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Analysis of Hazards of Dispersant Constituents and Review of Toxicological Studies

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ABSTRACT

The response to the 2010 Macondo oil well blow-out in the Gulf of Mexico used significant quantities of dispersants. The materials that comprise the oil dispersant, COREXIT 9500® present minimal toxicities. Risk to spill responders would be reduced through the use of personal protective equipment. At the time, oil spill dispersants were not well understood outside of the oil spill response industry. The apparent data gap resulted in a rush to generate data on these materials without consideration of the existing toxicity data used by the consumer product industry. A review of new *in vitro* and *in vivo* toxicology studies indicated numerous examples where the study design was not clearly defined, leading to difficulties in the evaluation of study quality and uncertain relevance of the studies to human health risk assessment. The lack of transparent communication of the results to the scientific investigators and the public has led to a mistrust of oil dispersants, due to a misunderstanding of their potential hazards and risks to human health. This paper will examine the hazardous properties of individual dispersant constituents and technological considerations of published toxicology studies of oil spill dispersants. This summary will objectively evaluate oil dispersant ingredients for human health risk assessments and provide guidance to future scientific investigators on high quality study designs.

INTRODUCTION

In response to the 2010 Deepwater Horizon oil well blow-out in the Gulf of Mexico, ~1.8 million gallons of oil dispersants were used at the water surface and at the subsurface well head. Oil dispersants are typically composed of food-grade surfactants that are mixed into a

hydrocarbon solvent. This solvent is used as a carrier for the surfactants to introduce the surfactant molecules into the oil matrix. The surfactant then combines with oil to form small droplets (<70 μm), increasing the surface to volume ratio of oil, and allows the oil droplets to mix into the water column as a result of wave and current actions. Once dispersed, oil droplets can be consumed by indigenous microbes (Prince, 2013; Prince, 2014; Prince, 2015). Corexit 9500®, in particular, has been shown to dramatically increase the surface area of oil droplets resulting in greater access to microbes, thus stimulating the rate of biodegradation (Prince, 2014).

The evolution of dispersants has been toward the use of constituents with lower toxicity and higher efficacy profiles. The oil dispersant COREXIT 9500® was specifically designed to address limitations of previous dispersants that had a reduced window of opportunity on spills of weathered and heavy oils. The resulting surfactant and solvent combination for COREXIT 9500® was tested and found to expand the window of opportunity, using less hazardous ingredients. The goal of this analysis is to provide information about the human health hazards of the constituents of COREXIT 9500® and examine some of the toxicology studies that have been reported. This paper provides a fundamental understanding of these materials so that future studies of dispersants might avoid findings that have limited relevance to human health risks.

METHODS

The individual chemicals in COREXIT 9500®'s formulation were provided by the manufacturer and are presented in Table 1 (Nalco, 2014). Many of these chemicals have been studied in great detail and have robust toxicological profiles developed specifically to address hazard potential. Two international programs, the Organization for Economic Co-operation and Development (OECD) High Production Volume (HPV) challenge and the European Union's Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) program have

collected data on all of the dispersant constituents. Additional toxicology profiles from the Federal Drug Administration (FDA), the Environmental Protection Agency (EPA), and the Joint FAO/WHO Expert Committee on Food Additives (JECFA) were also consulted. The individual chemical toxicology profiles were examined; where a study summary was insufficient to characterize a health endpoint, the primary reference was examined if possible. PubMed and ToxPlanet were used to conduct additional searches for hazard information.

As a starting point, a systematic review of peer-reviewed literature was conducted to evaluate *in vivo* and *in vitro* toxicology studies on COREXIT 9500® as a whole, in order to gain an understanding of the research conducted after the Deepwater Horizon spill. A number of search terms, available in Table 2, were used in combination for the systematic review and examined in the following databases: SciSearch®, Current Contents®, BIOSIS Previews®, BIOSIS® Toxicology, Embase®, MEDLINE®, ToxFile®, Gale Group Health Periodicals Database, Toxicology Abstracts, TOXLINE, PASCAL, Health & Safety Science Abstracts, Ei Compendex®, Ei EnCompassLIT, TULSA™, Immunology Abstracts, Neurosciences Abstracts, Lancet Titles, Embase® Alert, EMCare®, and New England Journal of Medicine.

