

RECEIVED
OPPT NCIC

2002 AUG -7 PM 1:16

AR201-13902B

Appendix B.

ROBUST SUMMARY
OF INFORMATION ON

Substance Group:

WAXES
AND
Related materials

Summary prepared by: American Petroleum Institute

Creation date: SEPTEMBER 19, 2000

Printing date: AUGUST 6, 2002

Date of last Update: JULY 23, 2002

Number of Pages: 48

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

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

A systematic approach for evaluating the quality of experimental toxicological and ecotoxicological data.
Regulatory Toxicology and Pharmacology 25, 1-5.

1.1 GENERAL SUBSTANCE INFORMATION

- Substance type** : Petroleum product
- Physical status** : Solid
- : This robust summary covers the waxes and related products which includes:
 - Slack wax
 - Petrolatum
 - Paraffin wax
 - Microcrystalline wax

Petroleum waxes are obtained from paraffinic refinery streams in lubricating oil manufacture. The wax is separated by filtering a chilled solution of waxy oil in a selected solvent (usually a mixture of methyl ethyl ketone and toluene).

SLACK WAX is obtained from the dewaxing of refined or unrefined vacuum distillate fractions. If the material has been separated from residual oil fractions it is frequently called PETROLATUM. The slack waxes are de-oiled by solvent crystallization or "sweating" processes to manufacture commercial waxes with low oil content. The oil that is separated from these processes is known as FOOTS OIL. The refined petroleum waxes are known as PARAFFIN WAXES. MICROCRYSTALLINE WAXES have higher molecular weights than the paraffin waxes and consist of substantial amounts of iso- and cycloalkanes.

1.2 SYNONYMS

- : Paraffin wax
- Slack wax
- Petrolatum
- Microcrystalline wax

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUES

- Type of limit** : TLV (US)
- Limit value** : 2 mg/m³
- Remark** : The UK HSE have established an occupational exposure limit of 2 mg/m³ (8 hour TWA) and a 15 minute Short Term Exposure Limit (STEL) of 6 mg/m³.

(2) (47)

Date 8/6/02

1.17 REVIEWS

Memo Remark : EU SCF
 : The EU Scientific Committee for Food (SCF) reviewed the available information on mineral hydrocarbons, which included the petroleum waxes. Their opinion was published in 1995. The SCF reached the following conclusion:

There are sufficient data to allow a full Group ADI of 0-20 mg/kg bw for waxes conforming to the following specification:-

Highly refined waxes derived from petroleum based or synthetic hydrocarbon feedstocks, with
 viscosity not less than 11 mm²/s (cSt) at 100° C
 Carbon number not less than 25 at the 5% boiling point
 Average molecular weight not less than 500

(43)

Memo Remark : WHO JECFA
 : The WHO Joint Expert Committee on Food Additives (JECFA) reviewed the available information on food grade mineral hydrocarbons. Their evaluation was published in 1996. With respect to waxes they made the following conclusions:

Substance

ADI

	ADI (mk/kg bw)
Paraffin waxes	
LMPW (Low melting point wax)	ADI withdrawn
IMPW (Intermediate melting point wax)	ADI withdrawn
Microcrystalline waxes	
HSW (High sulfur wax)	0-20
HMPW (High melting point wax)	0-20

(33)

Memo Remark : CTFA
 : An independent expert panel reviewed data supplied to them by the Cosmetics, Toiletries & Fragrances Association (CTFA). A report of the evaluation was published in 1984. However, few experimental details are available and the conclusions of the panel cannot be verified. Their overall conclusion was:

Toxicological test data on Ozokerite, Ceresin, Montan Wax, Paraffin, Microcrystalline Wax, Emulsifying Wax N.F., and Synthetic Beeswax are presented. Based on the documented animal and clinical test data, it is concluded that these waxes are safe for use as cosmetic ingredients in the present practices of concentration and use.

(18)

2. Physico-Chemical Data

Id Waxes

Date 8/6/02

2.1 MELTING POINT

Value : 36 - 95° C
: See additional remarks section 2.12

2.2 BOILING POINT

Value : ca. 350 - 500° C
: In a survey of the composition of food grade waxes and oils the boiling range for paraffin wax was reported to be 350-485°C. Microcrystalline waxes boiled in excess of 500 °C.

(11)

2.3.1 GRANULOMETRY

: Not relevant

2.5 PARTITION COEFFICIENT

Log Pow : 4.7 - \geq 6.7
Method : Calculated: KOWWIN Version 1.65 (EPIWIN)
Year : 2001
Test substance : Wax and related materials
Remark : As hydrocarbon number increases above C13, as is the case for the majority of the wax constituents, Log P values >6 are predicted. Substances having Log P estimates greater than 6 are characterized by extremely large molecular weight and subsequent hydrophobicity, therefore no significant aqueous exposures or bioaccumulation are expected to occur.
Result : Octanol-water partition coefficients (log P or Kow) were modeled with isomers of the lowest molecular weight component (C13 hydrocarbons) in waxes. These partitioning estimates are characteristic of only a small fraction of component molecules in a given wax. Because of the diversity of compounds encompassing waxes, it is not feasible to model the physicochemical endpoints for each potential compound. Since molecular weight and structural conformation determines in large part the solubility and vapor pressure characteristics of the hydrocarbons, modeling focused on the lower molecular weight hydrocarbons. These would be selected C13 and C20 hydrocarbons since waxes consist mostly of C20 to C85 compounds, with some minimal percent of C13 through C20 hydrocarbons. Therefore, the majority of the physicochemical modeling was performed on various paraffinic, naphthenic and aromatic representatives containing 13 and C20 carbon atoms.
Reliability : (2) valid with restrictions

(41)

2.6.1 WATER SOLUBILITY

Value : 0.027 - 5.96 mg/l at 25° C
Method : WSKOW Version 1.36 (EPIWIN)
Year : 2001
Test substance : Wax and related materials
Result : The water solubility of waxes cannot be determined due to their complex mixture characteristics. Therefore, the water solubility of individual C13 hydrocarbons was modeled. The highest solubilities would be exhibited by only a small fraction of the hydrocarbon molecules present in waxes. Increasing carbon number results in rapidly decreasing solubility, so that the most-soluble (predominantly methyl-substituted diaromatic) C18 and C20 analogues yield model values of 0.01195 and 0.00125 mg/l, respectively. Higher molecular weight (higher carbon number) components are even less water-soluble. Based on water solubility modeling for C13 components of complex mixtures, aqueous solubilities of these waxes are typically much less than 1 ppm, due to differential partitioning of components between the aqueous and organic phases.

Reliability : (2) valid with restrictions

(13)

2.8 AUTO FLAMMABILITY

: Not relevant

2.9 FLAMMABILITY

: Non flammable

2.10 EXPLOSIVE PROPERTIES

: Not relevant

2.11 OXIDIZING PROPERTIES

: Not relevant

2. Physico-Chemical Data

Id Waxes

Date 8/6/02

2.12 ADDITIONAL REMARKS

: Physico chemical properties for typical grades of wax and petrolatum are shown in the following table.
See also Bennet (1975), Kauffman et al (1993) and EWF (1990).

Melting Point (°C)	Kinematic Penetration viscosity at 100 °C	Oil content (%m/m) (mm ² /sec)	Carbon number range	(25°C)
ASTM D127	ASTM D445	ASTM D721 or D3235	ASTM D2505	ASTM D1321 or D937*
<u>Slack wax</u> 45-85	3-30	2-30	12-85	9-80*
<u>Lower Melt Paraffin Wax</u> 43-74	3-10	<2.5	18-75	9-50*
<u>Microcrystalline Wax</u> 60-95	10-30	<5	23-85	3-60*
<u>Petrolatum</u> 36-60	3-30	>10	12-85	>60

NB * The second value given for penetration was determined using method D937

(6) (20) (35)

3. Environmental Fate and Pathways

Id Waxes

Date 8/6/02

3.1.1 PHOTODEGRADATION

Type : Atmospheric oxidation
Method : Calculated: AOPWin Version 1.89 (EPIWIN)
Year : 2001
Test substance : Wax and related materials
Remark : Although waxes typically have low vapor pressures, volatilization of some lower molecular weight components exhibit relatively high atmospheric oxidation half-lives. Therefore, those compounds that may partition to the atmosphere will be removed through indirect photochemical degradation. All modeled components exhibited rapid degradation in the atmosphere; the value presented represents both the most volatile component and the longest modeled half-life. All other modeled C13 components had both lower volatility and shorter half-lives.
Result : $T_{1/2} = 0.913$ days (10.96 hr) for most volatile C13 component modeled
Reliability : (2) valid with restrictions

(40)

3.1.2 STABILITY IN WATER

Remark : Hydrolysis of an organic chemical is the transformation process in which a water molecule or hydroxide ion reacts to form a new carbon-oxygen bond. Chemicals that have a potential to hydrolyze include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters. Materials in the waxes category are not subject to hydrolysis, as they lack these reactive groups.
Reliability : (1) valid without restriction

(28)

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type : Calculated according to Mackay Level I
Media : Soil, air, water, suspended sediment, and sediment
Year : 2000
Remark : Fugacity-based computer modeling indicated that the majority of high molecular weight hydrocarbons with carbon numbers of C20 and greater in waxes would be distributed to soil. Percent distribution estimates were modeled with C13 to C29 branched paraffins as this class of wax hydrocarbons shows the greater distribution to air. Aromatic compounds with carbon numbers from C13 through C85 will partition principally to soil. Linear paraffins and naphthenes distribute to both soil and air, with increasing partitioning to soil for hydrocarbons greater than C20 as vapor pressure decreases. Physical properties input are those calculated by the EPIWIN Estimation 3.04 program and included in this summary. Since the majority of hydrocarbon components in waxes are primarily normal paraffins of C20 and greater, with moderate to minimal amounts of naphthenics, isoparaffins and trace amounts of aromatics, volatility is not a significant fate process for these petroleum substances due to negligible vapor pressures at ambient temperatures and their high molecular weight. As hydrocarbon number increases above C20, partitioning to soil is the

Concentration of test chemical: Test substance loading was approximately 20 mg/l of medium.

