

MINERAL OILS

**High Viscosity, Class I Medium and Low Viscosity, Class II Medium and Low Viscosity, and Class III Medium and Low Viscosity
(per the World Health Organization classification)**

ORAL RISK ASSESSMENT DOCUMENT



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EXECUTIVE SUMMARY

Mineral Oil, USP or Food Grade – Oral Risk Assessment (oil classification per the World Health Organization)						
Mineral Oil Class	NOAEL mg/kg-day	Uncertainty Factor	Oral RfD, mg/kg-day	TAC ^{1,4} mg/L	SPAC ^{2,4} mg/L	STEL ^{3,4} mg/L
High viscosity, ≥ 11 centistokes	2,000	100	20	700	70	700
Medium and low viscosity, Class I 8.5-11 centistokes	2,000	100	20	700	70	700
Medium and low viscosity, Class II 7.0-8.5 centistokes	200	100	2	40	4	40
Medium and low viscosity, Class III 3.0-7.0 centistokes	20 20 20	100	0.2	1	0.1	2
¹ Group TAC ² Group SPAC ³ Group STEL ⁴ The solubility of a mineral oil in actual use as a direct or indirect drinking water additive should not be exceeded.						
KEY STUDY and KEY REVIEWS	BIBRA Toxicology International. 1992a. A 90-day feeding study in the rat with six different white 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. Sponsored by CONCAWE, Brussels, Belgium. Project no. 3.1010. Report no. 1010/3/92. BIBRA Toxicology International. 1992b. Ninety-day feeding study in Fischer 344 rats of highly refined petroleum-derived food-grade white oils and waxes. Presented in part at The Toxicology Forum Special Meeting on Mineral Hydrocarbons, Green College, Oxford, United Kingdom, Sept. 21-23, 1992 and The Toxicology Forum 1993 Annual Winter Meeting, The Capital Hilton, Washington, D.C., February 15-17, 1993. WHO (World Health Organization). 1995a. Evaluation of certain food additives and contaminants. Technical Report Series No. 859. Forty-fourth report of the Joint FAO/WHO Expert Committee on Food Additives. Geneva. WHO (World Health Organization). 2002. Joint FAO/WHO Expert Committee on Food Additives. Fifty-ninth meeting. Geneva 4-13 June 2002. Summary and Conclusions (full report in preparation).					
CRITICAL EFFECTS	The critical effects depended to some extent on the physical properties of the mineral oils tested. The two highest viscosity oils did not show any effects considered adverse at the highest dose tested. Other oils produced liver and/or spleen weight effects with liver granulomas or other liver pathology.					
TOXICITY SUMMARY	The available toxicology information on USP and food grade mineral oils has been summarized by the World Health Organization at a number of meetings of the Joint FAO/WHO Expert Committee on Food Additives, and was not re-summarized in this document. The World Health Organization has taken the lead in the risk assessment of mineral oils, requesting or requiring additional studies as needed for clarification. It is clear from both human data and animal studies that mineral oil can accumulate to a small extent in organs and tissues. The liver is a target organ for the lower viscosity oils, based on liver weight effects, granulomas or micro-granulomas in the liver, and biochemical changes indicative of mild liver damage. Immune system effects of pigmented macrophages and lymph node histiocytosis have so far been observed in F-344 rats, but not in other rat strains or in Beagle dogs. Most genetic toxicity studies have shown that test results on mineral oils correlate directly with their polycyclic aromatic hydrocarbon content, suggesting the oil itself is not genotoxic. Oral exposure of humans to USP or food grade mineral oil in food and pharmaceuticals over many decades has not produced any evidence of carcinogenicity. Several older long-term oral studies in laboratory animals have shown no evidence of carcinogenicity, although these studies were not conducted according to current regulatory guidelines. Since there are no human epidemiological studies and no adequate animal studies on mineral oil by the oral route, the <i>“data are inadequate for an assessment of human carcinogenic potential”</i>.					
CONCLUSIONS	The drinking water action levels derived in this document are based on NOAEL values from well conducted subchronic studies of well characterized mineral oils. Based on these NOAEL values and appropriate uncertainty factors, the action levels are considered protective of the public health.					

