FOREWORD INTRODUCTION

TRIACETIN

CAS N°:102-76-1

SIDS Initial Assessment Report

For

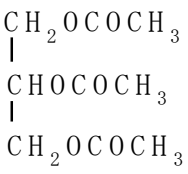
SIAM 15

Boston, 22-25 October 2002

1. Chemical Name:	Triacetin
2. CAS Number:	102-76-1
3. Sponsor Country:	Japan **National SIDS Contact Points in Sponsor Country**: Mr. Yasuhisa Kawamura Director Second Organisations Div. Ministry of Foreign Affairs 2–2-1, Kasumigaseki, Chiyoda-ku Tokyo 110
4. Shared Partnership with:	
5. Roles/Responsibilities of the Partners:	
• Name of industry sponsor /consortium	Dr. Tsuneo Baba Daicel Chemical Industries, Ltd. E-mail: ts_baba@daicel.co.jp
• Process used	
6. Sponsorship History	
• How was the chemical or category brought into the OECD HPV Chemicals Programme ?	This substance is sponsored by Japan under the ICCA Initiative and is submitted for first discussion at SIAM 15
7. Review Process Prior to the SIAM:	The industry consortium collected new data and prepared the updated IUCLID, draft versions of the SIAR and SIAP. Japanese government peer-reviewed the documents, audited selected studies.
8. Quality check process:	No testing (X) Testing ( )
9. Date of Submission:	13 August 2002 Deadline for Circulation: 9 August 2002
10. Date of last Update:	
11. Comments:	The Industry contact point is Dr. Tsuneo Baba, Daicel Chemical Industries, Ltd. acting on behalf of the Triacetin Consortium

Industries, Ltd. acting on behalf of the Triacetin Consortium (consortium members: Bayer AG, Cognis Deutschland GmbH, Eastman Chemical Company, Tessenderlo Chemie NV and Uniqema)

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	102-76-1
Chemical Name	Triacetin
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Triacetin is readily hydrolyzed to free glycerol and acetic acid, when incubated with rat intestine *in vitro*. The chemical infused in dogs undergoes intravascular hydrolysis and the majority of the resulting acetate is oxidized nearly quantitatively.

The acute oral and dermal toxicity of triacetin are very low: in an oral acute toxicity study in rats [OECD TG 401], a limit dose of 2,000 mg/kg bw caused no mortality and no signs of systemic toxicity during the 14-day observation period. The LD_{50} in rats by gavage is determined to be >2,000 mg/kg bw for both sexes, and dermal LD_{50} in rabbits and guinea pigs were >2,000 mg/kg bw. Acute inhalation toxicity is considered to be very low, since the LC_{50} in an acute inhalation toxicity study in rats was >1,721 mg/m^3 for both sexes [OECD 403] and repeated daily exposure of rats to 73,700 mg/m^3 produced no sign of toxicity after 5 days.

In an oral study in rats by the OECD combined repeated dose and reproductive/developmental toxicity screening test [OECD TG 422], animals received gavage doses of 0 - 1,000 mg/kg bw/day of triacetin for 44 days from 2 weeks prior to mating for males and for 41 - 48 days from 14 days before mating to day 3 postpartum for females. Triacetin had no effects on clinical signs, body weight, food consumption, and organ weight or necropsy findings. No histopathological changes ascribable to the compound were observed in either sex. There were no abnormalities in haematological or blood chemical parameters in males. The NOAEL for repeated dose oral toxicity is thus considered to be 1,000 mg/kg bw/day for both sexes.

An inhalation study was conducted in rats given triacetin for 90 days at a dose of 249 ppm (2,220 mg/m^3) under non-GLP condition. No toxic signs were noted during the exposure. The NOAEL is considered to be 249 ppm (2,220 mg/m^3) for 90 days. Although the inhalation study is considered to be useful, it does not fully comply with the current testing protocol.

The combined repeated dose and reproductive/developmental toxicity study in rats at doses of 0 - 1,000 mg/kg bw/day [OECD TG 422] showed no statistically significant adverse effects on reproductive parameters including the mating index, fertility index, gestation length, numbers of corpora lutea and implantations, implantation index, gestation index, delivery index, parturition and maternal behavior at delivery and lactation. In addition, there were no significant differences in numbers of offspring or live offspring, the sex ratio, the live birth index, the viability index or body weight. Developmental toxicity, clinical signs of toxicity, and change in necropsy findings were not found in offspring. Therefore, the NOAEL is considered to be 1,000 mg/kg bw/day for parental animals and offspring.

Triacetin did not induce gene mutation in bacteria at concentrations up to 5,000 ug /plate (OECD TG 471 and 472). Induction of chromosome aberrations, however, was observed in the Chinese hamster cultured cells only at the highest concentration (2.2 mg/mL, 10 mM) in the presence of an exogenous metabolic activation system (OECD TG 473). Because of high toxicity (75 %) that might be caused by low pH (4.9) at the end of the treatment, the chromosomal aberration observed might not be biological relevant. Under un-physiological culture condition, such as low pH, it was reported that the frequency of chromosomal aberrations could be increased. Polyploidy was not induced under any of the conditions tested. Taking all data into consideration, triacetin could be considered to be

non-genotoxic.

Triacetin is not irritating to skin [OECD TG 404] and to eyes [OECD TG 405] in rabbits. There is no skin sensitisation in guinea pigs by triacetin. In the tests using human volunteers, triacetin induced no skin irritation or skin sensitization. However, one case concerning allergic contact eczema caused by triacetin has so far been reported in a cigarette factory.

Based on the available data and anticipated daily intake (7.8 mg/day/adult), triacetin and a group of related triglyceride did not represent a hazard to human health (JECFA, 1975, Commission, 1992 and SCF, 1995). Triacetin was given GRAS status by FEMA (1965) and is approved by the FDA for human food use.

Environment

Triacetin is a liquid with a boiling point of 258 °C and vapour pressure of 0.003306 hPa at 25°C. It is soluble in water (70 g/L at 25°C) and miscible with alcohols, aromatic hydrocarbons and diethyl ether.

