HYDROCARBON RESIN, HYDROGENATED

SYNONYMS

Hydrocarbons, C6-20, polymers, hydrogenated

CHEMICAL STRUCTURE

Hydrocarbons, C6-20

CHEMICAL FORMULA

Hydrocarbons, C6-20

IDENTIFIER DETAILS

CAS Number	:	69430-35-9
CoE Number	:	-
FEMA	:	-
EINECS Number	:	-
E Number	:	-

CLP CLASSIFICATION

Ingredient CLP Classification: No

Endpoint	Classification	Category
Acute Oral Toxicity	-	-
Acute Dermal Toxicity	-	-
Acute Inhalation Toxicity	-	-
Skin Corrosive/irritant	-	-
Eye Damage/Irritation	-	-
Respiratory Sensitisation	-	-
Skin Sensitisation	-	-
Mutagenicity/Genotoxicity	-	-
Carcinogenicity	-	-
Reproductive Toxicity	-	-
Specific Target Organ Toxicity	-	-
Aspiration Toxicity	-	-

SPECIFICATIONS

Melting Point: No specific data available
Boiling point: No specific data available.

STATUS IN FOOD AND DRUG LAWS

CoE limits:

Beverages (mg/kg)	Food (mg/kg)	Exceptions (mg/kg)
-	-	-

Acceptable Daily Intake:

ADI (mg/kg)	ADI Set by	Date Set	Comments
-	-	-	-

FDA Status:[CFR21]

Section Number	Comments
-	-

HUMAN EXPOSURE

Natural Occurrence: Although derived from natural sources, hydrogenated hydrocarbon resins are synthetically manufactured.

Reported Uses: Wide range of applications including; synthetic fibre manufacture, lubricants, and as additives in inks and paints.

TOXICITY DATA

Although no specific data has been identified for hydrocarbon resin, hydrogenated, it is believed to be toxicologically similar to other complex hydrocarbon mixtures e.g. liquid paraffin.

In Vivo Toxicity Status

Acute data [obtained from [RTECS, 2002]]:

Oral-Mouse	LD_{50}	22g/kg
Ihl-Man	TCL_0	5 mg/m^3/ 5 yr intermittent treatment
Ipr-Mouse	TDL_0	14 g/kg
Ipr-Mouse	TD	60 g/kg/17 wk intermittent treatment
Ipr-Mouse	TD	50 g/kg/9 wk intermittent treatment
Ipr-Mouse	TD	72 g/kg/26 wk intermittent treatment
Skin-Rat	TDL_0	5200 ul/kg/13 wk intermittent treatment
Skin-Mouse	TDL_0	20800 ul/kg/13 wk intermittent treatment
Skin-Mouse	TDL_0	332 g/kg/ 20wk intermittent treatment

The probable human oral lethal dose is reported to exceed 15 g/kg for a 70 kg person [HSDB].

Male Sherman rats administered a dose of 2ml/kg bw mineral oil [gavage] for a period of three months was reported to be without toxic effects [HSDB, 2002].

The injection [i.p] of 30 cc paraffin oil into rabbits was reported to produce 'well-spread' metaphases in the peritoneal cavity [2.8 %] [HSDB, 2002].

In a recent review of the toxicity of mineral oils JECFA (2003) examined toxicity data for the following classes of mineral oils:

P100 oil, crude: paraffinic, viscosity (40°C): 100 mm^2/s
P70 oil, crude: paraffinic, viscosity (40°C): 70 mm^2/s
P70(H) oil, crude: paraffinic, viscosity (40°C): 70mm^2/s, hydrotreated (catalytic hydrogenation).
N70(H) oil, crude: naphthenic, viscosity (40°C): 70mm^2/s, hydrotreated (catalytic hydrogenation
P15(H) oil, crude: paraffinic, viscosity (40°C): 15mm^2/s, hydrotreated (catalytic hydrogenation.
N15(H) oil, crude: naphthenic, viscosity (40°C): 15mm^2/s, hydrotreated (catalytic hydrogenation).