1.0 INTRODUCTION

This document has been prepared to allow toxicological evaluation of the unregulated contaminant **mineral oil** in drinking water, as an extractant from one or more drinking water system components evaluated under NSF/ANSI 61 (2003e), or as a drinking water treatment chemical evaluated under NSF/ANSI 60 (2003e). Both non-cancer and cancer endpoints have been considered, and risk assessment methodology developed by the U.S. Environmental Protection Agency (U.S. EPA) has been used. USP grade, white, and commercial mineral oils will be evaluated using criteria developed in this document, with potential impurities in the lower grades evaluated separately under the requirements of NSF/ANSI 60 (2003e) or 61 (2003e).

1.1 NSF Risk Assessment Procedures

Non-cancer endpoints are evaluated using the reference dose (RfD) approach (Barnes and Dourson, 1988; Dourson, 1994; U.S. EPA, 1993; U.S. EPA, 2002a), which assumes that there is a threshold for these endpoints that will not be exceeded if appropriate uncertainty factors (Dourson et al., 1996; U.S. EPA, 2002a) are applied to the highest dose showing no significant effects. This highest dose is derived from human exposure data when available, but more often is derived from studies in laboratory animals. Either the no-observed-adverse-effect level (NOAEL) taken directly from the dose-response data, or the calculated lower 95% confidence limit on the dose resulting in an estimated 10% increase in response (the LED₁₀ or BMDL₁₀ from benchmark dose programs) can be used (U.S. EPA, 2003a). The lowest-observed-adverse-effect level (LOAEL) can also be used, with an additional uncertainty factor, although the benchmark dose approach is preferred in this case. The RfD is expressed in mg/kg-day. It is defined by the U.S. EPA as “an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime” (Barnes and Dourson, 1988; U.S. EPA, 1993; U.S. EPA, 2003b).

NSF uses the RfD to derive three product evaluation criteria for non-cancer endpoints. The total allowable concentration (TAC), generally used to evaluate the results of extraction testing normalized to static at-the-tap conditions, is defined as the RfD multiplied by the 70 kg weight of an average adult assumed to drink two liters of water per day. A relative source contribution (RSC), to ensure that the RfD is not exceeded when food and other non-water sources of exposure to the chemical are considered, is also applied in calculating the TAC. The relative source contribution should be data derived, if possible. Alternately, a 20% default contribution for water can be used (U.S. EPA, 1991a). The TAC calculation is then as follows:

$$\text{TAC (mg/L)} = \frac{[\text{RfD (mg/kg-day)} \times 70 \text{ kg}] - [\text{total contribution of other sources (mg/day)}]}{2 \text{ L/day}}$$

or

$$\text{TAC (mg/L)} = \frac{\text{RfD (mg/kg-day)} \times 70 \text{ kg}}{2 \text{ L/day}} \times 0.2 (\text{RSC})$$

The single product allowable concentration (SPAC), used for water treatment chemicals and for water contact materials normalized to flowing at-the-tap conditions, is the TAC divided by the estimated total number of sources of the substance in the drinking water treatment and distribution system. In the absence of source data, a default multiple source factor of 10 is used. This accounts for the possibility that more than one product in the water and/or its distribution system could contribute the contaminant in question to drinking water.

Finally, a short-term-exposure level (STEL), at a higher level than the TAC, may be calculated for contaminants such as solvents expected to extract at higher levels from new product, but also expected to decay rapidly over time. The STEL is calculated from the NOAEL or the LED₁₀ of an animal study of 14- to 90-days duration, with uncertainty factors appropriate to the duration of the study. The contaminant level must decay to a level at or below the TAC under static conditions, or to a level at or below the SPAC under flowing conditions within 90 days, based on the contaminant decay curve generated from over-time laboratory extraction data.

Endpoints related to cancer are evaluated using modeling to fit a curve to the appropriate dose-response data (U.S. EPA, 1996a; U.S. EPA, 1999; U.S. EPA, 2003c). If there is sufficient evidence to use a non-linear model, the LED₁₀ or BMDL₁₀, divided by the anticipated exposure, is calculated to give a margin of exposure. If there is insufficient evidence to document non-linearity, a linear model drawing a straight line from the LED₁₀ or BMDL₁₀ to zero, is used as a default. If a linear model (generally reflecting a genotoxic carcinogen) is used, a target risk range of 10^{-6} to 10^{-4} is considered by the U.S. EPA to be safe and protective of public health (U.S. EPA, 1991a). For the purposes of NSF/ANSI 60 (2003e) and 61 (2003e), the TAC is set at the 10^{-5} risk level, and the SPAC is set at the 10^{-6} risk level. Use of a higher risk level is not ruled out, but would generally require documentation of a benefit to counteract the additional risk.