Temp of incubation: 20 ±2°C

Dosing procedure: Each 2-liter vessel contained 1 liter of inoculated medium. The wax was dissolved in heated carbon tetrachloride, then the solution applied to glass fiber filters (13 mm) to obtain about 20 mg wax/filter after evaporation of the solvent. One filter was added to each test material vessel. Controls and reference standards also received glass fiber filters to which CCl₄ was added and allowed to evaporate.

Sampling frequency: Carbon dioxide production was monitored weekly through day 28, and then every other week to day 84. Wax residues were measured only at test termination.

Controls: Yes (blank and positive controls per guideline); abiotic and toxicity checks were not included. Sodium acetate was used as the positive control.

Analytical method: Carbon dioxide production was measured by titrating residual base with 0.1 N HCl. Wax residues were measured by extracting filters with warm heptane and the volume of extract adjusted prior to GC-FID analysis.

Method of calculating biodegradation: Wax was assumed to have a mean composition of [CH₂] for the purpose of calculating ThCO₂ (3.14 mg CO₂/mg wax). The report does not include the mechanics of calculation of the mineralization endpoint. Total hydrocarbon remaining at 84 days was determined by area integration of the chromatograms, and primary biodegradability was determined by comparing the amount of hydrocarbons at the end of the test with the amount on wax-dosed filters prepared at the start of the test.

Other: Two grades of paraffin wax, 52/50 and 58/60 were tested; only the 52/50 grade was tested for 84 days, and in all, three tests were carried out for 52/50. Result below for 28 days is mean of 52/50 average and 58/60 result. An intermediate wax was also tested as noted in results.

Test substance was incubated in the inoculated mineral medium in sealed vessels containing a vial of 0.4 M NaOH (5 ml) suspended in the headspace above the medium (similar to EPA 835-3100). Carbon dioxide evolution resulting from mineralization of the test substance was trapped in the base for periodic quantitation. Base was renewed at each sampling period. GC analysis for parent compound was carried out on the solid phase of the test medium at study termination.

Reliability

: (2) valid with restrictions

(27)

3. Environmental Fate and Pathways

Id Waxes

Date 8/6/02

Type : Aerobic
Inoculum : Oil-contaminated soil from land-farming project
Contact time : 28 - 84 day
Result : Inherently biodegradable
Method : Modified OECD 301B (significant modification)
Year : 1989
GLP : Yes
Test substance : Microcrystalline wax CAS 63231-60-7
Remark : Wax residue analysis showed 65% parent hydrocarbons (mostly n-alkanes greater than C43) remained after 84 days. Most iso-alkanes were degraded regardless of carbon number.

Result : Degradation % after time: 21% of ThCO₂ after 28 days;
25% after 84 days

Kinetic (for sample, positive and negative controls:

Reference (sodium acetate) - Not Reported
Test substance - 21% (28d)

Breakdown Products: None

Test condition : Inoculum: Soil was collected from land-farm used by the investigators to treat oil-contaminated soil. Soil contained 2200 mg/kg mineral oil (generally at greater retention times than wax components, based on chromatograms provided in report), and was a sandy loam comprising 68% sand, 14.2% clay and 10.2% silt with 5.4% OC. Elevated levels of heavy metals were measured in the soil but not considered to be inhibitory to the test. Soil was suspended in mineral medium prior to distribution to test vessels at a loading rate of approximately 80 mg/l. No microbial enumeration was undertaken but performance of the inoculum in degrading a reference standard (sodium acetate at 100 mg/l) provided evidence of inoculum adequacy.

Concentration of test chemical: Test substance loading was approximately 20 mg/l of medium.

Temp of incubation: 20 ±2°C

Dosing procedure: Each 2-liter vessel contained 1 liter of inoculated medium. The wax was dissolved in heated carbon tetrachloride, then the solution applied to glass fiber filters (13 mm) to obtain about 20 mg wax/filter after evaporation of the solvent. One filter was added to each test material vessel. Controls and reference standards also received glass fiber filters to which CCl₄ was added and allowed to evaporate.

Sampling frequency: Carbon dioxide production was monitored weekly through day 28, then every other week through day 84. Wax residues were measured at test termination.

Controls: Yes (blank and positive controls per guideline); abiotic and toxicity checks were not included. Sodium acetate was used as the positive control.

Analytical method: Carbon dioxide production was measured by titrating

3. Environmental Fate and Pathways

Id Waxes

Date 8/6/02

residual base with 0.1 N HCl. Wax residues were measured by extracting filters with warm heptane and the volume of extract adjusted prior to GC-FID analysis.

Method of calculating biodegradation: Wax was assumed to have a mean composition of $[CH_2]$ for the purpose of calculating $ThCO_2$ (3.14 mg CO_2 /mg wax). The report does not include the mechanics of calculation of the mineralization endpoint. Total hydrocarbon remaining at test termination was determined by area integration of the chromatograms, and primary biodegradability was determined by comparing the amount of hydrocarbons at the end of the test with the amount on wax-dosed filters prepared at the start of the test.

Other: Test substance was incubated in the inoculated mineral medium in sealed vessels containing a vial of 0.4 M NaOH (5 ml) suspended in the headspace above the medium (similar to EPA 835-3100). Carbon dioxide evolution resulting from mineralization of the test substance was trapped in the base for periodic quantitation. Base was renewed at each sampling period. GC analysis for parent compound was carried out on the solid phase of the test medium at study termination.

Reliability

: (2) valid with restrictions

(27)

3. Environmental Fate and Pathways

Id Waxes

Date 8/6/02

Type : Aerobic
Inoculum : Naturally-occurring leaf-litter and soil biota (microbes and invertebrates)
Contact time : 6 month
Year : 1989
Test substance : CAS 8002-74-2 and CAS 63231-60-7
Result : Decomposition in the 5 mm mesh bag, which were exposed to invertebrates as well as microbes, proceeded at a higher rate than in the 45 μ m bags. Decomposition in the 5 mm mesh bags was nearly complete within 13 weeks in the autumn/winter test and within 26 weeks in the spring/summer test, while in the 45 μ m bags 25 - 50% was still left after 6 months, based on visual observation. Wax residue analyses also indicated more rapid degradation in the cold-weather experiment.

Waxed and non-waxed (control) paper decomposed at the same rate.

Paraffin wax residue analysis showed after 6 months a complete or nearly complete degradation of the samples in the 5 mm mesh bags (the 52/54 paraffin wax showed 10% residues remaining after the spring/summer experiment and 0% after the autumn/winter experiment).

In the 45 μ m bags, wax residues remaining at the end of the summer exposure were 30 - 50% for the paraffins and intermediate wax, and 60% for the microcrystalline wax. After winter exposure, paraffin wax residues were 10 - 30% of initial, intermediate wax is reported as 80% of initial, and microcrystalline wax residues were 40% of initial. The winter value for the intermediate wax appears incorrect based on the chromatograms, which show smaller peaks for the winter vs. the summer analyses (same scale for both).

Test condition : Inoculum: Waxed paper was placed in nylon bags of different mesh size (45 μ m or 5 mm) to allow colonization by either microbes alone or by microbes and soil fauna. Leaf litter served as the source of the inoculum, and was placed in a layer over the mesh bags at the start of the test.

Concentration of test chemical: Approximately 20 mg of wax per mesh bag.

Temp of incubation: Ambient forest litter layer temperatures. Testing was carried out during two different seasons: spring/summer (April - October 1989) and autumn/winter (November 1989 - May 1990)

Dosing procedure: Each mesh bag contained four 2 x 2 cm squares of waxed paper, which were dried and weighed before they were placed in the bags. The squares were arranged in a single layer within the bags (10 x 10 cm) to avoid sticking together.

Sampling frequency: Samples were retrieved monthly and decomposition of the squares was estimated visually. The remaining sample material was then removed from the bags, cleaned, dried (50 °C) and weighed.

Controls: Non-waxed paper was used as a negative control.

Analytical method:

- 1) Physical decomposition of paper: Each piece of paper was assessed visually according to the scale 100%, 75%, 50%, 25%, 5%, and 0%

decomposition.

- 2) Wax residues were measured by extracting paper with warm heptane and the volume of extract adjusted prior to GC-FID analysis. To prevent interference of the analysis by the mesh bags, soil particles, and base paper, a cleanup step with aluminum oxide was used and as much of the bag material as possible was removed before extraction. The squares (or remnants thereof) from each treatment were pooled before extraction.

Method of calculating biodegradation: The extent of paper decomposition was determined by averaging the visual percent decomposition scores of the four squares. The degradation of the wax was calculated from the analysis of samples taken at the start of the test, combined with analyses of uncoated paper and of field blanks for determination of background interference. Weight differences were not used, as artifacts such as soil particles could not be removed from the waxed surfaces without removing the wax or destroying the paper.

Other: Two grades of paraffin wax, 52/50 and 58/60, intermediate wax, and microcrystalline wax were tested.

Conclusion

- : Waxed paper decomposes at about the same rate as unwaxed paper. Soil invertebrates contribute significantly to the decomposition of waxed paper in leaf litter. Decomposition of waxed paper occurs more rapidly during the autumn/winter, when there is a fresh layer of leaf litter on the ground, than during the spring/summer, when the last fall's leaf litter has been largely reduced to humus.