Differences in the disposition and pharmacokinetics of a low-viscosity mineral oil were assessed in rats of two strains given a representative mineral hydrocarbon component. Female Fischer 344 and Sprague-Dawley rats received a single dose by gavage of 2 ml/kg bw of a 4:1 mixture (v/v) of olive oil and a food-grade paraffinic white mineral oil meeting the specifications for medium- and low-viscosity mineral oil class III, containing [1-^{14}C]-1-eicosanylcyclo-hexane and a non-absorbable marker, [1,2-^{3}H]polyethylene glycol 4000. The dose of mineral oil was 340 mg/kg bw. The rats were placed in metabolism cages for collection of urine, faeces and expired air at regular intervals over 96 h. For the study of pharmacokinetics, the rats received the same single dose of the olive oil: mineral oil mixture containing [1-^{14}C]-1-eicosanylcyclohexane by gavage. The authors concluded that Sprague-Dawley rats can efficiently metabolize and excrete ^{14}C-containing compounds, whereas the inability of Fischer 344 rats to clear these compounds from the liver probably resulted in deposition and possible retention. The amount of radioactivity in the mesenteric lymph nodes was similar in Fischer 344 and Sprague-Dawley rats until the 96-h sampling time, when the percentage of the administered radioactivity increased by nearly 10-fold, from 0.002% to 0.02%, in Sprague-Dawley rats [JECFA 2003].

Animals on the C80 wax diets had increased food intake during weeks 1–4 of both studies. Increases in the absolute and relative (to body weight) weights of liver, spleen and mesenteric lymph nodes were observed with some of the mineral hydrocarbons at both 4 and 13 weeks. The liver weights were statistically significantly increased in the group given N15H low-viscosity oil at 4 weeks and in those given N15H and low-melting-point paraffin wax at 13 weeks. The weights of the mesenteric lymph nodes were increased in the groups given low-melting-point paraffin wax, C80 wax and N15H oil at 4 and 13 weeks and in those given N70H, but not the P70H medium-viscosity oil, at 13 weeks. At 4 weeks, spleen weights were increased only with the N70H and P70H medium-viscosity oils, while at 13 weeks increases in spleen weights were observed only with the low-melting-point paraffin wax, C80 wax and

N15H oil. Significant histopathological alterations were found in the cervical and mesenteric lymph nodes, liver, heart and small intestine. The incidence and severity of the findings were more marked at 13 than at 4 weeks and were associated primarily with ingestion of low-melting-point paraffin wax.

A qualitative investigation was conducted to determine whether low-melting-point paraffin wax accumulated in the liver and Kupffer cells of female Fischer 344 and Sprague-Dawley rats fed 0 or 2% in the diet for 14, 30 or 60 days. Extracts of livers from Fischer 344 rats fed 2% in the diet for 60 days and of Kupffer cells from Fischer 344 rats treated for 14 and 30 days contained detectable amounts of low-melting-point paraffin wax. In contrast, Sprague-Dawley rats did not accumulate detectable amounts in liver or Kupffer cells, as determined by gas chromatography and mass spectrometry [JECFA 2003].

The effects of low melting-point paraffin wax on cell infiltrates in the liver, mesenteric lymph node and selected cardiac mitral valves were evaluated in Fischer 344 and Sprague-Dawley rats. Increased grades of hepatocellular and Kupffer cell vacuolation were apparent in both rat strains in response to a diet containing low melting-point paraffin wax. The earliest observed change in the Fischer 344 rats was small, mostly centrilobular vacuoles at day 30, which increased in size and distribution with duration of treatment. Lipid-like pseudocysts and granulomatous inflammation associated with the lipid-like material developed with increasing grade as a function of duration of treatment. Vacuolar changes were also observed in hepatocytes of Sprague-Dawley rats but to a much lesser extent than in Fischer 344 rats. The primary change in mesenteric lymph nodes of both strains of rat in response to a diet containing low melting-point paraffin wax was formation of granulomas composed of epithelioid macrophages. The severity and incidence of the changes was greater in the Fischer 344 rats [JECFA 2003].

In a comparison of the effects of dietary administration of low melting-point paraffin wax on Kupffer-cell function and morphology in female Fischer 344 and Sprague-Dawley rats, the animals received either control diet or a diet containing 2% low melting-point paraffin wax for 60 days in two separate studies. Mean body weights were not affected by consumption of diets containing low melting-point paraffin wax. In treated female Fischer 344 rats, the serum activity of the liver enzymes was increased and the total leukocyte and neutrophil counts were significantly higher than those of untreated controls. No such differences were seen in Sprague-Dawley rats. The concentration of mineral hydrocarbon in the liver of treated Fischer 344 rats was 3.6 ± 0.65 mg/g liver, but none was detected in the livers of untreated control Fischer 344 rats or treated or untreated Sprague-Dawley rats. Microgranulomas were observed in the livers of all treated Fischer 344 rats but in only one treated Sprague-Dawley rat, in addition to small areas of focal necrosis, lymphoid cell aggregates and increased frequency of cytoplasmic vacuoles [JECFA 2003].