HAZARD ASSESSMENT

COREXIT 9500® constituents have been used in a wide array of consumer products for decades and there is sufficient toxicity data available to support this use. A hazard assessment of constituents reveal low potential for acute, irritation, sensitization, subchronic, reproductive, and developmental toxicity, as well as, low potential for mutagenicity, genotoxicity, and carcinogenicity from constituents. A summary of this information may be found in Tables 5-8. Hazard concerns for each hazard type are classified as low, moderate or high, based on the severity of clinical signs of toxicity reported in the available studies.

Table 1. COREXIT 9500® Ingredients		
CAS	**Ingredient**	**Common Consumer Product Uses**
57-55-6	2-Propanediol (Propylene Glycol)	Emulsifier in food and beverages
1338-43-8	Span™80 Sorbitan, mono-(9Z)-9-octadecenoate	Skin cream, body shampoo, emulsifier in juice
9005-65-6	Sorbitan, mono-(9Z)-9-octadecenoate, poly(oxy-1,2-ethanediyl) derivs.	Baby bath, mouth wash, face lotion, food emulsifier
9005-70-3	Sorbitan, tri-(9Z)-9-octadecenoate, poly(oxy-1,2-ethanediyl) derivs	Body/Face lotion, tanning lotions
577-11-7	Butanedioic acid, 2-sulfo-, 1,4-bis(2-ethylhexyl) ester, sodium salt (1:1)	cosmetic products, gelatin, beverages
29911-28-2	Propanol, 1-(2-butoxy-1-methylethoxy)	Household cleaning products
64742-47-8	Distillates (petroleum), hydrotreated light	Air freshener, cleaner

Dipropylene Glycol Monobutyl Ether (DPGBE) is part of the class of "p-series" (propylene) glycol ether solvents. DPGBE is alkyl ether of propylene glycol and has solvent properties. P-series ether solvents are typically used in degreasers, cleaners, paint removers, dyes, adhesives and could be used as an intermediate to create other chemicals. DPGBE, as part of the propylene glycol ethers, has been extensively studied. The European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC) reviewed the human health data and published two volumes describing their toxicity (ECETOC, 2005a,b) and the propylene glycol ethers were registered under ECHA's (European Chemicals Agency) REACH (ECHA, 2015a) and OECD's HPV initiative (OECD, 2003). DPGBE has minimal acute oral, dermal, and inhalation toxicity. DPGBE was slightly irritating in eye and skin tests and did not cause sensitization in animal or human skin tests. Repeated oral, inhalation, and dermal tests reported few and minor effects at the highest doses tested. There were no adverse reproductive or developmental effects reported and are not likely to be mutagenic or carcinogenic (OECD, 2003).

Sorbitan fatty acid esters are comprised of mono-, di-, and tri- esters of fatty acids and sorbitol-derived hexitol anhydrides. The polyethylene glycol (PEG) sorbitan fatty acid esters are

ethoxylated sorbitol and sorbitan esters of fatty acids. These fatty acid esters are hydrophilic nonionic surfactants and have a long history of use as inert ingredients in consumer products. Sorbitan fatty acid esters are approved by FDA as a Generally Recognized As Safe (GRAS) ingredient for many uses and are primarily used as emulsifiers, solubilizers, and stabilizers in food (eg. ice cream, mayonnaise), cosmetic (eg. moisturizer, deodorant), and pharmaceutical (eg. ointments) applications (Elder, 1984; Elder, 1985). An Acceptable Daily Intake (ADI) of 25 mg/kg bw for sorbitan oleate and polysorbate 80 was established by JECFA (JECFA, 2006a,b) and all three sorbitan fatty acid esters are listed as generally recognized as safe for all food producing species (livestock) (Official Journal of the European Union, 2006). In fact, a number of studies have examined the use of polysorbates as a therapy for lipid malabsorption syndromes in patients; these studies report no adverse effects with doses administered up to 15.0g for a few months or 6.0g when administered over several years (Krantz, 1951; Jones, 1948). In addition, sorbitan fatty acid esters have been approved by the FDA for use as emulsifiers, defoaming agents, food flavorants, stabilizers, and food thickeners (Zoller, 2008; Hartel and Hasenhuettl, 2013) and the Cosmetic Ingredient Review Expert Panel has determined they are safe for use as cosmetic ingredients (Elder, 1985). The PEG- and sorbitan fatty acid esters, as a class of chemicals, have low acute toxicity.