The generic fugacity model (Mackay Level III Fugacity Model) shows that triacetin will be distributed mainly to water if it is released into water, whereas approximately one third and two third of the chemical will stay in water and soil, respectively when released at equal amounts to water, soil and sediment (1:1:1). An estimated Henry's law constant of 1.23×10^{-8} atm m^3/mol indicates that the compound is essentially non-volatile from water.

The rate constant for the vapour-phase reaction with photochemically produced hydroxyl radicals has been estimated to be 7.81×10^{-12} cm^3/molecule sec at 25°C, which corresponds to an atmospheric half-life of about 48 hours at an atmospheric concentration of 5×10^5 hydroxy radicals/cm^3.

Triacetin is readily biodegradable (OECD TG 301C: 77 % after 14 days based on BOD, OECD TG 301B: 93 % after 28 days based on $ThCO_2$, OECD TG 301D: 79 % after 30 days based on BOD). The chemical is expected to have a low potential for bioaccumulation based on a low Log Pow (0.21).

The half-lives in water at pH 7 and 9 are estimated to be 60.4 days and 16.5 hours at 25 °C, respectively, whereas no hydrolysis at pH 4 occurs at 50 °C in 5 days. Triacetin is expected to have high soil mobility and may leach readily in soil based on Koc value of 10.5 from a regression-derived equation. Therefore, aqueous hydrolysis may be a major degradation process for triacetin in moist alkaline soils.

The 72-h toxicity of triacetin to alga (growth inhibition, *Selenastrum capricornutum*) is > 1,000 mg/L for EC_{50} and 556 mg/L for NOEC [OECD TG 201]. In *Daphnia magna*, EC_{50} values (48 h) for acute toxicity [OECD TG 202] are 768 mg/L, 810.9 mg/L and 380 mg/L, while the NOEC (21-d reproduction) for chronic toxicity [OECD TG 211] is 100 mg/L. The acute toxicity to fish is > 100 mg/L (Medaka; *Oryzias latipes*) and 165.3 mg/L (Fathead minnow; *Pimephales promelas*) for 96 h LC_{50} [OECD TG 203]. The prolonged toxicity to fish (Medaka; *Oryzias latipes*) is 100 mg/L for 14 d LC_0 [OECD TG 204].

Exposure

Triacetin is manufactured in a closed reaction system. The production volume in Japan is approximately 5,000 tonnes/year, while the estimated global production is 10,000-50,000 tonnes/year. Commercially available triacetin contains less than 0.1 % of diacetin and 0.01 % of monoacetin. Since triacetin produced in Japan is used industrially in a variety of applications including a solvent for basic dyes, fixative in perfumery, food additive, pharmaceuticals, CO_2 remover from natural gas and in manufacture of cigarette filters, celluloid, photographic films etc., in consumer products as well as at industrial sites, both workplace and consumer exposure has to be assumed according to the following three scenarios.

(1) Occupational exposure: inhalation and dermal route during operations such as cleaning of strainers, sampling, analysis and drum filling.
(2) Consumer exposure: intake and dermal/inhalation route in food additive and topical antifungal or perfume fixative and cigarette filter.
(3) Environmental exposure: emission to aquatic compartment from waste water and evaporative emissions associated with its use in the perfume and cosmetic industries and its use as a solvent and CO_2 remover from natural gas, and disposal of consumer products containing triacetin.

RECOMMENDATION

The chemical is currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

The chemical is currently of low priority for further work because of its low hazard potential.

FULL SIDS SUMMARY

CAS NO: 102-76-1		SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL				
2.1	Melting Point		Unknown	3 °C (276 K)
2.2	Boiling Point		Unknown	258°C (1,013 hPa)
2.3	Density		Unknown	1.1562 g/cm^3 (25 °C)
2.4	Vapour Pressure		Unknown	0.003306 hPa (25 °C)
2.5	Partition Coefficient (Log Pow)		OECD TG 107	0.21 (25 °C)
2.6 A.	Water Solubility		OECD TG 105	70 g/L (25 °C)
			Unknown	58 g/L (25 °C)
B.	pH		Unknown	7
	pKa			None.
2.12	Oxidation: Reduction Potential			None.
ENVIRONMENTAL FATE AND PATHWAY				
3.1.1	Photodegradation		Calculated (Atkinson)	$T_{1/2}$=48 hours (Indirect photolysis)
3.1.2	Stability in Water		OECD TG 111	Stable at pH 4 (50°C). $T_{1/2}$ = 60.4 days at pH 7 (25°C) $T_{1/2}$ = 16.5 hours at pH 9 (25°C)
3.2	Monitoring Data		Unknown	In air : None. In surface water : None. In soil/sediment : None. In biota : None.
3.3	Transport and Distribution		Calculated	Estimated distribution under four emission scenario
			(Mackay Level III Fugacity Model)	Water solubility: 70 g/L (58 g/L) at 25°C (Release 100% to air) Air Water Soil Sed. (%) 0.9 (1.1) 20.0 (19.9) 79.1 (79.0) 0.1 (0.1) (Release 100% to water) 0.0 (0.0) 99.7 (99.7) 0.0 (0.0) 0.3 (0.3) (Release 100% to soil) 0.0 (0.0) 12.9 (12.9) 87.1 (87.1) 0.0 (0.0) (Equal emission scenario 1:1:1) 0.3 (0.4) 30.1 (30.2) 69.5 (69.4) 0.1 (0.1)
			(Local exposure)	PEC_{local} : None.
3.5	Biodegradation		OECD TG 301C	Readily biodegradable.
3.7	Bioaccumulation		Calculated (Lyman)	1.3