Groups of 10 female rats of each strain were fed a standard diet containing 0.0, 0.2 or 2.0% low-melting-point paraffin wax (100% pure) (equal to 0, 160

and 1600 mg/kg bw per day) for 90 days or 0.0 or 2.0% for 30 or 60 days. For the analysis of mineral hydrocarbon, groups of five female rats of each strain were fed diets containing 0.0, 0.2 or 2.0% low-melting-point paraffin wax for 90 days or 2.0% for 30 or 60 days. No deaths occurred during the study. Treatment did not adversely affect body-weight gain, food consumption or physical parameters in either strain. In the Fischer 344 rats, statistically significant, treatment-related effects were observed in: haematological parameters (decreased erythrocyte count, erythrocyte volume fraction, haemoglobin concentration and platelet count; increased neutrophil count; clinical chemistry parameters (increased activity of alanine and aspartate aminotransferases, alkaline phosphatase and *gamma*-glutamyl transpeptidase; decreased serum albumin); organ weights (increased liver, mesenteric lymph node, spleen and ovary weights), macroscopic findings included (discoloured liver, enlarged mesenteric lymph nodes); and histological changes in the liver (increased incidence and severity of vacuolated hepatocytes, time-related development of microgranulomas, lymphoid-cell infiltrates or aggregates and scattered foci of necrosis), mesenteric lymph nodes (increased incidence and severity of microgranulomas and reticuloendothelial-cell hyperplasia), cervical lymph node (development of microgranulomas in 3/9 animals at the high dose), spleen (increased severity of extramedullary haematopoiesis) and heart (time-related increase in incidence of lymphoid-cell infiltrates in the base of the mitral valve).

In animals at the high dose, many of these effects were seen as early as 30 days into the study. With the exception of inflammation of the mitral valve (affecting 1/10, 2/10 and 5/10 rats in the control group and at the low and high doses, respectively) and microgranulomas in the cervical lymph node (affecting 0/10, 2/9 and 3/9 rats in the three groups, respectively), the histopathological changes affected all rats at the high dose (10/10). Slight reticuloendothelial cell hyperplasia was also observed in the Peyer patch of the jejunum of one of three Fischer 344 female rats at the high dose. The only treatment-related effects observed in the Sprague-Dawley animals were increased weight of the mesenteric lymph nodes accompanied by microscopic changes (microgranulomas and reticuloendothelial-cell hyperplasia) [JECFA 2003].

The authors also reported that the mineral hydrocarbon concentrations in tissues measured over the course of the study were also indicative of a clear strain difference. The Fischer 344 rats showed a significant, time- and dose-related accumulation of mineral hydrocarbon in the mesenteric lymph nodes and liver. No plateau was seen during the 90 days of the study. In Sprague-Dawley rats, slight accumulation of mineral hydrocarbon was observed only in the mesenteric lymph nodes and only after 90 days of treatment. There was no notable accumulation in the heart, kidney or spleen in either strain of rat, regardless of dose and treatment duration [JECFA 2003].

A 28-day study and a 90-day study were conducted to confirm the findings of previous feeding studies with mineral oils and waxes and to extend these observations to include a synthetic wax and a wider range of tissue samples for histopathological examination and chemical analysis. Groups of 12 female

Fischer 344 rats were fed diets for either 28 or 90 days containing 2% of low-melting-point wax, C80 synthetic wax or one of three white oils, N15H (mineral oil, medium and low viscosity, class III), N70H (mineral oil, medium and low viscosity, class II) or P70H (mineral oil, medium and low viscosity, class I), providing doses of 2500, 2600, 2500, 2600 and 2600 mg/kg bw per day, respectively, for the groups treated for 28 days and 2100, 2100, 2000, 2000 and 2100 mg/kg bw per day, respectively, for those treated for 90 days. Respective control groups received standard diet containing <0.01% mineral hydrocarbon by weight. No deaths were reported. Consumption of 2% mineral hydrocarbon in the diet did not affect body-weight gain. Food consumption was statistically significantly increased in the groups receiving the white oils (N15H, N70H and P70H) throughout most of the treatment period of each study. While increased food consumption was noted with diets containing low-melting-point paraffin wax at various times during the first 10 weeks of the 13-week study, no difference from controls was observed during the 4-week study.