Dioctyl Sodium Sulfosuccinate (DSS) is the dioctyl ester of sodium sulfosuccinate and is a white, waxy solid. DSS has detergent properties and is used in the food packaging and the pharmaceutical industry (eg. laxatives). Due to its wide use in consumer products, the FDA, EPA, and JECFA have evaluated DSS' safe use. JECFA established an Acceptable Daily Intake level with a 500 fold safety factor of 0.1 mg/kg bw/ day (JECFA, 1990) and the FDA has determined DSS meets the definition for GRAS (generally recognized as safe) for numerous

direct food additive applications (21CFR172.810). The sulfosuccinates, as a chemical category, were examined as part of the OECD High Production Volume during the SIAM 29 Assessment Meeting in 2009. The conclusions were that the sulfosuccinates have minimal acute toxicity and may be mildly irritating to the skin and eyes, but are not sensitizers. The sulfosuccinates are not mutagenic, reproductive/ developmental toxicants, or carcinogens.

Distillates (petroleum), hydrotreated light (CASRN: 64742-47-8) is a member of the hydrocarbon solvents. Hydrocarbon solvents are the liquid hydrocarbon fractions produced by the distillation of petroleum feed stocks or their synthetic analogs (e.g. gas to liquid technology). Hydrocarbon solvents are complex substances with variable compositions or UVCBs (Unknown or Variable Composition, Complex Reaction Products and Biological Materials). The chemical class of hydrocarbon solvents is comprised of alkane and aromatic molecules containing only carbon and hydrogen molecules with 5-20 carbon chains. The alkane molecule carbon chains can be straight ("normal"), branched ("isoparafins"), or acyclic ("naphthenic"), while the aromatic molecules are single or double alkylated aromatic rings, but are not polyaromatic hydrocarbons (i.e. PAHs). The CASRN 64742-47-8 describes hydrocarbon solvents comprised of mixed isomeric hydrocarbon molecules containing chains of 10-18 carbons with <2% aromatic molecules and <1 ppm benzene (McKee, 2015). Extensive toxicity data for the hydrocarbon solvents was available from the REACH database of registered substances and for the OECD HPV Initiative. In order to reduce animal testing and to maximize the utility of toxicity testing, a category approach was used for these regulatory activities. A category approach allows data from one member of a category to be used to assess hazard from another member of the category (and in some circumstances, to other categories). Distillates (petroleum), hydrotreated light (CASRN: 64742-47-8) belong to the "C9-C14 Aliphatic Hydrocarbon Solvents (<2% aromatics)" category

(McKee 2015). This toxicology data was compiled and discussed exhaustively in a review by McKee et. al (McKee, 2015). The C9-C14 Aliphatic Hydrocarbon Solvents (<2% aromatics) have few toxicological effects. If aspirated into the lungs, all hydrocarbon solvents can cause chemical pneumonitis. Hydrocarbons with 6 to 10 carbons are volatile and may cause acute CNS effects (narcosis) or cause eye or respiratory irritation at high concentrations that exceed accepted occupational exposure limits (e.g. ACGIH TLVs).