ECOTOXICOLOGY				
4.1	Acute/Prolonged Toxicity to Fish	*Oryzias latipes*	OECD TG 203	LC_{50} (96 hr) > 100 mg/L
			OECD TG 204	LC_{50} (14 d) > 100 mg/L LC_0 (14 d) = 100 mg/L
		Pimephales promelas	OECD TG 203	LC_{50} (96 hr) = 165.3 mg/L
		Cyprinus Carpio	Other (unkown)	LC_{50} (48 hr) = 174 mg/L
		Leuciscus idus	DIN38412	LC_{50} (48 hr) = 170 mg/L
		Branchydanio rerio	ISO-7346/2	LC_{50} (96 hr) = 300 mg/L
4.2	Acute Toxicity to Aquatic Invertebrates (*Daphnia*)	*Daphnia magna*	OECD TG 202	EC_{50} (24 hr) = 888 mg/L EC_{50} (48 hr) = 768 mg/L EC_0 (48 hr) = 309 mg/L
			OECD TG 202	EC_{50} (24 hr) > 974.4 mg/L EC_{50} (48 hr) = 810.9 mg/L EC_0 (48 hr) = 541.1 mg/L
			OECD TG 202	EC_{50} (48 hr) = 380 mg/L EC_0 (48 hr) = 65 mg/L
4.3	Toxicity to Aquatic Plants e.g. Algae	*Selenastrum Capricornutum (ATCC22662)*	OECD TG 201	EC_{50} (72 hr) > 1,000 mg/L NOEC (72 hr) = 556 mg/L (Growth inhibition: growth rate & biomass)
4.5.2	Chronic Toxicity to Aquatic Invertebrates (*Daphnia*)	*Daphnia magna*	OECD TG 211	EC_{50} (21 d) > 100 mg/L (Reproduction) NOEC (21 d) = 100 mg/L (Reproduction) LC_{50} (14 d) > 100mg/L (Parental Daphnia) LC_{50} (21 d) > 100mg/L (Parental Daphnia)
4.6.1	Toxicity to Soil Dwelling Organisms			None.
4.6.2	Toxicity to Terrestrial Plants			None.
4.6.3	Toxicity to Other Non-mammalian Terrestrial Species (Including Birds)			None.

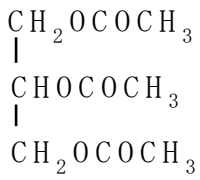
TOXICOLOGY				
5.1.1	Acute Oral Toxicity	Rat	OECD TG 401	LD_{50} > 2,000 mg/kg bw (m & f)
		Rat	Other (unknown)	LD_{50} = 3,000 mg/kg bw
		Rat	Other (unknown)	LD_{50} = 6,400-12,800 mg/kg bw
		Rat	Other (unknown)	LD_{50} = 12,700 mg/kg bw
		Mouse	Other (unknown)	LD_{50} = ca. 9,300 mg/kg bw (m)
		Mouse	Other (unknown)	LD_{50} = 1,800 mg/kg bw (m) LD_{50} = 1,100 mg/kg bw (f)
		Mouse	Other (unkown)	LD_{50} = 3,200-6,400 mg/kg bw
5.1.2	Acute Inhalation	Rat	OECD TG 403	LD_{50} > 1,721 mg/m^3 (m & f) No lethal effects observed.
	Toxicity		Other (unkown) (Inhalation for 5 days)	NOAEL=73,700 mg/m^3
5.1.3	Acute Dermal Toxicity	Rabbit	Other (unknown)	LD_{50} > 2,000 mg/kg bw
		Rabbit	Other (unknown)	LD_{50} > 5,000 mg/kg bw
		Guinea pig	Other (unknown)	LD_{50} > 20 mL/kg bw
5.2.1	Skin Irritation	Rabbit	OECD TG 404	Not irritating.
5.2.2	Eye Irritation	Rabbit	OECD TG 405	Not irritating.
5.3	Skin Sensitisation	Guinea pig	Maximization	Not sensitising.
5.4	Repeated Dose Toxicity	Rat	OECD TG 422 (Oral gavage)	NOAEL =1,000 mg/kg bw/day (m) NOAEL =1,000 mg/kg bw/day (f)
		Rat	Other (unknown) (Oral by feed)	NOAEL =10 g/kg bw /day (20 % of the diet)
		Rat	Other (unknown) (Inhalation for 90 days)	NOAEL =2,220 mg/m^3
5.5	Genetic Toxicity *In Vitro*			
A.	Bacterial Test (Gene mutation)	*S.typhimurium, E. coli*	Japanese TG and OECD TG 471 & 472	- (With metabolic activation) - (Without metabolic activation)
B.	Non-Bacterial *In Vitro* Test (Chromosomal aberrations)	CHL cells	Japanese TG and OECD TG 473	? (With metabolic activation) - (Without metabolic activation)
5.6	Genetic Toxicity *In Vivo*			None.
5.7	Carcinogenicity			None.
5.8	Toxicity to Reproduction	Rat	OECD TG 422	NOAEL Reproduction=1,000mg/kg bw/day
5.9	Developmental Toxicity/Teratogenicity			NOAEL F1 Offspring=1,000mg/kg bw/day
5.11	Experience with Human Exposure		Duhring-chamber	Very mild skin reaction. One case report of contact eczema.
			Other (a patch test)	Triacetin ingestion : 7.8 mg/day/adult

SIDS Initial Assessment Report

1. IDENTITY

1.1 Identification of the Substance

CAS Number: 102 – 76 – 1
IUPAC Name: Triacetin
Molecular Formula: $C_9H_{14}O_6$
Structural Formula:



Synonyms: (Chemical name)
1, 2, 3-Propanetriol, triacetate
1, 2, 3-Propanetriyl, triacetate
1, 2, 3-Triacetoxypropane
Acetic acid, glycerol triester
Acetic, 1, 2, 3-Propanetriyl ester
Acetin, Tri-
Glycerin triacetate
Glycerol triacetate
Glycerol, triester with acetic acid
Glyceryl triacetate
Propane-1, 2, 3-triyl triacetate
Triacetin
Triacetyl glycerin
Triacetyl glycerine
Triacetyl glycerol

(Trade name)
ENZACTIN
"ESTROBOND" B Plasticizer
FEMA NUMBER 2007
FUNGACETIN
GLYPED
KESSCOFLEX TRA
KODAFLEX TRIACETIN
VANAY

1.2 Physico-Chemical properties

Table 1 Summary of physico-chemical properties

ITEMS	PROTOCOL	RESULTS
Melting Point	Unknown	3 °C (276 K)
Boiling Point	Unknown	258 °C (1,013 hPa)
Density	Unknown	1.1562 g/cm^3 (25 °C)
Vapour Pressure	Unknown	0.003306 hPa (25 °C)
Flash point	DIN 51758/ISO2719	> 145 °C (Closed cup).
Auto flammability	ASTM D2155	432 °C
Partition Coefficient (Log Pow)	OECD TG 107	0.21 (25 °C)
Water Solubility	OECD TG 105	70 g/L (25 °C)
	Unknown	58 g/L (25 °C)

2. GENERAL INFORMATION ON EXPOSURE

Triacetin is a liquid with a boiling point of 258 °C and a vapour pressure of 0.003306 hPa at 25 °C. It is soluble in water. The Henry's Law constant (1.23×10^{-8} atm m^3/mol) for triacetin indicates that the compound is essentially non-volatile from water.