Histiocytosis was seen in the lymph nodes of rats in all groups except those receiving N70H medium-viscosity oil for 4 weeks or P70H medium-viscosity oil for either 4 or 13 weeks. The incidence, severity (progression to individual cell necrosis) and onset were greater in mesenteric than in cervical nodes and in proximal mesenteric than in distal mesenteric nodes. The combined incidence and severity scores indicated a rank order of low-melting-point paraffin wax > C80 wax, N15H oil > N70H oil > P70H oil. Other changes identified at 13 weeks in nearly all (6–8/8) rats receiving low-melting-point paraffin wax in the diet included: hepatic focal necrosis with inflammation, periportal vacuolation and granuloma; and focal inflammation of the mitral valve of the heart and macrophage accumulation, particularly in Peyer patches of the small intestine. Periportal vacuolation was also observed in the livers of 7/8 rats receiving dietary C80 wax; vacuolation of macrophages was found in the lamina propria of the small intestine; granuloma of lower severity was seen in the livers of 7/8 rats; and focal inflammation of the cardiac mitral valve was recorded in 3/8 rats receiving N15H low-viscosity oil. Calcification of the renal medulla was exacerbated at both 28 and 90 days by dietary treatment with the white oils and marginally by treatment with the waxes [JECFA 2003].

Carcinogenicity and mutagenicity

Thirty BD1, BD111 and W rats [unspecified sex] given 2 % liquid paraffin in the diet to give a total dose of 136 mg/animal in 500 days] did not show any signs of tumour induction, [HSDB, 2002]. Similarly a study in which three different grades of petroleum were administered to 50 male and female FDRL weanling rats in the diet at a concentration of 5 % for a period of 2 years did not reveal any treatment-related tumour effects [HSDB, 2002].

A group of 36 DBA/2 and 12 CBA female mice given a total of 1.5 ml of Primol D mineral oil in three i.p. injections over a period of 15 weeks and then survivor's sacrifices at 24 months revealed small intraperitoneal granulomatous nodules containing oil droplets in all animals. Forty-two percent of the mice [DBA/2] developed reticulosarcomatous growths in some

of the peritoneal nodules with leukemic infiltrations of varying severity found in the livers of several mice, [occurrence less frequent in other organs]. Only one of the CBA mice developed reticulum cell sarcoma. In contrast BALB/C mice given mineral oil i.p. developed plasma cell neoplasms in intraperitoneal nodules. However, the purity of the mineral oil samples in the study was unknown. The authors indicated that the sample contained an impurity having similar physical properties to those of carcinogenic polycyclic aromatic hydrocarbons [WHO, 1976].

RTECS, (2002) reported that liquid paraffin is a known human carcinogen [RTECS, 2002].

Untreated and mildly treated oils are carcinogenic to humans [IARC group 1] whereas highly refined oils are not classifiable as to their carcinogenicity to humans, [IARC group 3] [IARC evaluation, 1987].

Administration of either oil to Fischer 344 rats in the diet for 24 months did not affect survival. No treatment-related effects were seen on clinical signs, body weight, food consumption, food conversion efficiency, ophthalmic, haematological, serum chemical or urinary parameters, and no treatment-related changes were seen at gross necropsy. Dietary administration of both oils was associated with increased weight of mesenteric lymph nodes and increased grade of infiltrating cell histiocytosis; increased incidence and grade of vacuolation of periportal hepatocytes; increased incidence of combined cystic degeneration or angiectasis of the liver of male rats, with no dose–response relationship; and a quantifiable, reversible accumulation of mineral hydrocarbons in the liver to a similar level regardless of dose but dependent on the type of mineral oil. The effects were more marked in rats treated with P70H oil than with P100H oil, and there were sex-related differences in response. Neither oil was carcinogenic in this assay [JECFA 2003].