Reliability

- : (2) valid with restrictions, since positive control data not reported

(26)

3. Environmental Fate and Pathways

Id Waxes

Date 8/6/02

Type : Aerobic
Inoculum : Unacclimated domestic sewage sludge supernatant and forest soil
Contact time : 137 day
Deg. Product : No
Method : Shake flask test
Year : 1989
GLP : No data
Test substance : Paraffin wax CAS 8002-74-2
Result : Degradation % after time: 55 % of ThCO₂ after 31 days;
98.5% after 137 days

Kinetic (for sample, positive and negative controls):

Reference (cellulose) 88.7% after 31 days

Test substance - 55% (31d); 98.5% (137 d)

Test condition : Inoculum: Soil was collected from a state park in central NJ, and sewage sludge was obtained from a domestic sewage treatment plant in Pennington, NJ. The sludge was aerated for 30 minutes and allowed to settle for an additional 30 minutes before the supernatant was withdrawn and filtered through #1 filter paper prior to use as the sewage inoculum. Filtrate was used at a rate of 25 ml/l of test medium (2.5%). Soil was added directly to each test flask at a rate of 0.1 g/l.

Concentration of test chemical: Test substance loading was approximately 10 mg carbon/l of medium.

Temp of incubation: 25 °C

Dosing procedure: Test material was added by direct addition of 11.8 mg grated wax to each test flask. Reference material (cellulose) was also weighed (25 mg) and added to the reference flasks to provide 10 mg C/l.

Sampling frequency: Carbon dioxide production was monitored after 2, 4, 7, 10, 17, and 24 days, and approximately weekly thereafter through day 137.

Controls: Yes (blank and positive controls per guideline); abiotic and toxicity checks were not included. Cellulose was used as the positive control.

Analytical method: Carbon dioxide produced by mineralization of the test substances was absorbed in 0.2 N KOH solution in cuvettes in the headspace of the test vessels. CO₂ production was measured by titrating residual base with 0.2 N HCl.

Method of calculating biodegradation: Wax was assumed to contain 85% carbon for the purpose of calculating ThCO₂ wax). Average titration volumes at each sampling point were corrected for average blank volumes, then the amount of carbon dioxide produced was divided by ThCO₂ to determine percent biodegradation.

Conclusion : Not readily biodegradable; inherently biodegradable and extensively biodegradable in long-term exposures

Reliability : (2) valid with restrictions. Unable to determine GLP status. Study report is in the form of a memo from which some details are lacking. Same details (e.g., temperature log) are also lacking from the raw data provided with the

3. Environmental Fate and Pathways

Id Waxes

Date 8/6/02

report

(5)

Type : Aerobic
Inoculum : Unacclimated domestic sewage sludge supernatant and forest soil
Contact time : 137 day
Result : Extensively biodegraded in long-term test
Deg. Product : No
Method : Shake flask test
Year : 1989
GLP : No data
Test substance : Microcrystalline wax CAS 63231-60-7
Result : Degradation % after time: 27 % of ThCO₂ after 31 days;
67.2% after 137 days

Kinetic (for sample, positive and negative controls):

Reference (cellulose) 88.7% after 31 days
Test substance - 27% (31d); 67.2% (137 d)

Test condition : Inoculum: Soil was collected from a state park in central NJ, and sewage sludge was obtained from a domestic sewage treatment plant in Pennington, NJ. The sludge was aerated for 30 minutes and allowed to settle for an additional 30 minutes before the supernatant was withdrawn and filtered through #1 filter paper prior to use as the sewage inoculum. Filtrate was used at a rate of 25 ml/l of test medium (2.5%). Soil was added directly to each test flask at a rate of 0.1 g/l.

Concentration of test chemical: Test substance loading was approximately 10 mg carbon/l of medium.

Temp of incubation: 25 °C

Dosing procedure: Test material was added by direct addition of 11.8 mg grated wax to each test flask. Reference material (cellulose) was also weighed (25 mg) and added to the reference flasks to provide 10 mg C/l.

Sampling frequency: Carbon dioxide production was monitored after 2, 4, 7, 10, 17, and 24 days, and approximately weekly thereafter through day 137. Controls: Yes (blank and positive controls per guideline); abiotic and toxicity checks were not included. Cellulose was used as the positive control.

Analytical method: Carbon dioxide produced by mineralization of the test substances was absorbed in 0.2N KOH solution in cuvettes in the headspace of the test vessels. CO₂ production was measured by titrating residual base with 0.2 N HCl.

Method of calculating biodegradation: Wax was assumed to contain 85% carbon for the purpose of calculating ThCO₂ wax). Average titration volumes at each sampling point were corrected for average blank volumes, and then the amount of carbon dioxide produced was divided by ThCO₂ to determine percent biodegradation.

Reliability : (2) Valid with restrictions. Unable to determine GLP status. Study report is in the form of a memo from which some details are lacking. Same details (e.g., temperature log) are also lacking from the raw data provided with the report

3. Environmental Fate and Pathways

Id Waxes

Date 8/6/02

(5)

3. Environmental Fate and Pathways

Id Waxes

Date 8/6/02

Inoculum : Activated sludge, domestic
Contact time : 28 day
Method : OECD Guide-line 301 F "Ready Biodegradability: Manometric Respirometry Test"
Year : 1995
GLP : Yes
Test substance : Slack wax (petroleum), hydrotreated CAS 92062-09-4
Result : By day 28, 40% degradation of the test material was observed and indicated that the test material was inherently biodegradable. By day 5, >60% biodegradation of positive control was observed, which meets the guideline requirement. No excursions from the protocol were noted. Biodegradation was based on net oxygen consumption and the theoretical oxygen demand of the test material as calculated using results of an elemental analysis of the test material.

Sample	% Degradation* (day 28)	Mean % Degradation (day 28)
SN 60	50.20, 34.54, 33.92	39.55
Na Benzoate	82.04; 72.88	77.46

* replicate data

Test condition : Fresh activated sludge was obtained one day prior to test initiation, and homogenized in a blender for two minutes. After allowing the sample to settle for approximately 30 minutes, the homogenated supernatant was decanted, avoiding carry-over of solids. Microbial activity of an aliquot of the filtered supernatant was 1E6 CFU/ml, which was determined using microbial agar dip slides. Activated sludge supernatant was added to the test medium at 10 ml/l, and the inoculated medium was continuously aerated with CO₂-free air until the next day when the test systems were prepared. Test medium consisted of glass distilled water and mineral salts (phosphate buffer, ferric chloride, magnesium sulfate, calcium chloride). Test vessels were 1L glass flasks located in a water bath and electronically monitored for oxygen consumption. Test material was tested in triplicate; controls and blanks were tested in duplicate. Test material (Slack wax (petroleum), hydrotreated) concentration was approximately 37 mg/l, equivalent to a theoretical oxygen demand (ThOD) of 127 mg/l. Test material was weighed onto a Gelman type A/E 13 mm glass fiber filter, which was then added to each respirometer flask. Sodium benzoate (positive control) concentration was 53.54 mg/l, and was added using an aliquot of a stock solution. Test temperature was 22 ±1° C. All test vessels were stirred constantly for 28 days using magnetic stir bars and plates.

Reliability : (1) valid without restriction

(22)

4.1 ACUTE/PROLONGED TOXICITY TO FISH

: See remarks in section 4.9 below

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

: See remarks in section 4.9 below

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

: See remarks in section 4.9 below

4.9 ADDITIONAL REMARKS

: The physical size and number of carbon atoms in petroleum waxes and related materials severely limits the ability of these materials to be taken up into living organisms. It is accepted that the ecotoxicity of alkanes of carbon number greater than C₁₀ are not acutely toxic to aquatic organisms at their limit of solubility in water (Adema, 1986). The petroleum waxes, containing hydrocarbons greater than C₁₃, would not be expected to cause acute toxicity to aquatic organisms. The results of toxicity tests with lubricant base oils, which have similar hydrocarbon ranges and some structures in common, show no acute toxicity to freshwater fish, invertebrates, or algae and no chronic effects to aquatic life at concentrations below 1 mg/l. (CONCAWE, 1997)

(4) (12) (13)

: The values of log K_{ow} for individual hydrocarbons increase with increasing carbon number within homologous series of generic types. Quantitative structure activity relationships (QSAR), relating log K_{ow} values of single hydrocarbons to toxicity, show that water solubility decreases more rapidly with increasing K_{ow} than does the concentration causing effects (Abernathy, et al, 1988; Donkin, et al, 1991). This relationship varies somewhat with species, but it follows that there is a log K_{ow} limit for hydrocarbons, above which, they will not exhibit acute toxicity; this limit is at a log K_{ow} value of about 4 to 5 (Abernathy, et al, 1988; Donkin, et al, 1991). It has been confirmed experimentally that for fish and invertebrates, paraffinic hydrocarbons with a carbon number of 10 or higher (log K_{ow} >5) show no acute toxicity (Adema, 1986) and that alkylbenzenes with a carbon number of 14 or greater (log K_{ow} >5) similarly show no acute toxicity (Adema, 1991) From these well-demonstrated solubility 'cut-offs' for acute toxicity of hydrocarbon substances, which directly relate to their physico-chemical properties, it is clear that the same should hold for complex petroleum substances. QSAR equations for chronic toxicity also suggest that there should be a point where hydrocarbons with high log K_{ow}

values become so insoluble in water that they will not cause chronic toxicity, that is, that there is also a solubility cut-off for chronic toxicity (McCarty, L.S. et al, 1991; European Union, 1996). Thus, paraffinic hydrocarbons with carbon numbers of greater than 14 ($\log K_{ow} > 7.3$) should show no measurable chronic toxicity. The existence of this cut-off for chronic toxicity is supported for petroleum substances by the numerous chronic toxicity studies reported on lubricant base oils, which demonstrate that for these substances which are composed primarily of alkanes and naphthenes of C15 and greater, no evidence of chronic toxicity is seen (CONCAWE, 1997). Further evidence to support this generalization is provided by a lack of chronic toxicity for hydrocarbon based solvents (CEFIC, 2000)

(1) (3) (4) (10) (12) (16) (19) (39)

- : In February of 2001 discharge of slack wax to national parks along British Columbia (Canada) coastline occurred during tank washing activities, impacting approximately 100 km of Pacific Rim National Park beach. Canadian Wildlife Service (a branch of Environment Canada) and the Department of Fisheries and Oceans biologists agreed that the risk of acute toxicity to aquatic life in the area was minimal based on the low solubility of the components in the wax and given that the BC Parks staff observed no significant environmental impacts. Generally the consensus was that the material was relatively inert and would likely pose little environmental damage.