Triacetin is produced in a fully closed system in Japan. The production volume of triacetin in Japan is approximately 5, 000 tonnes/year (Daicel, 2001), while estimated global production is 10,000-50,000 tonnes/year according to IUCLID 2001. Other major manufacturers are Eastman (USA), Cognis (Germany) and Uniqema (UK).

Since triacetin has a variety of applications including as a plasticizer for cigarette filters and cellulose nitrate, solvent for the manufacture of celluloid, photographic films, fungicide in cosmetics, fixative in perfumery, component in binders for solid rocket fuels and a general purpose food additive, release of triacetin to the environment may occur at the production sites, specific industrial sites and consumers depending on the conditions of use in Japan.

The exposure of triacetin may occur mainly according to the following three scenarios.

(1) Occupational exposure: inhalation and dermal route in the industries.

(2) Consumer exposure: intake and dermal/inhalation route through the use as a food additive and topical antifungal and perfume fixative or cigarette filter, respectively.

(3) Environmental exposure: emission to aquatic compartment from waste water and evaporative emissions associated with its use in the perfume and cosmetic industries and its use as a solvent and CO_2 remover from natural gas, and disposal of consumer products containing triacetin.

2.1 Environmental Exposure and Fate

2.1.1 Sources of Environmental Exposure

Triacetin is readily biodegradable in activated sludge (OECD 301C: 77 % by BOD and 94 % by TOC (100 mg/L) after 14 days, OECD 301 B: 64 % (10 mg/L) and 93 % (20 mg/L) by $ThCO_2$, after 28 days, OECD 301 D: 69 % (2 mg/L) and 79 % (5 mg/L) by BOD, after 30 days) (Chemicals Evaluation and Research Institute, 1998, Unichema, 1990 and Henkel, 2001, respectively).

This chemical is stable to hydrolysis in water at pH 4, whereas it is hydrolysed at pH 7 and 9 with half-lives of 60.4 days and 16.5 hours at 25 °C, respectively (Chemicals Evaluation and Research Institute, 1998).

Triacetin is a triglyceride, and the shortest-chain fatty acid ester of glycerol, which will be readily hydrolyzed to give acetic acid and glycerol in alkaline environment.

Direct photodegradation is not expected because triacetin has no absorption band in the UV and VIS region, whereas indirect photodegradation may occur as a result of reactions with photochemically generated hydroxy radicals with an estimated rate constant of 7.81×10^{-12} cm^3/molecule*sec (Atkinson, 1987), which corresponds to an atmospheric half-life of about 48 hours at an atmospheric concentration of 5×10^5 hydroxy radicals/cm^3.

Triacetin has low bioaccumulative potential based on its Log Pow (0.21 at 25 °C, Chemicals Evaluation and Research Institute, 1998).

During the course of the regular use of consumer products, triacetin diffuses away into air. Although direct photodegradation is not expected, triacetin in air decomposes and disappears by photolytic reactions with photochemically generated hydroxy radicals.

For these reasons, there will be little potential for accumulation of triacetin in the atmosphere.

2.1.2 Other Information on Environmental Fate

In Japan, the annual quantity of triacetin production is estimated to be 5, 000 tonnes/year and 3.6 tonnes of this chemical is treated by activated sludge through process waste water (Daicel, 2001). Worst case and most likely case scenarios are based on the assumption that all of the annual production of 5,000 tonnes was discharged to water and the process waste water containing 3.6 tonnes of triacetin/year was released without sludge treatment within a single geographical area, respectively.

The Mackay level III fugacity model was employed to estimate the environmental distribution of triacetin in air, water, soil and sediment (Section 4.4). The calculation revealed that in the case of 100 % release to water, more than 99 % of triacetin is expected to stay in water due to its high solubility and low vapour pressure, but if it is released into air and/or soil, it is likely to be distributed to other compartments. The results also show that approximately one third of triacetin will be distributed to water, whereas two third will stay in soil when applied to the equal emission scenario to water, soil and sediment (1:1:1). In addition, the fugacity model using the solubility value of 58 g/L reveals that there is little change in the distribution of triacetin between the three compartments when compared to those obtained from 70 g/L (Section 4.4).

For exposure to surface water, PEC values of 0.00018 mg/L and 0.25 mg/L are calculated for most likely case and worst case modelling evaluations, respectively. PEC values are calculated based on the hypothetical model area such as inlet into the Tokyo bay (for parameters used, refer to Appendix in the SIDS dossier).

Assuming that individuals use untreated water as their sole source of drinking water (2 L/day for a 70 kg adult), EHE values of 0.00000514 mg/kg bw/day (most likely case) and 0.00714 mg/kg bw/day (worst case) are calculated.

Potential exposure via consumption of fish is anticipated to be negligible because triacetin is expected to have a low potential for bioaccumulation and is readily biodegradable in activated sludge (Chemicals Evaluation and Research Institute, 1998, Unichema, 1990, Henkel, 2001)

There is little potential for accumulation of triacetin in the atmosphere because of the decomposition by the reactions with photochemically generated hydroxy radicals with a half-life of ca. 48 hours.

2.2 Human Exposure

2.2.1 Occupational Exposure

Occupational exposure to triacetin can occur through dermal contact and inhalation at the production sites during operations such as cleaning strainer, sampling, analysis and drum filling.

The atmospheric concentration of this chemical was measured at a production site in Japan. The monitored data and Estimated Human Exposure (EHE) for triacetin are shown in Table 2.