The RfD, TAC, SPAC, and STEL values derived in this document are based on available health effects data and are intended for use in determining compliance of products with the requirements of NSF/ANSI 60 (2003e) and 61 (2003e). Application of these values to other exposure scenarios should be done with care, and with a full understanding of the derivation of the values and of the comparative magnitude and duration of the exposures. These values do not have the rigor of regulatory values, as data gaps are generally filled by industry or government studies prior to regulation. Data gaps introduce uncertainty into an evaluation, and require the use of additional uncertainty factors to protect public health.

The general guidelines for this risk assessment include those from the National Research Council (NRC, 1983) and from The Presidential/Congressional Commission on Risk Assessment and Risk Management (1997a; 1997b). Other guidelines used in the development of this assessment may include the following: Guidelines for Carcinogen Risk Assessment (U.S. EPA, 1986), Proposed Guidelines for Carcinogen Risk Assessment (U.S. EPA, 1996a), draft revised Guidelines for Carcinogen Risk Assessment (U.S. EPA, 1999), draft final Guidelines for Carcinogen Risk Assessment (U.S. EPA, 2003c), Guidelines for Developmental Toxicity Risk Assessment (U.S. EPA, 1991b), Guidelines for Reproductive Toxicity Risk Assessment (U.S. EPA, 1996b), Guidelines for Neurotoxicity Risk Assessment (U.S. EPA, 1998), A Review of the Reference Dose and Reference Concentration Process (U.S. EPA, 2002a), Recommendations for

and Documentation of Biological Values for Use in Risk Assessment (U.S. EPA, 1988), and Health Effects Testing Guidelines (U.S. EPA 1996c; U.S. EPA 2003d).

1.2 Evaluation of USP and Food Grade Mineral Oils by the World Health Organization

The World Health Organization has been actively involved in the evaluation of USP or food-grade mineral oils as food additives since the Fourteenth Meeting of the Joint FAO/WHO Expert Committee on Food Additives (WHO, 1970; WHO, 1971). Several conclusions were reached. First, that it was important to establish limits for polycyclic aromatic hydrocarbons in food grade mineral oil. Second, that ingested mineral oil was absorbed and stored in liver, kidneys, mesenteric lymph nodes, fat, and other tissues with no evidence of systemic toxicity. Third, that interference of mineral oil with the absorption of some fat-soluble vitamins was not toxicologically significant at the current levels of mineral oil intake, and finally that the intake of mineral oil was self-limiting because of its laxative effect. At that time, the use of mineral oil was limited only by good manufacturing practice. At the Seventeenth Meeting of the Joint FAO/WHO Expert Committee on Food Additives (WHO, 1974a) the Committee prepared a monograph summarizing the available toxicological information (WHO, 1974b) and recommended further work on the significance of stored mineral oil in the body. At the Twentieth Meeting of the Joint FAO/WHO Expert Committee on Food Additives (WHO, 1976a) the ADI was again not specified, and the Committee noted that impurities likely to result from the oleum but not the hydrogenation manufacturing process were known (WHO, 1976b).

The Thirtieth (WHO, 1987) and Thirty-third (WHO, 1989) reports of the Joint FAO/WHO Expert Committee on Food Additives discussed mineral oil specifications based on new manufacturing methods, and discussed the results of two recently completed subchronic ingestion studies of mineral oil in rats. These studies had deficiencies in terms of mineral oil specifications, so the results could not be reliably related to food grade mineral oil. Based on these discussions, the “not specified” ADI was retained but made temporary. The Thirty-seventh report (WHO, 1991) continued the temporary “not specified” ADI until 1995, at which time additional feeding studies were expected to be available for review. Results of subchronic studies in rats on several mineral oils as well as some paraffin waxes were available for review at the Forty-fourth Meeting of the Joint FAO/WHO Expert Committee on Food Additives (WHO, 1995a; WHO, 1995b). Based on these results, food grade mineral oils were categorized as high viscosity or Class I, Class II or Class III medium or low viscosity. An ADI of 0-20 mg/kg was established for high viscosity mineral oil. A temporary ADI of 0-1 mg/kg was established for Class I medium and low viscosity mineral oil. Temporary group ADIs of 0-0.01 mg/kg were established for Class II and Class III medium and low viscosity mineral oils. At the Fifty-ninth meeting (WHO, 2002) the temporary designation was removed for Class I and its ADI was revised to 0-10 mg/kg. The temporary group ADIs for Class II and Class III were retained, and information on the relevance to humans of the findings in two rat strains were required for evaluation in 2006.