SYSTEMATIC LITERATURE REVIEW

The systematic literature search yielded a number of results for articles published between June 2010 and July 2015. Of the 5,034 articles on COREXIT 9500®, 2,376 included toxicology key words. The search terms for mammals were used to identify studies that could be used as read-across data to human health; from this subset, 366 articles were identified. Lastly, this subset of articles was limited to exclude databases for news articles, yielding 143 results. The full abstracts for these results were then reviewed and limited to *in vivo* and *in vitro* toxicology studies. Article duplicates, as well as, review articles and conference abstracts were excluded. Final results yielded eleven articles. In total, six articles were identified examining the effects of COREXIT 9500® exposure *in vivo* (George, 2010; Krajnak, 2011; Li, 2015; Roberts, 2011; Roberts, 2014; Sriram, 2011), for which study design details are available in Table 4. Six articles were identified examining the effects of COREXIT 9500® exposure *in vitro* (Bandele, 2012; Judson, 2010; Li, 2015; Shi, 2013; Wang, 2012; Zheng, 2014), for which study design details are available in Table 3. One study, Li and colleagues, contained both in vivo and in vitro experimental data (Li, 2015).

Appropriate study design of *in vivo* and *in vitro* experiments is particularly crucial to the applicability and relevance of findings to human health risk assessment. The quality of a study

relies first and foremost on the transparency of the study design. It is crucial to publish clearly defined study methods for the purpose of both quality assessment and study reproducibility. According to EPA's Health Effects Testing Guidelines, high quality studies should define a number of method parameters, as seen in Tables 3 and 4 (40CFR798). A review of the identified studies revealed key information gaps in all of the *in vivo* studies examined. Of the studies examined, George and colleagues were most transparent with their study methodology and only lacked microscopic tissue observations (George, 2010). On the other hand, the study conducted by Li and colleagues lacked the most critical information by far. Missing were any mention or details regarding control organisms, life stage and source of test organisms, source of test organisms, husbandry conditions, number of organisms tested per group, euthanasia details, and macroscopic and behavioral observations (Li, 2015). Of the *in vitro* studies examined, two clearly delineated all key parameters tested (Bandele, 2012; Zheng, 2014). On the other hand, the study conducted by Judson and colleagues lacked details regarding source of test model, passage numbers used, details of culture media and culture conditions used, and statistical methods (Judson, 2010).

CONCLUSIONS

This paper examined the hazards and toxicology studies of one oil dispersant used during the Deepwater Horizon spill response. Components of these materials have been manufactured in US Commerce and utilized in numerous household and consumer products, medical products, and the food industry for decades. As a result, they have been studied extensively under a variety of EPA and European chemical assessment programs with a focus on human health effects. At the time of the aforementioned spill, dispersants were not well understood outside of the oil spill response industry. The apparent data gap resulted in a rush to generate data on these

materials without consideration of the existing toxicity data used by the consumer product industry. The lack of transparent communication of the results to the scientific investigators and the public has led to a mistrust of oil dispersants, due to a misunderstanding of their potential hazards and risks to human health.

The materials that comprise the oil dispersant, COREXIT 9500®, present minimal toxicities. Several of the constituents were found to produce irritation in dermal and eye testing. Furthermore, hydrotreated light petroleum distillates are damaging to lung tissues when aspirated. Use of personal protective equipment would prevent exposures and minimize risk to spill responders. A review of both *in vitro* and *in vivo* toxicology studies indicated numerous examples where the study design was not transparent, leading to difficulties in the evaluation of study quality. If these key attributes are not satisfied, the relevance of the study to risk assessment is uncertain. The production and publication of scientifically valid studies is absolutely fundamental and has been the cornerstone of toxicology. It is incumbent upon scientists examining dispersant materials to understand the body of scientific evidence. New analyses should focus to fill gaps in existing data. Those studies that test for potential health effects during an oil spill response should be designed in light of realistic exposure scenarios. This paper is meant to examine the hazardous properties of dispersant constituents and the toxicological design and transparency of published toxicology studies of COREXIT 9500®. This summary highlights the conclusions from existing extensive human health risk assessments of oil spill dispersant ingredients and provides guidance to future scientific investigators on research needs and high quality study designs.