Table 2: Workplace Monitoring Data and EHE values for Triacetin production

Operation	Working hours/day	Maximum concentration (mg/m^3)	Average concentration (mg/m^3)	Maximum EHE_{inh}	Average EHE_{inh}
Cleaning strainer	0.50	1.364	1.031	0.0122	0.0092
Sampling	0.25	1.333	1.167	0.0060	0.0052
Analysis	0.25	0.400	0.400	0.0018	0.0018
Drum filling	5.0	0.200	0.092	0.0179	0.0082
Combined EHE_{inh}				0.0379	0.0244
EHE_{der}				49.43	4.94
Combined (EHE_{inh} + EHE_{der})				49.47	4.96

EHE : Estimated Human Exposure

Source: Japan Industrial Safety and Health Association Report 2002

Monitoring method: Air sample was suctioned at the breathing zone (1.5 m in height) of a worker at the suction rate of 1 L/min and was passed through a filter. The substance collected on the filter was dissolved in a solvent and analysed quantitatively by GC method. The identity of the substance was confirmed by GC/MS.

Using the data in Table 2, if a single worker (body weight: 70 kg, respiratory volume: 1.25 m^3/hr) is assigned to implement all daily operation without protection, the highest daily intake (combined EHE_{inh}) is calculated to be 0.0379 mg/kg bw/day (e.g. for cleaning strainer, EHE_{inh} (0.0122) = (0.50 hr/day*1.364 mg/m^3*1.25 m^3/hr)/70 kg) for the worst case (maximum concentration) or as 0.0244 mg/kg bw/day (e.g. for cleaning strainer, EHE_{inh} (0.0092) = (0.50 hr/day*1.031 mg/m^3*1.25 m^3/hr)/70 kg) for most likely case (average concentration), respectively.

Dermal absorption can be a significant route of entry into the body for triacetin, however there is no information for the percutaneous absorption rate.

Based on the EASE model and an absorption rate of 0.1 – 1 mg/cm^2/day (worst case) or 0– 0.1 mg/cm^2/day (most likely case), using body weight (70 kg) and open body area (face + arms = 3,460 cm^2), a worker's daily dermal dose (EHE_{der}) for triacetin is calculated to range from 4.94 mg/kg bw/day (most likely case, EHE_{der}= (0.1 mg/cm^2/day*3,460 cm^2)/70 kg) to 49.43 mg/kg bw/day (worst case, EHE_{der}= (1 mg/cm^2/day*3,460 cm^2)/70 kg).

Typically, workers are using PPE (protective gloves) and RPE (respiratory protective equipment-mask) during these operations at the workplace, triacetin uptake is minimised and is practically negligible.

Triacetin has no significant irritant effects following skin contact or by inhalation.

No occupational exposure limits are established for triacetin (MSDS-OHS, 2001).

2.2.2 Consumer Exposure

According to HSDB 2001, triacetin has the following uses in consumer products: as a solvent for celluloid and photographic films, a plasticizer for cigarette filters, fungicide in cosmetics, fixative in perfumery, and a general purpose food additive.

Concentration of triacetin in consumer products is in the range of about 0.005-2 % for cosmetics, and has been reported to be as high as 15-33 % for one specific antifungal drug (Opdyke, 1978).

Dermal exposure (EHE_{der}) to triacetin by consumers is estimated using the equation based on EASE model.

Dermal dose (EHE_{der}) =($M*W_f*n*R_f$)/(W)

Where, Dermal dose (EHE_{der}): daily dermal dose (mg/kg bw/day)

M (mg) = amount /use (1,000 and 10 mg assumed, for cream for most likely case and antifungal ointment for worst case, respectively)

W_f (%): triacetin content (0.3 and 25 % assumed)

n: exposure frequency/day (1 and 3 assumed)

R_f (%): amount remained on the skin (100 % assumed)

W: body weight (70 kg)

Based on this hypothetical scenario, a consumer's daily dermal dose (EHE_{der}) for triacetin is calculated to range from 0.0429 mg/kg bw/day (most likely case, 1,000 mg*0.3*1/day*1.00/70 kg) to 0.107 mg/kg bw/day (worst case, 10 mg*0.25*3/day*1.00/70 kg).

According to a UK survey, an adult might ingest 7.8 mg triacetin/day as part of a total daily additive intake of 8.0 g (MAFF, 1993) and the daily intake is thus calculated to be 0.111 mg/kg bw/day (most likely case).

3. HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

Pharmacokinetics studies according to OECD TG are not available. Instead, a substantial amount of studies were conducted concerning mechanism on enzymatic hydrolysis of triacetin and its favorable effects on carbohydrate and protein metabolism because of the use regarding triacetin as a parenteral nutrient. Among them, two studies are identified as the key study because they were well conducted and described in detail. Details of the studies are described below.

When monoacetin, diacetin and triacetin were incubated with the sacs of everted intestine from rats for 1 hr at 37 °C, the glycerides entered the epithelial cells and were completely hydrolyzed to free glycerol and acetic acid. The acetate released appeared in higher concentrations on the serosal side. The activity of the preparation, as measured by acetate release, increased with the number of acetic acid residues in the glyceride (15 mM). Monoacetin, diacetin and triacetin released 92 ± 4, 206 ± 12 and 307 ± 11 umoles of acetate, respectively. With increasing concentrations of glyceride (5, 10 and 15 mM), the amount of acetate released increased linealy up to about a total amount of 300 umoles of acetates released. There was no absolute positional specificity, and all three ester linkages were split (Barry et al., 1966).

To investigate that triacetin may have a role as a parenteral nutrient, a 5 % (v/v) aqueous solution was administered intravenously to mongrel dogs at a rate of 47 umol/kg bw/min (estimated resting energy expenditure: REE) for an additional 4 hours, after [1-^{14}C] acetate was infused at a rate of ca. 30 kBq/min for 3 hours (continued to the end of study) to allow quantification of organ uptake of acetate as well as systemic turnover and oxidation (Bleiberg, 1993).

