observed	
Solvent dewaxed, light API 78-9	21 days 4h/day 3 days/week	5000	Acanthosis, parakeratosis Chronic dermal inflammation	None observed	29-33065
Solvent dewaxed, heavy API 78-10*	"	5000	Acanthosis, parakeratosis Chronic dermal inflammation	None observed	29-33105
79-3	"	5000	None	None observed	29-33067
79-4	"	5000	None	None observed	29-33066
79-5	"	5000	None	None observed	29-33068
5 Paraffinic base oils	28 days 5 days per week	1000	Minor irritation	None observed	Trimmer et al, 1989
Naphthenic distillates					
Solvent refined, light API 78-5	"	5000	Acanthosis, parakeratosis Chronic dermal inflammation	None observed	29-33106
API 79-1	"	5000	None	None observed	29-33065
Hydrotreated, light API 83-12	28 days 3 doses per week	2000	Moderate irritation	Reduced testis weight	33-30499
		1000	Males: slight irritation Females: moderate irritation	None observed	
		200	Minimal irritation	None observed	
Hydrotreated, heavy API 83-15	28 days 3 doses per week	2000	Slight irritation hyperplasia	Elevated SGOT & SGPT, decreased body weight. Subacute hepatitis. Increased relative liver weight in females	35-32430
		1000	Slight irritation	Elevated SGOT & SGPT	
		200	Minimal irritation	None observed	

* Although this material is not included in the HPV Lubricating base stocks category, it is similar to other materials in the category and provides supportive information.