These ADIs were based on currently available toxicological information and meet, in part, the data requirements for published risk assessments on substances regulated by other agencies under NSF/ANSI 60 (2003e) and 61 (2003e), Annex A Section A.3.3. These ADIs are supported by evaluations of mineral oils conducted by the U.S. Food and Drug Administration (U.S. FDA,

2004) and IARC (1984; 1987). The WHO (2002) evaluation served as a point of departure for this document. The present analysis highlights issues of toxicological significance considered by the World Health Organization in establishing the ADIs. The WHO (1995a) evaluation used NOEL rather than NOAEL values, and uncertainty factors not in conformance with U.S. EPA (2002a) risk assessment procedures. Therefore, data from 1995 and later have been evaluated or re-evaluated for the present assessment. The reader is referred to the WHO documents for information on studies prior to 1995.

The literature search for mineral oil under the USP, white mineral oil, and non-USP grade CAS registry numbers was conducted on June 5, 2003. This document includes relevant information retrieved as a result of that search that was not covered by the various World Health Organization evaluations.

2.0 PHYSICAL AND CHEMICAL PROPERTIES

Mineral oils are mixtures of highly refined paraffinic and naphthenic liquid hydrocarbons defined by their viscosity, molecular weight, and boiling point. Synonyms include white mineral oil, food grade mineral oil, liquid petrolatum, and liquid paraffin. White mineral oil has a CAS Registry Number of 8042-47-5. The primary CAS Registry Number for mineral oil USP grade is 8012-95-1, although there are many other registry numbers (Section 13.1). Non-USP grade mineral oils have a primary CAS Registry Number of 8020-83-5, and other registry numbers (Section 13.2). Mineral oils have been divided into two major classes, high viscosity and medium and low viscosity, with the latter group subdivided into Class I, Class II, and Class III. Properties of these classes are shown in Table 1.

Table 1. Classification of mineral oils (JECFA, 1995; JECFA, 2002)

Property	High Viscosity	Medium and Low Viscosity		
		Class I	Class II	Class III
Viscosity at 100 °C (mm ² /sec or centistokes)	≥ 11	8.5-11	7.0-8.5	3.0-7.0
Average Molecular Weight	≥ 500	480-500	400-480	300-400
Boiling Point, °C	> 350 °C	> 200 °C	> 200 °C	> 200 °C
Boiling Point, °C at the 5% Distillation Point	> 422 °C	> 391 °C	> 356 °C	> 287 °C
Carbon Number at the 5% Distillation Point	≥ 28	≥ 25	≥ 22	≥ 17

In addition to physical property requirements, USP grade mineral oils are required to meet certain purity requirements. High viscosity USP oils can have no more than 1 mg/kg arsenic or lead and no more than 10 mg/kg total heavy metals, and are required to pass an ultraviolet absorption test to limit total polycyclic aromatic hydrocarbon content. Medium and low viscosity oils have the same requirements on lead and polycyclic aromatic hydrocarbons. Most references indicate mineral oils are insoluble in water (Budavari et al., 1996; HSDB, 2004). Chemfinder (2004) lists mineral oil solubility as < 0.1 g/100 mL at 18 °C. RIVM (2004) provides several equations for the calculation of the solubility of liquid aliphatic compounds based on log K_{ow} . However, log K_{ow} values were not located for any class of mineral oils.

2.1 Organoleptic Properties

Refined (food grade, USP) mineral oil is reported to be odorless (JECFA, 1995; JECFA, 2002) and practically tasteless (Budavari et al., 1996), even when warmed.