Systemic acetate kinetics was obtained in all animals tested. Systemic acetate turnover accounted for approximately 70 % of triacetin-derived acetate, assuming complete hydrolysis of the triglyceride. Aapproximately 80 % of systemic acetate uptake was rapidly oxidized and significant acetate uptake was demonstrated in all tissues (liver, 559 ± 68; intestine, 342 ± 23; hind limb, 89 ± 7; and kidney, 330 ± 37 umol/min). The results demonstrate that during intravenous administration in dogs, the majority of infused triacetin undergoes intravascular hydrolysis, and the majority of the resulting acetate is directly oxidized (Bleiberg, 1993). This is consistent with the generally accepted view that short- and medium-chain fatty acids undergo near quantitative oxidation rather than being reesterificated or elongated to longer fatty acid chain (Groot and Hulsmann, 1973).

Effects on metabolism

(Mineral metabolism)

Triacetin was infused at 47 umol/kg bw/min for 3 hr at an isocaloric rate in mongrel dogs to test its effects on serum phosphorus, calcium, and magnesium metabolism (Bailey, et al. 1989). Arterial blood was sampled at 15-30 min intervals until the end of the study. Urine was collected during the equilibration period and again during triacetin infusion. There were no changes in serum P or Ca. Serum Mg decreased by approximately 20 %, probably because of cellular uptake rather than accelerated excretion and remained at this level for the remainder of the study. Thus, triacetin administered to dogs at a rate approximating resting energy expenditure has no demonstrable adverse effects on mineral metabolism (Bailey, et al. 1989).

(Protein metabolism)

To investigate the effects of intravenous administration of triacetin on leucine metabolism in dogs, infusion of **L**-[1-^{14}C]-leucine was conducted at 1.5 kBq/kg bw/min for 6 hr in mongrel dogs (Bailey, et al. 1993). Three hours after initiation of the isotope infusion, animals received infusion of 5 % triacetin at 47 umol/kg bw/min (1.0 x estimated resting energy expenditure: REE), at 70 umol/kg bw/min (1.5 x REE), glycerol (70 umol/kg bw/min), or saline during infusion. No overt toxic effects were observed. Leucine kinetics (the rate of leucine appearance (Ra): an estimate of leucine derived from endogenous protein breakdown, leucine oxidation, and the rate of no oxidized leucine disappearance (NOLD): an indicator of protein synthesis) were not significantly different among animals receiving saline, glycerol, or isoenergitic triacetin infusions. When triacetin was infused at 1.5 x REE, leucine Ra and leucine oxidation decreased 19 % and 53 %, respectively. NOLD did not change in any of the studies. The studies demonstrate that triacetin does not have adverse effects on protein metabolism and at relatively high doses actually suppresses endogenous proteolysis (Bailey, et al. 1993).

(Lipolysis)

Following ingestion, a natural long-chain triglyceride is eventually hydrolyzed to glycerol and corresponding fatty acid by pancreatic lipase in the presence of colipase, producing 2-monoglyceride, which in turn by the action of 2-monoglyceride lipase in plasma (Fielding, 1981 and Fossati et al., 1992) or liver (Fielding, 1972).

However, such mechanism cannot be necessarily applied to short- and medium-chain triglycerides because shorter-chain 2-monoglycerides are either cleaved by pancreatic lipase or rapidly isomerized to the 1-isomer, which rapidly hydrolyzed (Boudreau, 1965). Several studies confirmed that triacetin is readily hydrolyzed to glycerol and acetic acid by digestive enzymes, particularly intestinal lipase or liver and plasma carboxyesterases (Murphy & Cheever, 1968). Rat everted intestine was found to be equally active on mono-, di- and triacetin to produce glycerol and acetic acid (Barry et al., 1966). An intestinal lipase has been characterized in different species, including man (Serrero, 1975). In addition, the presence of a gastric lipase in adult man with an acidic optimum pH has also been characterized. This lipase is active on short- and medium-chain triglycerides (Cohen, et al., 1971).

Information on structurally related chemicals

(Monoacetin: glyceryl monoacetate)

The oral LD_{50} of monoacetin in rats was determined as 5.0 mL/kg bw (Li et al, 1941). Monoacetin caused no toxic effects in rats when administered at 0.1 mL/kg bw, daily subcutaneously for 70 days, and similar results were observed in dogs (Chenoweth et al, 1951). There are no reports on toxic effects of monoacetin for human beings, and the hazards from handling this chemical appear to be comparatively small.

(Diacetin: glyceryl diacetate)

The oral LD_{50} of diacetin in rats or mice was determined as 4.0 mL or 2.5 mL, respectively (Li et al, 1941). There are no reports on toxic effects of diacetin in man (von Oettingen, 1960).

From these results, it can be concluded that the toxicity of monoacetin and diacetin in mammals is not significant.

(Triproprionin: glyceryl tripropanoate)

The oral LD_{50} of triproprionin in rats was found to be ca. 15 mL/kg bw (Hodge, 1942). Rat exposed to heated vapour (about 750 ppm) for 6 hours/day for 90 days showed no symptoms or abnormalities in clinical data and histopathology (Hodge, 1942). Triproprionin is not a skin irritant or sensitiser in guinea pig (Fassett, 1963).

(Tributyrin: glyceryl tributyrate)

The oral LD_{50} of tributyrin in rats is about 13 g/kg bw. Weakness, ataxia and vasodilatation in the ears and feet were noted. There was no percutaneous absorption or irritation in the guinea pig. Inhalation of 78 ppm for 6 hours caused temporary hyperpnea, but no fatalities or other symptoms in rats (Fassett, 1963).

3.1.2 Acute Toxicity

Studies in Animals

Results from acute toxicities via the oral, inhalation and dermal route using rats, mice, rabbits and guinea pigs are summarized in Table 3.