(21)

5.1.1 ACUTE ORAL TOXICITY

Type : LD₅₀
Species : Rat
Strain : No data
Sex : Male/female
Number of animals : 10
Vehicle : Arachis oil
Value : > 5000 mg/kg bw
Year : 1976
GLP : No data
Test substance : R 9071 is a paraffin wax that was prepared as solutions in arachis oil for oral dosing. Two concentrations (20 and 100 mg/ml) were prepared for the two dose levels tested.
Method : Paraffin wax was administered orally as a solution in arachis oil to groups of 5 male and 5 female rats at dose levels of 1 and 5 g/Kg. The rats were observed for clinical signs of toxicity for the following 7 days. On the seventh day the animals were weighed, then killed and autopsied.
Result : There were no clinical signs of toxicity during the seven day observation period and growth rates were normal. There were no mortalities and no macroscopic changes were observed at autopsy. The LD₅₀ was found to be greater than 5g/Kg.
Reliability : (1) valid without restriction
 Although there is no indication that the study was carried out according to GLP, it nevertheless is a reliable study and full details are provided in the laboratory report.

(31)

Type : LD₅₀
Species : Rat
Strain : No data
Sex : Male/female
Number of animals : 10
Vehicle : Arachis oil
Value : > 5000 mg/kg bw
Year : 1976
GLP : No data
Test substance : R 9269 is a microcrystalline wax that was prepared as solutions in arachis oil for oral dosing. Two concentrations (20 and 100 mg/ml) were prepared for the two dose levels tested.
Method : Microcrystalline wax was administered orally as a solution in arachis oil to groups of 5 male and 5 female rats at dose levels of 1 and 5 g/Kg. The rats were observed for clinical signs of toxicity for the following 7 days. On the seventh day the animals were weighed, then killed and autopsied.
Result : There were no clinical signs of toxicity during the seven day observation period and growth rates were normal. There were no mortalities and no macroscopic changes were observed at autopsy. The LD₅₀ was found to be greater than 5g/Kg.
Reliability : (1) valid without restriction
 Although there is no indication that the study was carried out according to GLP, it nevertheless is a reliable study and full details are provided in the

laboratory report.

(32)

5.1.2 ACUTE INHALATION TOXICITY**5.1.3 ACUTE DERMAL TOXICITY**

Type : LD₅₀
Species : Rabbit
Strain : No data
Sex : No data
Vehicle : Petrolatum
Value : > 4000 mg/kg bw
Year : 1972
GLP : No
Test substance : Paraffin wax/Petrolatum (50/50)
Method : Method is not described.
Remark : The report does not provide sufficient information to fully evaluate the study.
Reliability : (4) Not assignable
 This information is taken from a published safety review conducted by an expert panel. Few experimental details are provided and the quality of the studies and the panel's conclusions cannot be verified.

(18)

5.2.1 SKIN IRRITATION

Species : Rabbit
Concentration : Undiluted
Exposure : Occlusive
Exposure time : 24 hour(s)
Number of animals : 9
Result : Not irritating
Year : 1984
GLP : No data
Remark : An expert panel on cosmetics reviewed the skin irritation data and reported:

- An undiluted paraffin wax was non-irritant in a 24 hour occluded patch test in rabbits
- A microcrystalline wax was slightly irritating in a 24 hour occluded patch test

Result : The report contains the following statement:
 A sample of 100% paraffin wax was applied full strength under a single closed patch to the skin of 9 rabbits. No irritation developed. Three samples of 50% paraffin in petrolatum were tested in repeated, open patch applications to 6 rabbits. Two samples produced erythema in four animals that lasted three days,

5. Toxicity

Id Waxes

Date 8/6/02

Reliability : and one produced erythema in one rabbit that lasted two days.
No other details are provided.
: (4) not assignable
This information is taken from a published safety review conducted by an expert panel. Few experimental details are provided and the quality of the studies and the panel's conclusions cannot be verified.

(18)

5.2.2 EYE IRRITATION

Species : Rabbit
Concentration : 50 %
Dose : 0.1 ml
Exposure Time : 72 hour(s)
Comment : Not rinsed
Number of animals : 6
Result : Slightly irritating
Year : 1984
GLP : No data
Result : The publication states:

Four 50% solutions of paraffin in petrolatum were each instilled into the eyes of six albino rabbits with no rinse. Eyes were observed for irritation for three days. Two of the samples caused mild irritation in one rabbit on day 1; the other samples were not irritating.

Reliability : (4) not assignable
This information is taken from a published safety review conducted by an expert panel. Few experimental details are provided and the quality of the studies and the panel's conclusions cannot be verified.

(18)

5.3 SENSITIZATION

No data

5.4 REPEATED DOSE TOXICITY

Species	: Rat
Sex	: Male/female
Strain	: Fischer 344
Route of admin.	: Oral feed
Exposure period	: 90 days
Frequency of treatment	: Continuous in food
Doses	: 0.002, 0.02, 0.2 & 2.0% in the diet
Control group	: Yes, concurrent no treatment
Method	: OECD Guide-line 408 "Subchronic Oral Toxicity - Rodent: 90-day Study"
Year	: 1992
GLP	: Yes
Test substance	: Three finished waxes and six mineral oils were tested in a series of three studies.

Only the information on waxes is included here.

The 3 finished waxes were:

Low melting point wax (LMPW)

High melting point wax (HMPW)

High sulphur wax (HSW)

The characteristics of these waxes has been published elsewhere (CONCAWE, 1993).

The waxes were powdered and incorporated in the diet at a concentration of 10% wt. This concentrate was further diluted with control diet to achieve test diets containing 2.0, 0.2, 0.02 and 0.002% wax. Analytical studies were carried out to ensure stability of wax in the diet and homogeneity of mixing. Throughout the study diets were analyzed for mineral hydrocarbon content.

An extra control diet containing 2.0% coconut oil was also prepared and this was analyzed throughout the study.

Results of analytical measurements throughout the study demonstrated that dietary mixing had been adequate and that dietary levels were within acceptable limits

Method	: Three separate studies were carried out at the same time. In the main study, groups of 20 male and 20 female rats were fed diets containing one of 3 different waxes at dietary concentrations of 0.002, 0.02, 0.2 and 2.0% for 90 days. Further groups of 60 male and 60 females were fed untreated control diet. Additionally groups of 20 rats of each sex were fed diets containing 2.0% coconut oil.
---------------	---

In a reversibility study, an extra group of 10 rats of each sex was fed diets containing one of the 3 different waxes at the 2.0% level or coconut oil at 2%. Groups of 30 rats of each sex served as controls for this reversibility study.

To determine tissue levels of hydrocarbons a study was also

5. Toxicity

Id Waxes

Date 8/6/02

included in which 5 rats of each sex were fed diets containing one of the 3 waxes or coconut oil at the 2.0% dietary level for 90 days. Extra groups of rats (5 of each sex) were fed control diet or coconut oil or one of the three waxes for 90 days followed by exposure to control diet only for a further 28 days.

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

A full necropsy was performed on the main and reversibility study animals and a full range of hematological parameters were measured on blood samples taken from the animals. Clinical chemical measurements were also made on serum separated from the blood samples. A selection of organs was weighed and a range of tissues retained for subsequent histopathological examination. All tissues from the high dose group and control groups were examined by light microscopy. Additionally the liver, lymph nodes, spleen, kidney, small intestine and lung were examined from all the intermediate dose groups.

Mineral hydrocarbon levels were measured in a limited number of tissues in those animals designated for tissue level determinations.

Remark

: The purpose of this study was to assess the safety in use of a variety of oils and waxes for food contact applications.

As a follow up to this study additional studies were carried out on other finished wax samples and the results are summarized in the table below.

The severity and incidence of the responses were related to the average molecular weights of the materials tested; the lower molecular weight materials causing the most severe effects (CONCAWE 1993).

Sample	Viscosity @ 100°C (mg/kg/day) (cSt)	Carbon Chain Length	Average Mol. Weight	NOAEL
LMPW	3.3	19-42	375	<2
Blend	8	19-80	470	<2
IMPW	6.3	21-49	480	<2
HSW	13.7	20-74	600	2000
HMPW	15.4	22-80	630	2000

LMPW: Low melting point finished wax
 Blend: Blend of LMPW and HMPW
 IMPW: Intermediate melting point finished wax
 HSW: High sulfur wax
 HMPW: High melting point finished wax

The findings from the above studies allowed the EU Scientific Committee for Food (SCF 1995) to set ADIs for the high sulphur (HSW) and high molecular weight waxes (HMPW), but not for the lower molecular weight materials since for these NOELS had not been established.

A further study has also been carried out in which Low Melting Point Wax was fed to F-344 and Sprague Dawley rats at dietary concentrations of 0.2 and 2.0% in the diet for 90 days.

The findings in the F-344 rats were essentially similar to those found in the studies summarized above but the Sprague Dawley rat was found to be a less sensitive strain.

The only effects of treatment seen were an increase in mesenteric lymph node weight and microscopic findings in the same tissue (microgranulomas and reticuloendothelial cell hyperplasia). These effects were less severe and less frequent than those seen in the F-344 rats.

Result

- : The results of a series of dietary studies done on multiple samples of food grade finished waxes are reported here.

Only minor treatment-related effects were observed in those animals fed either high sulfur wax or high molecular weight wax when compared to controls and then only at the highest dose level. Furthermore, for these two waxes, hydrocarbon levels in the tissues were no greater than those of the controls fed untreated diet.

Although growth rates, food intakes and clinical condition of animals fed LMPW were unaffected by exposure, there was a spectrum of changes that occurred as follows.