3.0 PRODUCTION AND USE

3.1 Production

Mineral oils are produced by a variety of methods and are available in a variety of grades (IARC, 1984). Production methods include vacuum distillation, acid treatment of oils of naphthenic or paraffinic origin, solvent-refinement, and hydrogenation. White oils are the most severely refined and are produced by acid and/or hydrogen treatment. Several mineral oils are listed as high production volume chemicals by both the United States and the European Union (U.S. EPA, 2002b; OECD, 2000).

3.2 Use

USP grade mineral oil is used as a laxative, as a vehicle or solvent in pharmaceuticals, and in cosmetics (Budavari et al., 1996). Food-grade mineral oil is used in direct and indirect additive applications (U.S. FDA, 2004). Uses of white mineral oil under 21 CFR 172.878 include as a release agent, binder, and lubricant in capsules and tablets of flavorings, spices, condiments, nutrients, and food for special dietary use and in the manufacture of yeast; as a defoamer in food; as a release agent and lubricant in bakery products; as a release agent in dehydrated fruits and vegetables and in egg white solids; as a protective coating on raw fruits and vegetables; as a hot-melt coating in frozen meat; as a protective float on brine used in the curing of pickles; in molding starch and as a release agent and sealing and polishing agent in the manufacture of confectionery; as an antidusting agent in sorbic acid for food use; and as a dust control agent for wheat, corn, soybean, barley, rice, rye, oats, and sorghum. Uses of synthetic isoparaffinic petroleum hydrocarbons under 21 CFR 172.882 and of odorless light petroleum hydrocarbons under 21 CFR 172.884 include as a coating on shell eggs, in the froth-floatation cleaning of vegetables, as a float on fermentation fluids in the manufacture of certain foods, and as a component of insecticide formulations for use on processed foods. Synthetic isoparaffinic petroleum hydrocarbons may also be used as components of coatings on fruits and vegetables, and odorless light petroleum hydrocarbons may also be used as a defoamer in processing beet sugar and yeast. White mineral oil is listed under 21 CFR 173.340 as a defoaming agent and under 175.230 as a hot-melt strippable food coating. Mineral oil may also be used in a number of indirect food additive applications, including up to 30% by weight as a plasticizer in rubber articles intended for repeated use under 21 CFR 177.2600.

Packaging of household products, drugs, and cosmetics containing greater than 10% low-viscosity hydrocarbons, including mineral oil, is regulated by the U.S. Consumer Product Safety Commission (2003). The U. S. Environmental Protection Agency (U.S. EPA, 2003e) regulates pesticide tolerances and exemptions from tolerances for mineral oil residues in food.

Other grades of mineral oil are widely used in industry as lubricants, plasticizers, or emulsifiers, as a component of cutting oils, and as a heat transfer medium in electrical transformers. Mineral oil is also used as an emulsifying agent in some direct drinking water additives, and can appear as an indirect drinking water additive as a result of its use in a variety of products.

4.0 ANALYTICAL METHODS

Mineral oils are complex hydrocarbon mixtures and can be analyzed as total mineral oil or as individual hydrocarbons.

4.1 Analysis in Water

Total mineral oil in water can be analyzed by total organic carbon, and unsaturated components of mineral oil can be analyzed by their ultraviolet absorption. Most often, mineral oil is analyzed using separation of components by gas chromatography or high-pressure liquid chromatography and detection of components by flame ionization, mass spectrometry, ultraviolet absorption, or by fluorescence for the aromatic oil fraction.

4.2 Analysis in Biological Matrices

Mineral oil components can be extracted from biological matrices and analyzed by the same methods as for water. Mineral oil droplets have been detected microscopically in tissues of humans and laboratory animals (WHO, 1970).

5.0 SOURCES OF HUMAN AND ENVIRONMENTAL EXPOSURE

5.1 Sources of Human Exposure

Occupational exposure to technical grade mineral oils may occur by the dermal route from handling of oils used in various manufacturing processes (ACGIH, 1991; ACGIH, 2000). Inhaled cutting oils have been problematic in those types of operations. Medication is a large but generally intermittent source of human exposure to USP grade mineral oil, while food is the largest consistent source of exposure to food-grade white mineral oils. According to the U.S. FDA (Benz, 1995), a total of 230.1 mg/person-day (~ 3 mg/kg-day for a 70 kg adult) of white mineral oil is ingested from foods in the customary United States diet. Sources include wheat, corn (overall), soybean (overall), barley, rice, rye, oats, sorghum, and other regulated uses at levels of 44.4, 17.6, 34.0, 8.3, 3.6, 0.2, 1.4, 0.6, and 120.0 mg/person-day, respectively. A more recent estimate of the mean mineral hydrocarbon exposure from food sources in the United States is 0.875 mg/kg-day (Heimbach et al., 2002). Exposures to food-grade white mineral oils from food sources in Europe were conservatively estimated to be in the range of 0.39-0.91 mg/kg-day for adults and 0.75-1.77 mg/kg-day for children (Tennant, 2004). These estimates decreased to 0.09-0.20 mg/kg-day for adults and 0.17-0.39 mg/kg-day for children when usage factors were applied. European exposure results in large part from imported grain de-dusted using mineral oil.