Treatment for 24 months with medium-viscosity white mineral oil (P70 (H)) resulted in a dose-related, statistically significant increase in mean mesenteric lymph node weight, both absolute and relative to body and brain weight, at all doses in female rats and at the highest dose, 1200 mg/kg bw per day, in males. Mesenteric lymph node weights were also statistically significantly increased in males at the highest dose after 12 months' feeding; this effect was no longer significant after the 12-month recovery period owing to an increased value for this parameter in the control group. No significant differences in mesenteric lymph node weights were observed in females after 12 months of treatment, although, after the 12-month recovery, a slight but significant increase was seen in females at the two higher doses, 240 and 1200 mg/kg bw per day. The grade, but not the incidence, of infiltrating cell histiocytosis of the mesenteric lymph nodes was increased in all treated groups after 24 months of treatment. In addition, there was a slight increase in the severity of this lesion in animals at the highest dose, the only group assessed, at the 12-month sacrifice. After the 12-month recovery period, these changes were apparent in all groups, at a severity greater than or comparable to that in the animals treated for 24 months [JECFA 2003].

Parallel studies were conducted to assess the long-term toxic and carcinogenic effects of P70(H) mineral oil (medium and low viscosity, class I) and P100(H) mineral oil (high viscosity) in male and female Fischer 344 rats after 2 years' administration in the diet. Five groups were used for each study: a control group and groups given concentrations in the diet corresponding to a dose of 60, 120, 240 or 1200 mg/kg bw per day. Groups of 50 male and 50 female animals were used in the main (24-month) study, with additional groups of 30 male and 30 female animals for the reversibility phase (treatment for 12 months followed by 12 months on control diet). Of the 30 animals of each sex per group in the reversibility phase, 10 animals of each sex per group were killed after the 12-month feeding period [JECFA 2003].

A dose-related increase in the incidence and grade of vacuolation of periportal hepatocytes was observed in the livers of males in all treated groups. The investigators did not consider this indicative of an adverse effect but rather a marker of prolonged exposure to mineral oil. Histological analysis revealed quantifiable amounts of hydrocarbon in the livers of treated animals; the hepatic concentrations of mineral hydrocarbon in animals at the highest dose reached nearly a maximum within 3 months and increased slowly up to 24 months of treatment. The values for animals at 60, 120 and 240 mg/kg bw per day at 12 and 24 months were 1200–1500 µg/g tissue, which were similar to each other and were approximately 60% of those of animals at 1200 mg/kg bw per day (1800 and 2300 µg/g tissue, respectively). After cessation of treatment, the hepatic concentrations had dropped substantially by 6 months and had returned to background levels by 12 months. The amount of mineral hydrocarbon in the spleen and mesenteric lymph nodes of most treated animals at higher doses was below the practical limit of reliable quantification.

After 24 months of treatment with high viscosity white mineral oil (P100 (H)), statistically significant increases in mean mesenteric lymph node weights (absolute and relative to body weight and brain weight) were observed in females at 1200 mg/kg bw per day. This effect was not evident at lower doses or in male rats or after the recovery period. A marginal increase in the grade, but not the incidence, of infiltrating cell histiocytosis in the mesenteric lymph nodes was observed in all treated groups at 24 months. No clear dose–response relationship was apparent in the males, and no effects were observed at 12 months of treatment [JECFA 2003].

A slight increase in the incidence and grade of vacuolation of periportal hepatocytes was observed in the livers of treated animals of each sex in all treated groups compared with controls. An increase in the incidence of combined angiectasis and cystic degeneration (focal sinusoidal dilatation) was observed in all treated male groups, without a dose–response relationship, which was statistically significant in animals given 1200 mg/kg bw per day. This lesion was not apparent at the 12-month sacrifice. In view of the nature and severity of the response, the investigators did not consider the increased grade of vacuolation to be indicative of an adverse toxicological effect but rather a marker of prolonged administration of white oil [JECFA 2003].

Histological analysis revealed quantifiable amounts of hydrocarbon in the livers of treated animals; the hepatic concentrations of mineral hydrocarbon in

animals at the highest dose reached nearly a maximum within 3 months (900 µg/g tissue) and increased slowly up to 24 months of treatment. The concentrations in the liver at 12 and 24 months were similar in all treated groups (800–900 and 1200–1400 µg/g tissue, respectively), suggesting that a steady-state level had been reached. After cessation of treatment, the hepatic levels had dropped substantially by 6 months and had returned to background levels by 12 months. Mineral hydrocarbon was found in mesenteric lymph nodes and spleen at some times. The concentrations in the spleen and mesenteric lymph nodes of most treated animals at the higher doses were below the practical limit of reliable quantification [JECFA 2003].