Organ weight changes were recorded in both sexes. Liver and spleen weights (absolute & relative) were increased at the 2 and 0.2% dose levels. Although some reduction was observed after the reversal period in the 2% dose groups, they were still higher than the corresponding controls.

Mesenteric lymph node weights were only available for the high dose level animals and these were increased following exposure to LMPW. Although the lymph node weights had reduced in the reversibility group they had not returned to normal by the end of the reversibility period.

The following hematological changes occurred at the dose levels shown for those animals fed LMPW:

Parameter	Dietary concentration	
	0.2%	2%
<u>Males</u>		
Hemoglobin content	Reduced (2%)	Reduced (2%)
MCH	Reduced (2%)	Reduced (2%)
Neutrophils	Increase (22%)	Increase (23%)
Platelets	Reduced (7%)	Reduced (13%)
<u>Females</u>		
Hemoglobin content	Reduced (6%)	

5. Toxicity

Id Waxes

Date 8/6/02

Erythrocyte count	Reduced (4%)	
Hematocrit	Reduced (4%)	
Reticulocytes	Increase (43%)	
Leucocyte count	Increase (26%)	Increase (48%)
Neutrophils	Increase (45%)	Increase (89%)
Lymphocytes	Increase (18%)	Increase (29%)
Monocytes	Increase (35%)	Increase (103%)
Eosinophils	Increase (41%)	
Basophils Actual value	0.003	0.004
(Control value = 0)		
Platelets	Reduced (14%)	Reduced (16%)

There were raised serum liver enzyme levels in the highest two dose groups of females but only at the highest dose in males. The enzymes affected were ALA, ALAT, ASAT and Gamma-GT. Serum bilirubin was also elevated in the highest dose group of females. Albumin/globulin ratios were reduced in the females at the highest 2 dose levels and in the highest dose level only for the males.

No mineral hydrocarbons were found in the kidneys of rats fed LMPW. However, it was found in the perirenal fat, liver and lymph nodes. After the reversal period mineral hydrocarbon was still found in these tissues, albeit at lower concentrations.

Histopathological lesions were observed in many tissues and were of a severity and nature consistent with the age of the animals and were not considered treatment-related. However, lesions in the liver, mesenteric lymph node, ileum & jejunum and heart were considered compound-related. These were as follows:

Liver

Granulomas were observed in the livers of male and female rats at the highest 2 dose levels. At the highest dose centrilobular vacuolation was also observed. After the one month reversal period, granulomas were still present at the same incidence but their severity was less.

Mesenteric lymph node

The lymph node lesions comprised focal collections of slightly vacuolated macrophages in the cortical region and after one month's reversal these were reduced in severity. Such lesions occurred to varying degrees of severity at all dose levels.

Ileum & jejunum

There was an increased incidence in macrophage accumulation in Peyer's Patches in both sexes at the highest two dose levels. There was also an increase in macrophage infiltration of the lamina propria in the high dose females.

Heart

A focal inflammatory lesion was observed within the cusps of the mitral valve. The lesion was characterized by an increased cellularity of the valve

5. Toxicity

Id Waxes

Date 8/6/02

with destruction of the fibrous core. The lesion was observed in 11/20 males and 11/20 females at the highest dose level and 5/20 females at the 0.2% group. Following the 28-day reversal period there was still an increased incidence of the lesion but this was less than that at the end of the 90-day feeding study.

Reliability : (1) valid without restriction
Study conducted to GLP and thoroughly reported.

(7) (8) (9)

5.5 GENETIC TOXICITY 'IN VITRO'

: No data available

5.6 GENETIC TOXICITY 'IN VIVO'

: No data available

5.7 CARCINOGENITY

Species : Mouse
Sex : Male
Strain : C3H
Route of admin. : Dermal
Exposure period : 80 weeks
Frequency of treatment : Twice weekly
Doses : 50 mg/application
Result : Negative
Control group : Untreated control and positive control (BaP)
GLP : No
Test substance : Slack wax CAS No. 64742-61-6
The sample was tested twice in the study summarized by Kane et al.

Method : 50 mg melted slack wax was painted on the skin of 50 individually housed male mice, twice weekly for 80 weeks. The animals were shaved bi-weekly with electric clippers and the test material applied to the shaven intrascapular region. Treatment was continued for 80 weeks. A concurrent negative untreated control and a positive control (benzo-a-pyrene) was included in the study. The study was repeated using 25 mg/application, twice weekly.

Remark : This report is a summary of results from an extensive program of studies. Consequently, not all the experimental details have been presented. The authors state that such details are available in the original laboratory reports.

Result : No skin tumors developed in any of the mice to which slack wax had been applied in either of the studies. The responses in the control groups are not reported.

5. Toxicity

Id Waxes

Date 8/6/02

Reliability

: (4) Not assignable
The report summarizes data from many studies and does not contain sufficient detail for a full evaluation.

(34)

5. Toxicity

Id Waxes

Date 8/6/02

Species : Mouse
Sex : Male
Strain : C3H
Route of admin. : Dermal
Exposure period : 80 weeks
Frequency of treatment : Twice weekly
Doses : 50 mg/application
Result : Negative
Control group : Untreated control and positive control (BaP)
GLP : No
Test substance : Petrolatum CAS No. 8009-03-8
Method : 50 mg petrolatum was painted on the skin of 50 individually housed male mice, twice weekly for 80 weeks. The animals were shaved bi-weekly with electric clippers and the test material applied to the shaven intrascapular region. Treatment was continued for 80 weeks. A concurrent negative untreated control and a positive control (benzo-a-pyrene) was included in the study. The study was repeated using 25 mg/application, twice weekly.

Remark : This report is a summary of results from an extensive program of studies. Consequently, not all the experimental details have been presented. The authors state that such details are available in the original laboratory reports.

Result : No skin tumors developed in any of the mice to which petrolatum had been applied in either of the studies. The responses in the control groups are not reported.

Reliability : (4) not assignable
 The report summarizes data from many studies and does not contain sufficient detail for a full evaluation.

(34)

Species : Mouse
Sex : Male/female
Strain : Swiss
Route of admin. : Dermal
Exposure period : Lifetime
Frequency of treatment : Twice weekly
Doses : Approximately 60 μ l per application
Result : Negative
Control group : Yes, concurrent vehicle
Year : 1966
GLP : No data
Test substance : 15% solution of Amber Petrolatum (NF Grade) in isooctane
Method : Three drops (approximately 60 μ l) of a 15% solution of amber petrolatum in isooctane was applied to the shaven skin of the mice, twice weekly for their lifetimes. 30 male and 40 female mice were treated in this way. A group of 50 males and 50 females served as vehicle controls and received 60 μ l of isooctane twice weekly for the lifespan of each animal. Animals were housed

5. Toxicity

Id Waxes

Date 8/6/02

Result

in groups of not more than 10 per cage.
 The occurrence of skin tumors and other lesions in the treated area and other visible lesions was noted and their progression recorded.
 Histological confirmation of each lesion was confirmed after autopsy of the respective animals.
 : Treatment with petrolatum caused moderate epidermal hyperplasia.
 The authors state that the incidence of internal tumors appeared within the limits observed in the control animals.
 Treatment did not appear to affect survival when compared to controls as follows:

Group	Survival (%) at weeks		
	30	50	70
<u>Petrolatum</u>			
Females	90	77	53
Males	93	83	35
<u>Controls</u>			
Females	90	80	64
Males	90	54	32

The skin tumor incidence is summarized below for the control and petrolatum groups. No data are included here for the various extracts of petrolatum that were tested, even though such data were given in the publication reviewed.

Animals	Total number of			Latency (weeks)
	Tumors	Carcinomas	Regressions	
<u>Petrolatum</u>				
Females				
1	2*	-	1	100
Males				
2	3**	-	2	69
<u>Solvent</u>				
Females				
-	-	-	-	-
Males				
2	2	1	-	63

* one papilloma on eyelid
 ** one papilloma under chin

Reliability

: (2) valid with restrictions
 The study was designed only to investigate skin carcinogenicity and consequently detailed pathological findings are not available. Detailed findings (histopathological) are not included in the paper, but the authors make reference to a source of such data.

(36)

Date 8/6/02

Species	:	Mouse
Sex	:	Male/female
Strain	:	Swiss
Route of admin.	:	Dermal
Exposure period	:	Lifetime
Frequency of treatment	:	3 times weekly
Doses	:	3 drops
Result	:	Negative
Control group	:	Yes, concurrent no treatment
Year	:	1962
GLP	:	No data
Test substance	:	<p>5 waxes were selected from 36 samples on the basis of their ultraviolet absorptivity, representing the range of aromatic contents</p> <p>Each of the 5 waxes was dissolved in warm benzene to achieve 15% solutions. These were warmed in a water bath prior to application to the skin.</p> <p>Additionally a benzene solvent control was included in the study as well as an aromatic extract (in is-octane) of one of the waxes and a 15% solution in benzene of a chromatographed wax.</p>
Method	:	<p>3 drops (approximately equivalent to 0.05 ml) of the solution of wax or the solvent control was applied to the skin of the intrascapular region over an area of approx. 2 X 2 cm. This treatment was continued 3 times weekly to groups of mice throughout the experiment. Observation was continued until spontaneous death or until the animals were killed when dying. All mice were subjected to a complete autopsy followed by a histological examination of all abnormal tissue.</p> <p>Group sizes were approximately 60 male and 30 female for each wax sample and 140 mice of each sex for controls.</p>
Result	:	<p>Survival rates of the mice were similar for treated and control animals with a better survival among females than males.</p> <p>Some desquamation and epilation occurred in the treated areas of skin after the first few applications and this persisted throughout the study.</p> <p>Histologically, moderate epidermal hyperplasia was observed in both treated and control animals. The wax treated animals also had some focal areas of hyperplasia of the sebaceous glands. No degenerative or necrotic changes were observed.</p> <p>The skin tumor incidences are shown in the following table. (overleaf)</p>

5. Toxicity

Id Waxes

Date 8/6/02

No. of mice	Benign papillomas	Malignant carcinomas	Sebaceous gland adenomas	Other
<u>Wax 2</u>				
61 M	1			
30 F				
<u>Wax 8</u>				
61 M	3	1		
31 F	1			
<u>Wax 12</u>				
58 M	4		1	1
34 F	1		1	
<u>Wax 15</u>				
57 M	2			
30 F	1			
<u>Wax 20</u>				
61 M	1		2	
36 F	1		2	
<u>Benzene</u>				
59 M		1		
35 F	1			

A number of other tumors were also observed at autopsy (mainly lung adenomas, mammary carcinomas and malignant lymphomas) but these were found in all groups and their incidence was similar in wax treated groups and controls. The authors judged that these studies were negative.