Table 2. Search terms used in Systematic Literature Review
corexit*
toxic* OR genotox* OR fetotox* OR neurotox* OR embryotox* Or embryoleth* OR reprotox* Or terat* OR mutate* OR mutation* OR mutagen* OR malform* OR developmental OR reproductiv* or cancer* OR carcino* OR tumor* OR tumour* OR neoplas* OR malignan* OR leukem* OR lethal* Or mortality Or oncogenic* Or adenoma* Or metastas* or health or immunotox* Or lymphoma* or micronucleus or LC50 OR LD50 OR subchrnonic OR chronic OR acute or subacute or bioconc* Or pharmacokinetic* or metabolism or bioaccumulat* Or biomarker* Or toxicokin* Or pharmacodynam* or skin OR sensitiz* Or sensitis* OR NOAEL OR irritan* OR irritat* OR demal OR dermatit* OR oral or immunolog* or CNS OR neurolog* OR gavage OR inhal* OR respir* or metabolit* or aberr* OR cytogen* OR genetic* OR ames OR salmonella OR chromatid* OR cytotox* Or microtox* or gene or genes or "sister chromatid*" Or "dominant lethal Or HPRT or micronucleus or genetox* or nasal* OR rhino* OR nostril* OR pharyngeal OR pharynx OR lung* OR alveol* OR pneumo* Or pulmo* OR thora* OR bronch* Or nasopharynx OR trache* OR respirat*
mammal* Or rodent* or rat OR rats OR mouse OR mice OR hamster* OR pig OR pigs OR dog OR dogs OR feline OR cats OR monkey* OR primate* OR rabbit* OR guinea*

Table 3. *In Vitro* Experiments

Reference	Bandele, 2012	Judson, 2010	Li, 2015	Shi, 2013	Wang, 2012	Zheng, 2014
Test substance details	Provided	Provided	Provided	Provided	Provided	Provided
Test substance source	Provided	Provided	Provided	Provided	Provided	Provided
Control details	Provided	Provided	N/A	N/A	N/A	Provided
Test model	Provided	Provided	Provided	Provided	Provided	Provided
Source of test model	Provided	N/A	Provided	Provided	Provided	Provided
Passage no. of test model	Provided	N/A	N/A	N/A	N/A	Provided
Culture media details	Provided	N/A	Provided	N/A	Provided	Provided
Culture condition details	Provided	N/A	N/A	Provided	Provided	Provided
No. of replicates	Provided	Provided	N/A	Provided	N/A	Provided
Concentrations evaluated	Provided	Provided	Provided	Provided	Provided	Provided
Length of treatment	Provided	Provided	Provided	Provided	Provided	Provided
Statistical methods	Provided	N/A	Provided	Provided	Provided	Provided

Table 4. *In Vivo* Experiments						
Reference	**George, 2010**	**Krajnak, 2011**	**Li, 2015**	**Roberts, 2011**	**Roberts, 2014**	**Sriram, 2011**
Test substance details	Provided	Provided	Provided	Provided	Provided	Provided
Test substance source	Provided	N/A	Provided	Provided	Provided	Provided
Control details	Provided	Provided	N/A	Provided	Provided	Provided
Test species	Provided	Provided	Provided	Provided	Provided	Provided
Life stage of test organism	Provided	Provided	N/A	N/A	N/A	N/A
Sex of test organisms	Provided	Provided	Provided	Provided	Provided	Provided
Source of test organisms	Provided	Provided	N/A	Provided	Provided	Provided
Husbandry conditions	Provided	Provided	N/A	Provided	Provided	Provided
No. per group	Provided	Provided	N/A	Provided	Provided	Provided
Concentrations evaluated	Provided	Provided	Provided	Provided	Provided	Provided
Exposure method	Provided	Provided	Provided	Provided	Provided	Provided
Exposure frequency	Provided	Provided	Provided	Provided	Provided	Provided
Length of treatment	Provided	Provided	Provided	Provided	Provided	Provided
Euthanization details	Provided	Provided	N/A	Provided	Provided	N/A
Macroscopic/Behavioral observations	Provided	N/A	N/A	N/A	N/A	N/A
Microscopic tissue observations	N/A	N/A	Provided	N/A	N/A	N/A
Statistical methods	Provided	Provided	Provided	Provided	Provided	Provided