A medium-viscosity white mineral oil (mineral oil, medium- and low-viscosity, class I), a blend of equal quantities of eight commercially available paraffinic white mineral oils obtained from eight member companies of the Japan Liquid Paraffin Industry, was fed in the diet to Fischer 344 rats. The oils also complied with the requirements of the Japanese food additive standards and the Japanese pharmacopoeia. Five of the component white mineral oils had been derived from petroleum by acid treatment, and the other three had been derived by hydrotreatment. The physical properties of the blended mineral oil were intermediate between those of P70H and N70H [JECFA 2003].

Groups of 50 male and 50 female Fischer 344 rats were fed diets containing 2.5% or 5% of the composite medium-viscosity white mineral oil (equivalent to 1250 and 2500 mg/kg bw per day), continually for 104 weeks. The food consumption and body weights of animals of each sex given 5% mineral oil were slightly increased. The frequency of clinical signs, mortality and haemato-logical parameters were unaffected by treatment. In the group given 5%, the absolute weights of the liver and kidney were increased in males and the absolute and relative weights of the submaxillary gland were reduced in females. The increased absolute organ weights were attributed to the slightly increased body weights of males at this concentration. The absolute and relative weights of the heart and spleen were unaffected by treatment. A variety of tumours developed in all groups, including the control group, but all the neoplastic lesions were histologically similar to those known to occur spontaneously in Fischer 344 rats, and no statistically significant increase in the incidence of any tumour type was found for either sex in the treated groups. An increased grade of small granulomatous foci of macrophages was observed in the mesenteric lymph nodes of both sexes at 2.5 and 5% in comparison with the respective control groups [Shoda *et al.,* 1997].

Fifteen rabbits fed 25 ml of a 1:1 mixture of olive and paraffin oil [undisclosed purity] and were sacrificed after a period of 60-406 days of treatment revealed a weight loss from the first to third week however, after this period weight gain was parallel to that of the control animals. There was a reported preferential deposition in the liver and the spleen, and on histological examination diffuse hyperplasia of reticuloendothelial cells was observed. The authors commented that the on histological examination cells resembled those seen in Whipples disease [WHO, 1976].

Dermal toxicity and irritation studies

100 mg of liquid paraffin [24 hour, not stated if covered patch] was reported to be a mild skin irritant. Similarly this concentration was reported to be a mild irritant to guinea pig skin [RTECS, 2002].

Liquid paraffin was reported to be a moderate irritant at 500 mg to rabbit eyes [RTECS, 2002].

Liquid petrolatum has been reported to be applied to human eyes without any reported discomfort or irritation, [HSDB, 2002]. However, another report stated that liquid petrolatum can cause folliculitis and miliaria [HSDB, 2002].

The injection of liquid petrolatum into the lacrimal system of patients already diagnosed as having chronic 'watery eye' due to narrowing of the tear duct apparatus produced inflammation in one eye and additional infiltration and altered eye motion in the other eye [HSDB, 2002].

Reproductive and developmental toxicity

25 chicken embryos [9 days] exposed to 10 or 20 ul mineral oil onto the egg-shell did not result in any mortalities, oedematous embryos, ascites or liver lesions. No histological changes were also reported in the liver or kidneys, however, at the concentration of 20 µl embryos were reported to have a slight dilation of the heart, body weights, crown length, body weight/crown-rump length ratio were not significantly different from that of the controls [HSDB, 2002].

Other relevant studies

Over half the Kupffer cells isolated from Fischer 344 rats treated with low melting-point paraffin wax contained large, irregularly shaped vacuoles, and another 10–20% had numerous smaller vacuoles. The vacuoles were membrane-associated, suggesting phagocytic uptake. Similar vacuoles were detected only rarely in Kupffer cells isolated from Sprague-Dawley rats. The indices of Kupffer cell function—production of superoxide anion and nitric oxide and phagocytic activity—were increased, and TNF-*alpha* and leukotriene B4 production were decreased in treated Fischer 344 rats compared with untreated controls. No significant changes in these functions were observed in Kupffer cells isolated from treated Sprague-Dawley rats [JECFA 2003].

The inflammatory changes in the mitral heart valve of Fischer 344 rats were slight and consisted of phenotypically mixed cell populations. They were also observed in one control animal, leading the investigators to conclude that the observation was of questionable significance. Only limited numbers of tissues were available for examination. The authors suggested that the data were consistent with a difference in pharmacokinetics between the strains, related to metabolic capacity, resulting in saturation of enzyme systems and accumulation of lipid-like crystalloids, cell disruption and inflammation [JECFA 2003].