Table 3: Acute Toxicity of Triacetin in Experimental Animals

Route	Animals	Values	Type	References
Oral	Rat	> 2,000 mg/kg bw (male & female)	LD_{50}	Unichema (1988)[2]
Oral	Rat	3,000 mg/kg bw	LD_{50}	von Oettingen (1960)
Oral	Rat	6,400 - 12,800 mg/kg bw	LD_{50}	Fassett (1955)[1]
Oral	Rat	12,700 mg/kg bw	LD_{50}	Fassett (1948)
Oral	Mouse	ca. 9,300 mg/kg bw (male)	LD_{50}	Lawrence et al. (1974)
Oral	Mouse	1,800 mg/kg bw (male) 1,100 mg/kg bw (female)	LD_{50}	Gast, J.H. (1963)
Oral	Mouse	3,200 - 6,400 mg/kg bw	LD_{50}	Fassett (1955)[1]
Inhalation	Rat	> 1,721 mg/m^3 (4 hrs), (male & female)	LC_{50}	Bayer AG (1985)
Inhalation	Rat	73,700 mg/m^3 (5 days)	NOAEL	Fassett (1955)[2]
Dermal	Rabbit	> 2,000 mg/kg bw	LD_{50}	Unichema (1994)
Dermal	Rabbit	> 5,000 mg/kg bw	LD_{50}	Bailey (1976)
Dermal	Guinea pig	> 20 mL/kg bw	LD_{50}	Fassett (1967)

Among the above, an oral rat study (Unichema, 1988[2]) was identified as the key study because it was well conducted and described in detail in compliance with GLP for non-clinical studies (US FDA, EPA and OECD). Details of the study are described below.

Male and female Wistar rats were administered orally at a single, maximum dose (2,000 mg/kg bw, a limit dose level) to one group of five male and five female rats according to OECD TG 401. No mortality occurred and no signs of systemic toxicity were observed during the 14-day observation period. Gross pathology revealed no treatment-related changes at the end of two weeks for both sexes. From these results, triacetin has no toxic effect when administered as a single oral dose to

rats at a level of 2,000 mg/kg bw. When triacetin was administered orally to rats, in another study, at doses that caused fatality, weakness and ataxia were reported (Fassett, 1955[1]).

Studies in Humans

There is no information available.

Conclusion

Acute toxicity of triacetin is low in rodents because LD_{50} values are greater than 1,000 mg/kg bw by oral or dermal route and greater than 1,000 mg/m^3 by inhalation.

3.1.3 Irritation

Studies in Animals

Skin Irritation

Application of triacetin induced no skin irritation in rabbits (Kaestner, 1988 and Hem, 1974-1975) and slight irritation in guinea pigs (Fasset, 1967).

Eye Irritation

Most of the studies report that triacetin caused no irritation to rabbit eye (Jacobs, 1989, Kaestner, 1988, Conquet, 1977, Lailer, 1976, Hughes, 1976) except one report where slight irritation was observed in rabbits (Fasset, 1967).

Conclusion

Triacetin is neither classified nor labelled as irritant according to European regulation and Directive 67/548/EWG.

Studies in Humans

Human data is not available in detail except one case report (Unna and Schultz, 1963). Triacetin caused mild skin irritation when tested at 50% in 20 volunteers with 24-hr occlusive skin contact (Matthies W., 1988). Triacetin (20 % in petrolatum) did not irritate the skin of 33 volunteers when tested in a 48-hr covered patch test (Epstein, 1976). Contact with a solution containing 50 % triacetin in ethanol was not irritant to 20 eczema patients in covered test for 24 and 48hr (Unna and Schulz, 1963).

No skin reactions occurred in 33 volunteers treated with 20% triacetin in petrolatum in an attempt to induce skin sensitisation using the maximization test (Klingman, 1966, Klingman & Epstein, 1975). However, there is one case report so far concerning allergic contact eczema in a cigarette factory, which was based on sensitisation towards triacetin used for the production of cigarette filters and identified as the key study because of detailed description of the case. The allergy was demonstrated in a patch test. In addition to triacetin, monoacetin and diacetin also produced positive results (Unna and Schulz, 1963).

3.1.4 Sensitisation

Application of triacetin did not induce skin sensitisation in guinea pigs (Opdyke, 1978 and Eastman Kodak Company, 1955).

Conclusion

Triacetin is not irritating to skin and to eyes in rabbits. Triacetin does not induce skin sensitisation in guinea pigs.

3.1.5 Repeated Dose Toxicity

Some of the results from repeated toxicity studies via oral, feeding and inhalation route in rats and sheep are summarized in Table 4.

Table 4: Repeated Dose Toxicity of Triacetin in Experimental Animals

Route	Animals	NOAEL	Exposure period	References
Oral	Rat	1,000 mg/kg bw/day (male) 1,000 mg/ kg bw /day (female)	44 days 41 - 48 days	MHW (1998)
Feed	Rat	10 g/kg bw /day (male)	90 days	Shapira (1969)
Feed	Sheep	10 %/day (male & female)	175 days	Bull (1970)
Inhalation	Rat	2,220 mg/m^3	90 days	Fassett (1955)[2]

Although several studies are available, all but one of these studies were run prior to the publication of GLP standards. In addition, these studies were not conducted according to currently approved laboratory methods for toxicity testing. Therefore, the repeated dose study by gavage conducted by MHW, Japan, 1998 was identified as the best quality and the key study because it was well conducted and described in detail. Other studies including by inhalation (Fassett, 1955[2]) and oral by feed (Bull, et al. 1970 and Shapira, 1969, 1975) were also reviewed because these studies were cited elsewhere and afford the experimental evidences concerning that triacetin is a safe substance in a variety of uses including food, cigarette filters and cosmetics (MSDS-OHS, 2001). Details of these studies are described below.

Oral

(Oral by Gavage)

Using the OECD combined repeated dose and reproductive/developmental toxicity screening test [OECD TG 422], SD (Crj: CD) rats received gavage doses of 0 (vehicle; distilled water), 40, 200 and 1,000 mg/kg bw/day; for males for 44 days from 2 weeks prior to mating and for females for 41-48 days from 14 days before mating to day 3 postpartum (MHW, Japan: 1998).

Triacetin had no effects on clinical signs, body weight, body weight gain, food consumption, and organ weight or necropsy findings. No histopathological changes ascribable to the compound were observed even at the highest dose for both sexes. There were no abnormalities in haematological or blood chemical parameters in males, although urinalysis was not conducted. The NOAEL for repeated dose toxicity is thus considered to be 1,000 mg/kg bw/day for both sexes.

(Oral by Feed)

(Rat) To develop diets which contain virtually all the calories as purified organic compounds for long-duration space missions, growing male rats were fed diets containing triacetin and/or glycerin (20 - 60 %) for 90 days. The animals well tolerated up to 20 % triacetin, which corresponds to 10

g/kg bw/day. Greater percentage caused a decrease in weight gain. A large loss in weight and considerable mortality was associated with diets containing either glycerol or triacetin at 60 % of the diet (Shapira, 1969), while increased liver weight occurred in the 30 % groups (Shapira, 1975). The NOAEL for the feeding study is considered to be 10 g/kg bw/day for male rats.