Table 5. Propanol, 1-(2-butoxy-1-methyloxy) (Dipropylene Glycol Monobutyl Ether)				
CASRN: 29911-28-2				
Hazard Type		**Hazard Concern**		**Reference**
Acute Toxicity	Oral	Low	LD50: 1850 – >4000 mg/kg	OECD, 2003
	Dermal	Low	LD50 >2000 mg/kg	
	Inhalation	Low	LC50 >328 mg/m3	
Irritation	Dermal	Low	NOAEL was 91 mg/kg bw/day	OECD, 2003; ECETOC, 2005b;

	Inhalation	Low	NOAEC was 200 mg/m3	Weterings & Daamen, 1987a,b; Vanderkom, 1987
Sensitization		Low	No sensitization reported	OECD, 2003; ECETOC, 2005b; Weterings & Daamen, 1987a,b; Vanderkom, 1987
Subchronic Toxicity	Oral	Low	NOAEL was 450 mg/kg bw /day; LOAEL was 1000 mg/kg bw/day	OECD, 2003; Thevenaz, 1989
	Dermal	Low	NOAEL was 91 mg/kg bw/day	ECETOC, 2005b; Lina, 1988
	Inhalation	Low	NOAEC was 200 mg/m3	ECETOC, 2005b; Cieszlak, 1991
		Low	NOAEC was 320 mg/m3	OECD, 2003
Mutagenicity/ Genotoxicity		Low	No genotoxicity reported	OECD, 2003
Carcinogenicity		Low	No carcinogenic effects reported; NOEL (rats) 300 ppm; NOAEL (mice) 1000 ppm	Spencer, 2002
Reproductive Toxicity		Low	No effects reported	OECD, 2003; Thevenaz, 1989
Developmental Toxicity		Low	NOEAL of 910 mg/kg bw/day	OECD, 2003; Wilmer and van Marwijk, 1988

Table 6. Sorbitan Fatty Acid Esters and Polyethylene Glycol (PEG) Sorbitan Fatty Acid Esters [Sorbitan, Mono-(9Z)-9-octadecenoate (Sorbitan Oleate); Sorbitan, mono-(9Z)-9-octadecenoate, poly (oxy-1,2-ethanediyl) derivs (Polyoxyethylene sorbitan monooleate or Polysorbate 80); Sorbitan, tri-(9Z)-9-octadecenoate, poly (oxy-1,2-ethanediyl) derivs (Polyoxyethylene Sorbitan Trioleate or Polysorbate 85)]

CASRN: 1338-43-8; 9005-65-6; 9005-70-3

Hazard Type		**Hazard Concern**		**Reference**
Acute Toxicity	Oral	Low	LD_{50} = 33 g/kg	Elder, 1985
			LD50 >25 g/kg bw	Elder, 1984
	Dermal	Low	LOEL = 6.8 g/kg	Elder, 1985
Irritation		Moderate	Mild dermal irritation reported; Studies conducted	Elder, 1985

			in animals and with human volunteers	
			No dermal irritation reported; Studies conducted in animals and with human volunteers	Elder, 1984
Sensitization		Low	No sensitization reported; Studies conducted in animals and with human volunteers	Elder, 1984; Elder, 1985
Subchronic Toxicity	Oral	Low	NOAEL > 5% of diet	Atlas, 1970
			NOAEL = 5% of diet	Chatelanot & Simon, 1969
			NOAEL = 5% of diet; LOEL = 10% of diet; LOAEL = 20% of diet	Oser and Oser 1956a,b, 1957a,b; Elder, 1984
	Dermal	Low	NOAEL > 3000 mg/kg	Elder, 1985
	Inhalation	Low	NOEL = 25,000 ppm; LOEL = 50,000 ppm	NTP, 1992
		Low	NOEL = 50,000 ppm	NTP, 1992
Mutagenicity/ Genotoxicity		Low	No mutagenicity reported	NTP, 1992; ECHA, 2015b,c
			No clastogenicity reported	CIR, 2000
			No genotoxicity reported	ECHA, 2015b,c
Carcinogenicity		Low	No carcinogenicity reported	NTP 1992; Greim, 2009; Setala, 1956; Elder,1985; Hendy, 1978
Reproductive Toxicity		Low	No reporductive toxicity reported; NOAEL = 1000 mg/kg bw/day	ECHA, 2015b,c
Developmental Toxicity		Low	No developmental toxicity reported; NOAEL = 1000 mg/kg bw/day	ECHA, 2015b,c
			No developmental toxicity reported; NOEL = 2500 mg/kg/day	Kavlock, 1987; CIR, 2000