Czerczak and Kupczewska, (2002) reported the Maximum Allowable Concentration [weighted average concentration during an 8-hour shift system and 42 hour week that should not cause adverse health effects in a worker or their descendants] as 5 mg/m^3 and the short-term exposure limit value of 10 mg/m^3 [concentration not causing adverse health effects in workers or their descendants if they remain in the working environment no longer that 30 minutes during a working shift] for Poland [Czerczak and Kupczewska, 2002].

The time-weighted average for liquid paraffin in Belgium [TWA] was reported to be 5 mg/m^3 [RTECS, 2002].

Peachee *et al*., (2001) reported differences in humoral immune foreign body responses to mineral oil [90 days included in feed] between F344 [fed 0.02 or 2 %] and SD [fed1 or 2 %] rats. No effect was observed with the SD rats however, a significant reduction of 40 % was reported in the F344 rats, [Peachee *et al*., 2001].

The use of mineral oil is not advisable in children under the age of 6, [as children in this age group are more prone to aspiration of oil droplets, which may produce lipid pneumonia] bedridden, geriatric, debilitated, or pregnant patients and in patients with oesophageal or gastric retention, dysphagia or hiatal hernia [HSDB, 2002].
Mineral oil is considered to be relatively non-toxic and in cases of chronic mineral oil pneumonia, [caused by laxative administration] expectoration has been reported to improve patient prognosis [HSBD, 2002].

Mineral oil has been reported to produce lipid pneumonitis on access to the lungs [usually in cases when used as a vehicle for nasal drug application]. However, it has also been reported after oral ingestion [HSDB, 2002]. It has also been claimed that mineral oil can alter postoperative wounds in anorectal regions, with the continual presence of oil in the rectum affecting defecatory reflexes [HSDB, 2002].

Granulomatous reactions in lungs observed after the usage of nasal drops and sprays which include mineral oils usually result in marked fibrosis and encystment with a similar effect observed with daily oral doses of 30 – 90 ml for a period of many months. Fatality has been reported as a result of this complication, [HSDB, 2002]. The oral ingestion of mineral oil is also reported to result in visceral lipid deposition [HSDB, 2002].

An incidence in which mineral oil was injected into the pleural cavity, [Granugenol, unknown amount] for the treatment of empyema resulted in an immediate loss of vision, severe headache, convulsions and coma. A recovery period of approx. 3 weeks was required for vision to return to normal [HSDB, 2002].

The chronic oral administration of mineral oil during pregnancy is reported to result in hypothrombinemia and hemorrhagic disease [due to reduced absorption of vitamin K] in the newborn [HSDB, 2002].

An investigation into complains from workers exposed to oil mist [below 5 mg/m^3] did not reveal any evidence of skin or respiratory tract irritation, [HSDB, 2002]. However, a similar study into five workers exposed to mineral oil vapours for a period of 5-35 years showed an increased prevalence of slight basal lung fibrosis, [HSDB, 2002]. But a study into 5189 workers exposed to oil mist for a period of 1 year, [unknown concentration] did not reveal an increased incidence of digestive or respiratory tract cancers [HSDB, 2002].

Lipoid pneumonia has been reported in people with a heavy exposure to oil mist in the absence of an adequate ventilation system [HSDB, 2002].

The administration of mineral oil with meals has been reported to interfere with fat-soluble material [e.g. vitamin] absorption. In the intestines mineral oil can elicit foreign body reactions in the intestinal mucosa, mesenteric lymph nodes, liver and spleen. The safe long-term use of mineral oil is therefore reported to be questionable [HSDB, 2002].

The continual ingestion of large amounts on mineral oil is thought to impair appetite [HSDB, 2002].

The i.p. injection of mineral oil in vaccines has been reported to result in granulomatous reactions at the site of injection, with similar reactions observed when mineral oil has been used as a lubricant [HSDB, 2002].

The injection of mineral oil into the anterior chamber of rabbits to replace the aqueous humor has been reported to produce glaucoma. The authors suggest that this is possibly a mechanical effect rather than a toxic reaction [HSDB, 2002].