Reliability

: (2) valid with restrictions
 Although not conducted to GLP, the study was nevertheless, robust and is acceptable for the purpose of assessing the skin carcinogenicity potential of paraffin wax solutions in benzene.

(45)

5. Toxicity

Id Waxes

Date 8/6/02

Species : Mouse
Sex : Male
Strain : White albino
Route of admin. : Dermal
Frequency of treatment : Three times weekly for lifetime
Year : 1951
GLP : No
Test substance : Eight slack waxes and eight aromatic hydrocarbon extracts derived from the slack waxes were tested.
[Because of the lack of detail in the publication it is not possible to establish which aromatic extract was derived from which specific slack wax].

The extracts were obtained by eluting, with an unspecified solvent, silica gel columns charged with the individual slack waxes. No additional information was provided on the preparation of the aromatic test materials. [However, in parallel studies on aromatic extracts collected from catalytically cracked oils, the investigators reported that the silica gel columns were eluted first with n-heptane to collect non-aromatic components of the oils and then with acetone to recover the aromatic components. In the parallel studies the recovered aromatics were tested on mice after evaporation of the acetone.]

Method : Approximately 15 mg of warmed test material were applied as a thin film by means of a small brush on Monday, Wednesday and Friday to the shorn scapular region of groups of 30 albino male mice. Test material application was continued until death. After tumors had appeared the test materials were applied around the viable base of the growths, not on their often "dead tops".

For each material at autopsy, sections were taken of representative tumors and any internal lesions of interest. These tissue sections were then examined microscopically.

For each test material a cancer and a tumor index was calculated as follows:

$$\text{Tumor index} = 100 \times \frac{\text{Total No of animals in which tumors developed}}{\text{Original No. animals less No dead at 90 days without tumors}}$$

$$\text{Cancer Index} = 100 \times \frac{\text{Total No animals in which cancer developed}}{\text{Original No less No. dead at 90 days from causes other than cancer}}$$

$$\text{Potency was calculated:} = \frac{\text{Cancer index}}{\text{Tumor index}}$$

Result : Results are summarized in the following two tables:

Date 8/6/02

Slack waxes

Wax Sample	Oil (%) ¹	CI/TI at Days	
		250	450
145	25	4/23	8/10 ³
147	17	0/3	7/7
150	20	0/0	4/4
141	10	0/3	0/7
142	21	0/4	0/4
144	21	0/4	0/4
140	20	4/7	4/4 ³
146	12	0/0	4/4

Aromatic extracts

Sample	Aromatic (%) ²	CI/TI at Days	
		250	450
231	18	14/38	24/38
233	0	19/30	23/35 ⁴
235	12	17/35	17/43 ⁴
228	7	3/17	14/34
229	0	0/0	0/13
230	12	0/42	8/30 ^{3,5}
231	11	4/22	4/30 ⁴
232	8	0/8	4/10

¹ Oil content of the slack waxes (w/w)

² Aromatics content of the slack wax (w/w)

³ The lower tumor index (TI) at the later date is due to spontaneous disappearance of some papillomas

⁴ The experiment was discontinued after 335 days

⁵ The experiment was discontinued after 490 days

The authors concluded that the slack waxes showed only a low order of carcinogenicity at 250 days. However by 450 days every sample of slack wax had elicited papillomas and for 5 of them cancers as well.

The aromatic extracts on the other hand exhibited a greater potency. At 250 days all but one sample had produced papillomas and 5 samples had produced cancers. At 450 days all but one sample had elicited cancers and all had elicited papillomas.

The authors concluded that the carcinogenicity of slack wax

1. Can be attributed to the aromatic compounds found in the oils from which the waxes were pressed and which are retained on the waxes as impurities.
2. Is not due to paraffins.

Another study from the same laboratory (Dietz et al, 1952) on 11 slack waxes (it is unclear whether some were the same samples as in Smith et al, 1951) produced similar results. The tumor potency of each sample was low to marginal.

Reliability

: (4) not assignable

The study summarized here was conducted to identify the carcinogenic component(s) of slack waxes.

5. Toxicity

Id Waxes

Date 8/6/02

Although not conducted to GLP and lacking experimental details the study is important since it identifies the residual oil in the slack wax and not the paraffins as being responsible for carcinogenic activity.

(15) (46)

5. Toxicity

Id Waxes

Date 8/6/02

- Species** : Rabbit
Sex : Male/female
Strain : New Zealand white
Route of admin. : Dermal
Frequency of treatment : Three times weekly
Control group : Yes, concurrent vehicle
Year : 1962
GLP : No
Test substance : 5 waxes were selected from 36 samples on the basis of their ultraviolet absorptivity, representing the range of aromatic contents
Each of the 5 waxes was dissolved in warm benzene to achieve 15% solutions. These were warmed in a water bath prior to application to the skin.
Additionally a benzene solvent control was included in the study.
- Method** : Solutions of the waxes as well as the benzene alone were applied three times weekly to the shorn skin of the intrascapular region (approximately 10 X 10 cm) of 4 male and 4 female rabbits. Each application consisted of approximately 0.08 ml.
The authors state that a few rabbits were added in some groups to compensate for death of other rabbits before one year of treatment. Specific details are not provided.
- Remark** : This study had not been completed at the time of publication of a paper on the toxicity of petroleum waxes (Shubik et al). However, the information is useful in assessing the skin carcinogenicity of petroleum waxes since it provides data from an additional species.
- Result** : Some reddening, desquamation and epilation of the painted skin area occurred after a few paintings with the wax solutions and the benzene alone; these changes persisted throughout the study without any notable modifications.
2 small skin papillomas were observed in the male group painted with one of the waxes. One of these papillomas developed after 48 weeks of treatment and was still present at the 105th week. The other papilloma developed after 93 weeks and regressed at the 110th week.
No other skin lesions were found in any of the groups.
- Reliability** : (4) Not assignable
This study was not reported thoroughly, nor was it complete at the time of publication. However, it does provide supportive information from a species other than the mouse.

(45)

5. Toxicity

Id Waxes

Date 8/6/02

Species : Rat
Sex : Male/female
Strain : FDRL
Route of admin. : Oral feed
Exposure period : 2 years
Frequency of treatment : Ad libitum
Doses : 5% in the diet
Result : Negative
Control group : Yes, concurrent no treatment
Year : 1965
GLP : No data
Test substance : Three blends of petrolatum were examined. They were as follows:

Blend A, a snow-white grade meeting USP XVI specifications. This sample was a blend in equal proportions of six commercially available materials, each meeting the US specification.

Blend B, a white petrolatum, somewhat darker than Blend A, but nevertheless meeting the USP XVI specification. This blend was also prepared as a mixture of six commercially available materials in equal proportions.

Blend C, a yellow petrolatum meeting NF XI specification. This blend was prepared as a mixture in equal proportions of 5 commercially available products.

The three blends were kept with minimum air space refrigerated in metal containers for the duration of the study.

Analytical characteristics of the blends were as follows:

Blend	UV absorptivity (290 m μ)	Lovibond color (2 in. cell)	Specific gravity (60 °C)	Melting point (°C)
A	0.136	2Y	0.830	53.5
B	0.424	12Y 0.5R	0.835	52.2
C	1.48	35Y 10R	0.844	51.3

Method : 50 rats of each sex, individually housed were fed diets containing 5% of one of three blends of petrolatum ad-libitum for two years. A group of 100 rats of each sex served as controls and were fed normal diet ad-libitum that had been supplemented with 1% vitamin mix and 0.2% Aurofac 10.

The animals were observed daily for appearance, behavior and survival.

Weekly measurements were made of body weight for the first

12 weeks of the study and biweekly thereafter. Weekly measurements were also made of food intake for the first 12 weeks for 10 rats of each sex fed the diets containing petrolatum and for 20 rats of each sex fed control diet.

At 12, 26, 52, 72 & 100 weeks the following determinations were made on representative animals from each of the groups: red cell count and/or hematocrit, total and differential white cell counts, hemoglobin content, blood glucose and blood urea nitrogen levels.

Rats that died and survivors at the end of the study were autopsied and the following organ weights were recorded: liver, kidneys, spleen, heart, adrenals, thyroids and pituitary.

For all rats that died, that were killed in a moribund state or from representative surviving animals at the end of the 2 year feeding period (10 of each sex in the petrolatum groups, 20 of each sex controls) the following organs were fixed and examined histologically: liver, spleen, stomach, large and small intestine, pancreas, kidney, urinary bladder, adrenal, thyroid gland, testis or ovary, salivary gland, lymph node, heart, lung, muscle, skin, spinal cord, brain, thymus, bone marrow and "growths of any description".

Result

: Growth rates were unaffected by exposure to petrolatum when compared to controls.

Although there were small statistically significant differences in food utilization values between control and some petrolatum exposed animals these were not of biological significance.

Survival at two years was unaffected when compared to controls. Survival of males was approximately 68% and that for females was 58%.

Neither hematological nor clinical chemical measurements were affected by exposure to any of the petrolatum samples either during or at the end of the study.

No differences were found at autopsy between petrolatum exposed and control animals. Furthermore, there were no histological changes that could be attributed to dietary exposure to petrolatum. Histological changes that occurred did so in both sexes and in all treatment and control groups and were considered to be ageing related.