5.2 Sources of Environmental Exposure

Traces of n-alkanes occur naturally in plants (WHO, 1974b). Environmental exposure of land, water, or air may occur through many different industrial processes in which mineral oil is used. Discarding of industrial or household chemicals, pharmaceuticals, or foods containing mineral oil contributes to environmental release.

RIVM (2004) published environmental risk limits for mineral oil. In soil and sediment, serious risk concentrations for the ecosystem (SRC_{eco}) for aliphatic fractions ranging up to 12 equivalent carbon numbers were in the range of 14-26 mg/kg dry weight. Aliphatics having 12-16 equivalent carbon numbers had an SRC_{eco} of 280 mg/kg dry weight, and aliphatics of higher carbon equivalents posed negligible risk. In water, the lowest aliphatic group with equivalent carbon numbers of > 5-6 had an SRC_{eco} of 330 $\mu\text{g/L}$. Aliphatics in the range of > 6-8 to > 12-16 equivalent carbon numbers had SRC_{eco} values in the range of 74-1.3 $\mu\text{g/L}$. Again, aliphatics of higher carbon equivalents posed negligible risk.

6.0 COMPARATIVE KINETICS AND METABOLISM IN HUMANS AND LABORATORY ANIMALS

Information in this section has been briefly summarized from the numerous referenced WHO documents. Information reviewed by the WHO was largely from older observations and studies lacking details on the class and purity of the oils, and is therefore very general. Orally administered mineral oil is poorly absorbed (~2%). The small portion that is absorbed is widely distributed and minimally metabolized. The remainder is eliminated in feces.

6.1 Absorption

It has been estimated that 2% of ingested mineral oil is absorbed by the intestinal mucosa in humans, while up to 20% may be absorbed in laboratory animals (WHO, 1970). This estimate does not consider the effect of dose level on absorption.

Mineral oil can interfere with the absorption of the fat soluble vitamins (A and precursors, D, E, and K), fatty acids, and digestible lipids. As long as the dietary intake did not exceed 6,000 ppm (6,000 mg/kg of diet) this interference was not considered by WHO (1970) to be significant for adults, but the effect in children was less certain.

6.2 Distribution

Mineral oil droplets have been observed in mesenteric lymph nodes, nodes of the porta hepatis, liver, spleen, and adipose tissue in humans after ingestion (WHO, 1970). These droplets were seen in approximately 50% of post mortem examinations in the United States and in 10% of post mortem examinations in Western Europe (WHO, 1974b). Mineral oil used as an emulsifier for subcutaneous injections is also widely distributed in the human body (WHO, 1970).

Similar droplets, proportional to the exposure duration, have been observed in rabbits, rats, and guinea pigs. Approximately 20% of ^3H -labeled mineral oil administered orally to rats was found

in the carcass, with 1-5% as unchanged mineral oil and 15% as ^3H -labeled mineral oil substance. The latter portion in part reflected exchange of ^3H with available H, but also may have reflected some metabolism. Most of the radioactivity associated with tritiated mineral oil was detected in the liver, fat, kidney, brain, and spleen (WHO, 1970).

Fleming et al. (1998) reviewed the available information on mineral oil granulomas (lipogranulomas) in humans, noting that oil droplets in human tissues were first reported in 1941. Oil droplets are generally localized in the lymph nodes, spleen, liver, and bone marrow. Up to 85% of portis hepatic lymph nodes, 24-75% of spleens, and 48% of livers contain oil droplets. An increasing incidence with age has been observed, along with higher tissue levels in North America and Australia. The lesions are initially described as collections of oil or lipid droplets that aggregate over time to form a lipogranuloma. This lesion is distinct from the follicular epithelioid granuloma observed in rats. According to the authors, no convincing effects on organ function as a result of the presence of lipogranulomas have been reported. They attributed the presence of oils in human tissue primarily to use of mineral oil as a laxative, but also to food.