Dogs, rats, mice and gerbils exposed to a mineral oil based mist [5 and 100 m^3] 6-hours a day, 5 days a week for a period of 2 years was reported to produce microgranulomas in dogs and rats only at the concentration of 100 m^3 [HSDB, 2002]. Similarly ‘lung inflammatory reactions’, lipoid granuloma formation and lipoid pneumonia, were reported in single and repeated exposures up to a period of six months [concentrations in excess of 100 mg/ m^3]. In studies where exposure has been extended for up to a period of a year [100 mg/ m^3] has also resulted in lung inflammatory reactions and lipoid granuloma formation. It must be noted however that carcinogenic effects have not been reported in any species including studies with susceptible strains of mice [HSDB, 2002].

Mineral oil is reportedly minimally absorbed following its administration orally or rectally [HSDB, 2002].

On administration of H^3-labelled mineral oil [i.p or orally] at 0.66 mg/kg bw it was shown that within five hours of dosing 80 % was not absorbed but excreted in the faeces, 1-5 % was absorbed unchanged and another 15 % appeared in the carcass as H^3-non mineral oil substance, [WHO, 1970].

Radioactivity was found in the liver, fat, kidney and brain. Following the i.p administration only slow excretion was observed. Eight days after injection 11 % was seen in the faeces and only traces were observed in the urine [WHO, 1970].

Labelled mineral oil emulsions given to rats, squirrels and monkeys, [subcutaneous or intramuscular] revealed that mineral oil was retained at the injection site with 60% remaining after a period of one month, with this reducing to 25 % after a period of 10 months, [HSDB, 2002]. The deposition of small quantities of liquid petrolatum in the rabbits, rats and guinea pigs mesenteric lymph nodes, intestinal mucosa and spleen has also been reported after injection of large quantities of liquid paraffin [HSDB, 2002].

The concurrent use of mineral oil with laxatives [acting as a stool softener] may lead to the absorption of mineral oil resulting in the formation of tumour like deposits in tissue [HSDB, 2002].

WHO, (1976) reported that 'mineral oils' have been demonstrated in human tissues after ingestion with no demonstrable pathological consequences. However, its storage is considered to be undesirable and exposure should therefore be kept to a minimum [WHO, 1976].
The toxicity and carcinogenicity of chlorinated paraffins containing C12 with 60% chlorine, and C23 with 43% chlorine, were assessed by Bucher et al., (1987) in prechronic and 2-year gavage studies using F344/N rats and B6C3F1 mice of both sexes. Single administrations of chlorinated paraffins were nonlethal in rats and mice, but repeated-dose and 2-year studies demonstrated toxic responses that differed with the paraffins. The C23, Cl43% paraffin produced a granulomatous inflammation in the liver of female rats in 13-week studies, while the C12,Cl60% paraffin caused deaths of rats and mice in 16-day studies and marked liver enlargement in 13-week studies. In 2-year studies, the C23,Cl43% paraffin caused hepatic and lymphatic granulomatous inflammation and hyperplasia in both sexes of rats, and was associated with marginal increases in adrenal medullary pheochromocytomas in female rats and hepatocellular neoplasms in female mice and with clear increases in malignant lymphomas in male mice. The C12,Cl60% paraffin caused marked liver enlargement in rats and increased the severity of nephropathy in male rats and the incidence of nephropathy in female rats. C12,Cl60% also caused hepatocellular neoplasms in both sexes of rats and mice: kidney tubular cell adenomas and adenocarcinomas in male rats, thyroid follicular cell neoplasms in female rats and female mice, and a marginal increase in mononuclear cell leukaemia in male rats. The authors conclude that the short-chain, heavily chlorinated paraffin appears to have a greater potential for chronic toxicity and carcinogenicity than the longer-chain, lightly chlorinated paraffin.

In both the United Kingdom and the USA, the average total intake of the sum of white mineral oil, paraffin wax and microcrystalline wax from use in food (as direct and indirect food additives) was estimated to be 0.47 mg/kg bw per day, whereas the dietary intake of naturally occurring hydrocarbons from plant and

animal foods was estimated to be 0.47 mg/kg bw per day for the population of the European Union, 0.25 mg/kg bw per day for that of the United Kingdom and 0.19 mg/kg bw per day for that of the USA. As naturally occurring hydrocarbons make a significant contribution to overall hydrocarbon intake in consumers in both the United Kingdom and the USA, it was concluded that the risk assessment of mineral oil residues from various food applications must include the dietary intake of naturally occurring hydrocarbon sources [JECFA 2003].

Behavioural data

No data identified.

***In Vitro* Toxicity Status**

Carcinogenicity and Mutagenicity

Paraffin Waxes have been reported to be nonmutagenic in bacteria (unspecified strain) (NTP, 1986).

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