Neither of the 3 petrolatum blends caused an increased tumor incidence in any tissue/organ examined.

**Test substance
Reliability**

: (2) valid with restrictions

This study is well conducted and reported, but was carried out prior to the need for GLP. Nevertheless the study is valid.

(42)

Date 8/6/02

Species	:	Rat
Sex	:	Male/female
Strain	:	Sprague-Dawley
Route of admin.	:	Oral feed
Exposure period	:	2 years
Frequency of treatment	:	Continuous
Post. obs. period	:	
Doses	:	5000mg/kg bw/day
Result	:	Negative
Control group	:	Yes, concurrent no treatment
Year	:	1962
GLP	:	No
Test substance	:	5 waxes were selected from 36 samples on the basis of their ultraviolet absorptivity, representing the range of aromatic contents Each of the 5 waxes was ground into a powder and added to powdered diet and mixed in the proportion 1:9 w/w
Method	:	Each of the five waxes was fed ad-libitum to male and female rats at a dietary concentration of 10% for 2 years. Additional groups of 140 male and 157 females were fed control diet. The rats inspected and weighed every second week and all gross lesions were recorded. This was continued until the rats died or were killed when dying and were then submitted to complete autopsy followed by histological examination of all abnormal tissue.
Result	:	Survival rates and growth rates were unaffected by oral exposure to any of the waxes tested. A number of tumors were found in all groups at autopsy. The incidence of each tumor type was reported. The number of tumor bearing animals was similar to that of controls and furthermore the incidence of the various tumor types was also similar in treated and control animals. No other toxic effects were found at histological examination. The authors concluded that the five waxes were devoid of carcinogenic or other toxic action when fed at a level of 10% in the diet.
Reliability	:	(2) Valid with restrictions Study not carried out according to GLP and only "abnormal" tissue examined histologically. Study provided supportive information only and could not be used as a definitive study.

(45)

5. Toxicity

Id Waxes

Date 8/6/02

Species : Rat
Strain : BD I, BD III and W
Route of admin. : Various
Exposure period : Up to approximately 2.5 years
Frequency of treatment : Various
Year : 1953
GLP : No
Test substance : Various, including yellow vaseline
Remark : The following is taken from the method section of an English translation of the German report:

"
Liquid paraffin (DAB. 6) was injected into 30 rats, 2.5 ml once subcutaneously and intraperitoneally in a total dose of 9 ml per animal divided over 15 individual injections over a period of 40 weeks. Another 30 rats obtained the liquid paraffin in the food. The total dose was 136 ml/animal in 500 days.

Yellow vaseline (DAB. 6) was also injected after warming. Eight rats obtained 3 ml intraperitoneally and 26 rats 1 ml subcutaneously besides. All animals were observed until spontaneous death....."

The following is taken from the results section of the publication.

"
In the experiment with vaseline a tumor developed at the injection point after a latent period of 658 days. Histologically this tumor turned out to be an osteo-sarcoma....."

Reliability

(3) invalid

This study is of historical interest only and is included for completeness only.

(44)

5. Toxicity

Id Waxes

Date 8/6/02

Species : Mouse
Sex : Male/female
Strain : Swiss Webster
Route of admin. : s.c.
Frequency of treatment : Single subcutaneous dose
Post. obs. period : 18 months
Doses : 100 mg
Result : Negative
Control group : Yes
Year : 1965
GLP : No
Test substance : Three blends of petrolatum were examined. They were as follows:

Blend A, a snow-white grade meeting USP XVI specifications. This sample was a blend in equal proportions of six commercially available materials, each meeting the US specification.

Blend B, a white petrolatum, somewhat darker than Blend A, but nevertheless meeting the USP XVI specification. This blend was also prepared as a mixture of six commercially available materials in equal proportions.

Blend C, a yellow petrolatum meeting NF XI specification. This blend was prepared as a mixture in equal proportions of 5 commercially available products.

The three blends were kept with minimum air space refrigerated in metal containers for the duration of the study.

Analytical characteristics of the blends were as follows:

Blend	UV absorptivity (290 m μ)	Lovibond color (2 in. cell)	Specific gravity 60 °C	Melting point (°C)
A	0.136	2Y	0.830	53.5
B	0.424	12Y 0.5R	0.835	52.2
C	1.48	35Y 10R	0.844	51.3

Method

Stripped lard was used as negative control substance.
 : A single dose of 100 mg of one of the three petrolatum blends or stripped lard was administered subcutaneously into the intrascapular region of 28-day-old mice. 50 male and 50 female mice were used for each group and these were housed individually for the following 18-month observation period. The mice were allowed food and water ad-libitum. Growth, physical appearance and behavior were observed throughout the study and special attention was paid to the injection site.

Result

Representative mice sacrificed at 9 months and all mice that died or were sacrificed at the end of the 18-month observation period were examined at autopsy for evidence of pathological change. Weights of liver, spleen and kidneys were recorded. After fixation, histological examination was made of: liver, spleen, stomach, small and large intestine, pancreas, kidney, urinary bladder, adrenal, thyroid, testis or ovary, salivary gland, lymph node, heart, muscle, lung, skin, spinal cord, brain, thymus and bone marrow and any macroscopically observed growths.

- : Growth rates, food intakes and food utilization was unaffected by s.c. administration of any of the petrolatum samples when compared to the control group. The males consumed slightly more food than the females, but there were no differences between the various treatment groups. Mortality was similar in the control and petrolatum groups and overall survival ranged between 12 and 24% at the end of the study (78 weeks). Liver, kidney and spleen weights were not affected by exposure to any of the petrolatum blends. Gross observations at autopsy were spread equally amongst all groups and were not specifically related to exposure to petrolatum. At about 7-9 months, there had been a significant rise in mortality in all groups and histopathological examination confirmed widespread leukemic infiltration with secondary septicemic involvement in some animals in all groups. Gross findings at the end of the study were consistent with ageing animals. The responses were largely either of a chronic inflammatory or fibrotic nature. Many of the observations in the lymphatic system showed chronic changes associated with the clearance of the foreign material that had been injected subcutaneously. There was no specific relationship between tumor incidence and the test material injected.

Reliability

- In conclusion, no toxic or carcinogenic response resulted as a consequence of the s.c. injection of a 100 mg dose of either of the 3 petrolatum blends.
- : (2) valid with restrictions
This study is well conducted and reported, but was carried out prior to the need for GLP. Although survival of mice was poor, nevertheless the study is considered valid.

(42)

5. Toxicity

Id Waxes

Date 8/6/02

Species : Mouse
Sex : Male/female
Strain : Swiss
Route of admin. : s.c.
Exposure period : Lifetime
Frequency of treatment : Once only administration of test material
Post. obs. period : Lifetime
Year : 1962
GLP : No
Test substance : Paraffin wax
Method : A single wax disc (2 cm. diameter, 2 mm. thick and weighing 0.5 g) was implanted subcutaneously in groups of approximately 45 male and 50 female Swiss mice. This was done for 5 different waxes. Additionally, 0.5 g of one of the waxes was implanted as a powder in a further group of 48 and 46 female Swiss mice. The animals and their controls were observed for their lifetimes.

Result : Tumors developed at the implantation sites of the wax discs. No tumors developed at the sites of the powdered wax.

This finding is consistent with other reports on the tumorigenicity of implanted inert materials. It is generally believed that tumorigenicity at subcutaneous implantation sites is a function of the physical form of the material rather than of the material itself. If however, the material had been tumorigenic it would be expected that tumors would have developed at the site of the implanted powder.

Reliability : (2) Valid with restrictions
Although the study was not GLP compliant it nevertheless was properly conducted and reported.

(45)

5.8 TOXICITY TO REPRODUCTION

No data

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

No data

5.11 EXPERIENCE WITH HUMAN EXPOSURE

- Memo Remark** : **Slack wax**
 : There are no published reports of acute effects in humans with slack waxes, but they are expected to be essentially non-toxic because both the residual oil and the wax components themselves are not acutely toxic.

There have been several reports of human occupational cancer amongst wax pressmen, during the preparation of paraffin wax (Hendricks et al, 1959; Lione and Denholm, 1959). In the process of wax pressing the unrefined or poorly refined oil was chilled and the solidified crude wax (slack wax) removed from the viscous oil on filter presses. This crude wax may have contained as much as 20-40% unrefined/poorly refined oil, which was reduced to less than 0.5% in subsequent processing. It should be noted that wax pressing is no longer used as a process and has been replaced by more modern techniques.

(29) (37)

- Memo Remark** : **Paraffin wax**
 : A review of the clinical studies with two undiluted paraffin waxes and formulated products containing various concentrations of paraffinic (5-16%) and microcrystalline (4.35-15%) waxes was published (Elder, 1984). These studies include a range of acute and repeat application tests in groups of humans for skin irritation and skin sensitization. All products gave, at most, slight erythema and none caused skin sensitization.

The widespread use in cosmetic and in cosmetic surgery over many years demonstrates the low toxicity of refined waxes and many guidelines exist for their safe use (Hjorth, 1987). Notwithstanding this, there are occasional reports of adverse effects with these products. Subcutaneous deposits, often referred to as paraffinoma, have been described frequently following injection of these materials under the skin but these are not normally associated with other progressive changes.

There has been one report where an outbreak of skin rashes was attributed to occupational exposure to wax fume (Halton & Piersol, 1994).

(18) (25) (30)

- Memo Remark** : **Petrolatum**
 : Despite the widespread use of petrolatum for many years as a vehicle in human skin patch testing, isolated cases of allergy to petrolatum have been reported. Nevertheless, petrolatum is still considered to be a good vehicle for patch testing. Fisher has concluded that although allergic reactions to petrolatum are rare, white, and not yellow petrolatum should be used as a vehicle in human skin patch testing.