6.3 Metabolism

Several studies using ^3H -labeled and unlabeled mineral oil have suggested that metabolism could occur to a very small extent, but no metabolites were identified (WHO, 1970).

6.4 Elimination/Excretion

Approximately 80-98% of orally administered mineral oil is eliminated in the feces of humans and laboratory animals (WHO, 1970).

7.0 EFFECTS ON HUMANS

7.1 Irritation and Sensitization

USP white mineral oil is a major or sole component of many baby oils and therefore is expected to cause minimal skin irritation and/or sensitization. It is used as an emollient in bath oil, and has been described as helpful in the treatment of pruritic and chronic eczematous dermatosis (HSDB, 2004). Material Safety Data Sheets have mixed information on irritation and sensitization. USP white mineral oil is not expected to cause skin irritation upon single or repeated and prolonged contact (Glo Germ, 2000) while white mineral oil may cause skin irritation, defatting of the skin, and dermatitis (Fisher Scientific, 2000).

Inhaled mineral oil or aspiration of ingested mineral oil may lead to a lipid pneumonia or granuloma, with shortness of breath and cough (HSDB, 2004; Glo Germ, 2000).

7.2 Eye Irritation

USP grade mineral oil can be applied to the human eye without discomfort (HSDB, 2004). Material Safety Data Sheets have mixed information on eye irritation of industrial grade mineral oils, with one indicating minimal irritation upon contact (Glo Germ, 2000) and another

indicating severe eye irritation (Fisher Scientific, 2000). The value of this information is very limited given the absence of information on the composition of the various oils and the dose.

7.3 Single-Exposure Studies

The oral lethal dose of mineral oil to humans has been reported as 15 g/kg, rendering it practically non-toxic (HSDB, 2004). Acute symptoms of over-exposure include diarrhea, vomiting, abdominal pain, lassitude, thirst, weakness, and edema.

7.4 Repeated Dose Exposure

Although ingested mineral oil can accumulate to a small extent in various human organs and tissues, no adverse health effects associated with this observation have been identified (WHO, 1970; WHO, 1974b). Some reports that accumulation was accompanied by inflammatory or granulomatous reactions could not be fully evaluated because of inadequate details regarding the level of intake (WHO, 1995a). Data are inadequate to determine whether accumulation occurs as a result of low-level exposures from food sources or higher-level exposures from laxative and other pharmaceutical exposures.

Post mortem examination of a 55-year-old man who had consumed ~ 10 mg/day of n-alkanes in apples for 18 years had small granulomas, particularly in the axillary and apical lung areas but also in other organs and tissues. Needle-like inclusions consisting of long-chain n-alkanes were microscopically observed in giant macrophage cells.

Occupational exposure to mineral oils is common (ACGIH, 1991). The oils used in industry are not generally highly refined and may include carcinogenic impurities such as polycyclic aromatic hydrocarbons. Occupational exposure generally occurs by the inhalation and/or dermal routes. “There is sufficient evidence from studies in humans that mineral oils (containing various additives and impurities) that have been used in occupations such as mulespinning, metal machining and jute processing are carcinogenic to humans” (IARC, 1984).

8.0 EFFECTS ON LABORATORY ANIMALS AND *IN VITRO* TEST SYSTEMS

Information in this section prior to the definitive studies reported in the mid 1990s has been briefly summarized from the numerous referenced WHO documents. Studies and reports prior to 1995 generally do not describe the oil type, class, dose, or impurities in sufficient detail for them to be useful in quantitative risk assessment and have not been re-evaluated.

The irritation and sensitization potential of mineral oil appears to depend upon its purity. Repeated dose oral studies of well-classified oils in laboratory animals have identified systemic accumulation of some oils at high doses in F-344 rats, including mesenteric lymph node histiocytosis and liver granulomas. These effects were reproducible in F-344 rats but did not occur in Sprague-Dawley CRL:CD rats in a comparative study. These effects were also not observed in Long-Evans rats or in Beagle dogs, although the maximum doses given these animals was lower than the maximum doses in the other studies.