Table 7. Succinic acid, sulfo-, 1,4-bis(2-ethylhexyl)ester, sodium salt

CASRN: 577-11-7				
Hazard Type		**Hazard Concern**		**Reference**
Acute Toxicity	Oral	Low	LD50 = 1.5 – 4.8 g/kg bw (mice)	Schultz, 1941; Hooper, 1949; Olsen, 1962; JECFA,1974
			LD50 = 1.8 – 5.7 g /kg bw (rat)	
	Dermal	Low	LD50 > 10g/ kg bw	OECD, 2009
Irritation		Moderate	Irritation reported	OECD, 2009
Sensitization		Low	No sensitization reported	OECD, 2009
Subchronic Toxicity	Oral	Low	NOAEL = 500 mg/kg bw/day	Taylor, 1966; JEFCA, 1974
Mutagenicity/ Genotoxicity		Low	No increases in mutation frequency	OECD, 2009
			No induction of chromosomal abberations	
Carcinogenicity		Low	No effects reported; NOEL = 0.1% DSS in diet	Fitzhugh & Nelson, 1948
Reproductive Toxicity		Low	No effects reported; NOEL = 0.1% DSS in diet	MacKenzie, 1990
Developmental Toxicity		Low	NOAEL = 500 mg/kg bw/day	OECD, 2009

Table 8. Distillates (petroleum), hydrotreated light				
CASRN: 64742-47-8				
Hazard Type		**Hazard Concern**		**Reference**
Acute Toxicity	Oral	Low	No toxicity reported; NOAEL >15.8 g/kg	ECHA, 2015d; Amoruso, 2008; Nilsen, 1988; McKee, 2015
	Dermal	Low	No toxicity reported; NOAEL = 2000 mg/kg bw	
	Inhalation	Low	No toxicity reported; NOAEC = 23500 mg/m3	

Irritation		Low	No irritation reported; Studies conducted in animals and with human volunteers	ECHA, 2015d; OECD, 2015; Amoruso, 2008
Sensitization		Low	No sensitization reported; Studies conducted in animals and with human volunteers	ECHA, 2015d; OECD, 2015; Amoruso, 2008
Subchronic Toxicity	Oral	Low	NOAEL = 5000 mg/kg/day	OECD, 2015; ECHA, 2015d; McKee, 2015
			NOAEL = 1000 mg/kg/day	
			NOAEL = 1000 mg/kg/day	
			NOAEL = 1000 mg/kg/day	
	Dermal	Low	LOAEL = 2000 mg/kg bw/day	McKee, 2015; OECD, 2015
	Inhalation	Low	NOAEC = 10,400 mg/m3 (1444 ppm)	OECD, 2015; ECHA, 2015d; McKee, 2015
			NOAEC = 5220 mg/m3 (900 ppm)	
			NOAEC = 5220 mg/m3 (900 ppm)	
			NOAEC = 6000 mg/m3	
			NOAEC = 1390 mg/m3 (200 ppm)	
			NOAEC = 6257 mg/m3 (900 ppm)	
			NOAEC = 4200 mg/m3 (615 ppm)	
Mutagenicity/ Genotoxicity		Low	No mutagenicity reported; No genotoxicity reported; No clastenoginicity reported	OECD, 2015; ECHA, 2015d; McKee, 2015
Carcinogenicity		Low	No carcinogenicity reported	NTP, 2004; Greim, 2009
Reproductive Toxicity		Low	No reproductive toxicity reported; NOAEL = 3000 mg/kg bw/day for male rats; NOAEL = 1500 mg/kg bw/day for female rats	ECHA, 2015d; OECD, 2015
Developmental Toxicity		Low	No developmental toxicity reported; NOAEL = 750 mg/kg bw/day	ECHA, 2015d; OECD, 2015
Neurotoxicity		Moderate	Acute Narcosis; in confined spaces	McKee, 2015

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