(14) (17) (23) (24)

5. Toxicity

Id Waxes

Date 8/6/02

- (1) Abernathy, S., D. Mackay, L. McCarty (1988).
Volume fraction correlation for narcosis in aquatic organisms: the key role of partitioning, Environ Toxicol Chem 7, 469-481
- (2) ACGIH (1998) Threshold limit values (TLVs) for chemical substances and physical agents and biological exposure indices (BEIs)
Cincinnati OH, American Conference of Governmental Industrial Hygienists
- (3) Adema, D.M.M. (1991)
The acute aquatic toxicity of alkylbenzenes. Dutch contribution to collecting data with respect to Annex II of Marpol 1973/1978.
Progress report no. 1 for 1990 and 1991.
Report No. R 91/198. Delft: TNO
- (4) Adema, D.M.M. and van den Bos Bakker, G.H. (1986)
Aquatic toxicity of compounds that may be carried by ships (Marpol 1973, Annex II).
Progress report for 1986 from TNO to the Dutch Ministry of Housing, Physical Planning and Environment.
Report No. R 86/326a. Delft: TNO.
- (5) American Petroleum Institute
- (6) Bennet, H. (1975)
Industrial waxes. Volume 1: Natural & synthetic waxes.
New York: Chemical Publishing Company Inc.
- (7) BIBRA (1992)
A 90-day feeding study in the rat with six different mineral oils [N15 (H), N70 (H), N70 (A), P15 (H), N 10(A) and P100 (H)], three different mineral waxes (a low melting point wax, a high melting point wax and a high sulphur wax) and coconut oil.
BIBRA Project No: 3.1010
- (8) BIBRA (1993)
A 90-day feeding study in the rat with two mineral waxes identified as paraffin wax 64 (OFH-064) and micro/paraffin wax mixture.
BIBRA Project No. 3.1205
- (9) BIBRA (1999)
A subchronic 90-day dietary toxicity study of a low melting point paraffin wax in two rat strains
Study No. 95-2394, API study No. HES1516-L-00880-Oral
- (10) CEFIC (2000)
The classification of petroleum solvent streams and related complex hydrocarbon solvents for aquatic environmental effects under the EU dangerous substances directive. Brussels: Hydrocarbon Solvents Producers Association

5. Toxicity

Id Waxes

Date 8/6/02

- (11) CONCAWE (1984)
Assessment and comparison of the composition of food-grade white oils and waxes manufactured from petroleum by catalytic hydrogenation versus conventional treatment.
Report No. 84/60
CONCAWE, Den Haag. August 1984
- (12) CONCAWE (1997)
Lubricating oil basestocks
Product dossier No. 97/108
CONCAWE, Brussels
- (13) CONCAWE (2001)
Environmental classification of petroleum substances - Summary data and rationale.
Report 01/54
CONCAWE, Brussels
- (14) Conti, A., Manzini, B. M., Schiavi, M. E. and Motolese, A. (1995)
Sensitization to white petrolatum used as a vehicle for patch testing.
Contact Dermatitis Volume 33, pages 201-202.
- (15) Dietz, W. A., King Jr., W. H., Priestley Jr. W. and Rehner, J. (1952)
Properties of high boiling petroleum products
Ind. Eng. Chem. Vol. 44., No 8., pp. 1818-1827
- (16) Donkin, P., J. Widdows, S.V. Evans, M.D. Brinsley (1991). QSARs for the sublethal response of marine mussels (*Mytilus edulus*) Sci Tot Environ 109/110, 461-474
- (17) Doms-Goosens, A. and Degreef, H. (1983)
Contact allergy to petrolatums (1) Sensitizing capacity of different brands of yellow and white petrolatums.
Contact Dermatitis Volume 9, Pages 175-185.
- (18) Elder, R (1984)
Final Report on the Safety Assessment of Fossil and Synthetic Waxes
Editor R. Elder
J. Am. College of Toxicology Volume 3, number 4, pages 43-99
- (19) EU (1996)
Technical guidance document in support of Commission Directive 93/67/EEC on risk assessment for new notified substances and Commission Regulation (EC) 1488/94 on risk assessment for existing substances. Part IV, Chapter 4: Use of quantitative structure activity relationships (QSARs) in risk assessment. Luxembourg Office for Official Publications of the European Communities
- (20) EWF (1990)
Specifications for petroleum derived hydrocarbon waxes - food grade
Brussels: European Wax Federation
- (21) Exxon Biomedical Sciences Inc.
C. Lee Personal Communication to S. Fraser, Environment Canada
01EMBSI.748;2001EMBSI.ZZJNK; and 01EMBSI.749;2001EMBSI.ZZJNK

5. Toxicity

Id Waxes
Date 8/6/02

- (22) Exxon Biomedical Sciences, Inc. (1995).
Ready Biodegradability, Manometric Respirometry.
Study #102094A.
- (23) Fisher, A. A. (1981)
Cutaneous reactions to petrolatum
Cutis, Volume 28 Pages 23--, 24, 31, 57 & 93.
- (24) Frankei, E. B. (1985)
Letter to the editor: Acne secondary to white petrolatum use
Arch. Dermatol. Vol. 121, pages 589-590.
- (25) Halton, D. M. and Piersol, P. (1994)
Investigations into an outbreak of rashes in a wax coating treatment process.
Appl. Occup. Environ. Hyg. Vol 9, No 12, pp 941-944
- (26) Hanstveit, (1991).
A study of the fate of waxed paper materials in a woodland litter layer.
TNO Report No. R 90/243a
- (27) Hanstveit, A. O. (1990)
Inherent Biodegradability of Waxes. TNO-Report No R 90/198b
- (28) Harris, J.C. 1982.
Rate of Hydrolysis. In Handbook of Chemical Property Estimation Methods. p. 7-6.
W. J. Lyman, W.F. Reehl and D.H. Rosenblatt, eds. McGraw-Hill Book Company, New
York, NY, USA.
- (29) Hendricks, N. V. et al (1959)
Cancer of the scrotum in wax pressmen
I. Epidemiology. AMA Arch. Ind. Health Vol 19, pp 524-529
- (30) Hjorth, N. (1987)
Diagnostic patch testing.
In: Marzuli, F. N. and Maibach, H. I. (Eds)
Dermato-toxicology (3rd edition). Chapter 13, pp 307-317
Washington DC: Hemisphere Publishing Corp.
- (31) IBR (1976)
Akute Toxizitotsprufung von "R 9107" nach oraler applikation
an der ratte
International Bio-Research Inc. Report No. 1-4-195/1-76
- (32) IBR (1976)
Akute Toxizitotsprufung von "R 9269" nach oraler Applikation
an der ratte.
International Bio-Research Inc. Report No. 1-4-195/2-76.
- (33) JECFA (1996)
Toxicological evaluation of certain food additives and
contaminants. Prepared by the 44th meeting of the Joint
FAO/WHO Expert Committee on Food Additives (JECFA).
WHO Food Additives Series 35. Geneva.

5. Toxicity

Id Waxes

Date 8/6/02

- (34) Kane, M. L., Ladov, E. W., Holdsworth, C. E. and Weaver, N. K. (1984)
Toxicological characteristics of refinery streams used to manufacture lubricating oils.
American Journal of Industrial Medicine Vol 5. 183-200
- (35) Kaufman, J. J. and Weisberger, G. A. (1993)
Petroleum waxes, including petrolatums.
ASTM Manual on significance of tests for petroleum products (6th ed). Chapter 10.
- (36) Lijinsky, W., Saffiotti, U. & Shubik, P. (1966)
Skin Tumorigenesis by an Extract of Amber Petrolatum.
Toxicology and Applied Pharmacology Vol. 8, 113-117
- (37) Lione, J. G. and Denholm, J. S. (1959)
Cancer of the scrotum in wax pressmen
II. Clinical observations. AMA Arch. Ind. Health Vol 19, pp 530-539
- (38) Mackay, D, A. DiGuardo, S. Paterson, & C. Cowan, EQC Model, ver. 1.01, 1997, available from the Environmental Modeling Center, Trent University, Canada.
- (39) McCarty, L.S. et al (1991)
Interpreting aquatic toxicity QSARs: the significance of toxic body residues at the pharmacologic endpoint.
In: Hermens, J.L.M. and Opperhuizen, A. (Eds).
QSAR in environmental toxicology. Volume IV, p. 515-525.
Amsterdam: Elsevier.
- (40) Meylan, M, SRC 1994-1999.
AOPWIN is contained in the computer program EPIWIN (Estimate ver. 3.04), available from Syracuse Research Corp.
- (41) Meylan, M, SRC 1994-1999.
LOGKOWWIN is contained in the computer program EPIWIN (Estimate ver. 3.04), available from Syracuse Research Corp.
- (42) Oser, B. L., Oser, M., Carson, S. & Sternberg, S. S. (1965)
Toxicologic Studies of Petrolatum in Mice and Rats
Toxicology and Applied Pharmacology Vol 7, 382-401
- (43) SCF (1995)
Opinion on mineral and synthetic hydrocarbons (expressed on 22 September 1995).
CS/ADD/MsAd/132-Final. Brussels, European Commission
- (44) Schmähl, D. and Reiter, A. (1953)
Experiments to create cancer with liquid paraffin, yellow petrolatum and wool fat.
Arzneimittel-Forschungen, Volume 3, pp 403-406
- (45) Shubik, P., Saffiotti, U., Lijinsky, W., Pietra, G., Rappaport, H., Toth, B., Raha, C. R., Tomatis, L., Feldman, R. and Ramaha, H. (1962)
Studies on the Toxicity of Petroleum Waxes.
Toxicol. Appl. Pharmacol. Volume 4, Supplement 1-62

5. Toxicity

Id Waxes

Date 8/6/02

- (46) Smith, W. E., Sunderland, D. A. and Sugiura, K. (1951)
Experimental analysis of the carcinogenic activity of certain petroleum products.
Arch. Ind. Hyg. Occ. Med. Volume 4, pp 299-314
- (47) UK HSE (1999) Occupational exposure limits 1999.
HSE Guidance Note EH40/99.
Health and Safety executive, London