(Sheep) A feeding experiment using rams and ewes was conducted for 175 days to study the efficiency of utilization for growth-fattening, of the energy of diets in the ruminal ingesta. Triacetin, employed as a source of acetic acid, was added to the basal diets to comprise 10 % of the total dietary dry matter. Faeces were collected and analysed for the proximate chemical constituents and heat of combustion and samples of urine were analysed for urinary energy. Utilization rates were 62.0 % for the metabolizable energy (ME) provided by the diets containing triacetin in a 175 day feeding study with sheep. No toxicity was reported (Bull et al. 1970).

Inhalation

To determine if the plasticiser, when used in cellulose acetate cigarette filters, would have any toxic effect on the individuals inhaling the compound, long-term vapour inhalation toxicity for 90 days was studied for rats at a dose of 249 ppm (2,220 mg/m^3). Average daily weight gain was 2.2 g/rat. Inhalation was further extended for another week at 73.72 ppm (660 mg/m^3) and 8,271 ppm (73,700 mg/m^3, saturated vapour) (Fassett, 1955[2]). No symptoms were noted during the exposure. Haematological studies and urinalysis showed no abnormalities in any of the animals. No histopathological changes were observed at the time of autopsy. The NOAEL is estimated to be 8,271 ppm (73,700 mg/m^3) for the 5-day study and 249 ppm (2,220 mg/m^3) for the 90-day study. Although the inhalation studies are considered to be useful, they do not fully comply with the current testing protocol.

Conclusion

An oral repeated dose study in rats showed no adverse effects even at the highest dose, 1,000 mg/kg bw/day. In a 90-day feeding study with rats up to 10 g/kg bw/day were tolerated without signs of toxicity. An inhalation study reveals no abnormalities attributable to exposures of 8,271 ppm (73,700 mg/m^3) for 5 days and 250 ppm (2,200 mg/m^3) for 90 days. Therefore, the NOAEL for repeated dose oral toxicity in rats is 1,000 mg/kg bw/day for both sexes. The NOAEL for the feeding study is considered to be 10 g/kg bw /day for male rats. The NOAEL for repeated inhalation toxicity in rats is considered to be 8,271 ppm (73,700 mg/m^3) for 5 days and 250 ppm (2,200 mg/m^3) for 90 days.

3.1.6 Mutagenicity

In vitro Studies

Several *in vitro* studies are available. Triacetin did not induce gene mutation in bacteria (MHW, Japan: 1998, Uniquema, 1988[3], Henkel, 1982) and induced chromosomal aberrations in mammalian cultured cells (MHW, Japan: 1998). Among these studies, MHW studies were identified to be the key study because they were most recent, well conducted and published.

A reverse gene mutation assay was conducted using the pre-incubation method (OECD TG 471 and 472). Triacetin was not mutagenic in *Salmonella typhimurium* TA100, TA1535, TA98, TA1537 and *Escherichia coli* WP2 *uvr*A at concentrations up to 5,000 ug /plate, with or without an exogenous metabolic activation system (MHW, Japan: 1998).

A chromosomal aberration test according to OECD TG 473 was conducted in cultured Chinese hamster lung (CHL/IU) cells. Induction of chromosome aberrations, however, was observed in the Chinese hamster cultured cells only at the highest concentration (2.2 mg/mL, 10 mM) in the

presence of an exogenous metabolic activation system (OECD TG 473). Because of the high toxicity (75 %) and also low pH (4.9) at the end of the treatment, the chromosomal aberration observed might not be biological relevant. Under un-physiological culture condition, such as low pH, it was reported that the frequency of chromosomal aberrations could be increased (Morita et al., 1990). Polyploidy was not induced under any of the conditions on continuous and short-term treatment with and without an exogenous metabolic activation system (MHW, Japan: 1998).

In vivo Studies

There are no data on genotoxicity *in vivo* available.

Conclusion

Triacetin is not genotoxic with and without an exogenous metabolic activation system in bacterial tests. The chemical however induced chromosomal aberrations *in vitro* (however under un-physiological conditions). Taking all data into consideration, triacetin should be considered non-genotoxic *in vitro*.

3.1.7 Carcinogenicity

There is no available information on carcinogenicity.

3.1.8 Toxicity for Reproduction

Studies in Animals

One study was available. The data from the OECD repeated dose and reproductive toxicity study by the oral route (MHW, Japan: 1998) was identified as the key study because it was well conducted and reported. Details of this study are as follows.

Effects on Fertility

Using the OECD combined repeated dose and reproductive/developmental toxicity screening test [OECD TG 422], SD (Crj: CD), rats received gavage doses of 0 (vehicle; distilled water), 40, 200 and 1,000 mg/kg bw/day. Males were exposed for 44 days from 2 weeks prior to mating and females were exposed for 41-48 days from 14 days before mating to day 3 postpartum. Female animals were sacrificed on day 4 of lactation (MHW, Japan: 1998).

No effects related to chemical exposure were observed maternally at any dose levels, although there was a single undelivered animal at 200 mg/kg bw which was not statistically significantly different from the control ($p<0.05$). Similarly, no effects related to the chemical exposure were observed at any dose levels on reproductive parameters including the mating index, fertility index, gestation length, numbers of corpora lutea and implantations, implantation index, gestation index, delivery index, parturition and maternal behaviour at delivery and lactation.

In summary, it can be concluded that reproductive toxicity of triacetin in rats by oral administration was not observed up to the highest dose tested. The NOAEL is thus established to be 1,000 mg/kg bw/day.

Developmental Toxicity

As described the above, using the OECD combined repeated dose and reproductive/developmental toxicity screening test [OECD TG 422], female rats received gavage doses of 0 - 1,000 mg/kg bw /day, for 41-48 days from 14 days before mating to day 3 postpartum. The animals were sacrificed

on day 4 of lactation to evaluate the potential maternal and developmental parameters of triacetin (MHW, Japan: 1998).

On examination of neonates, there were no statistically significant differences from the control in numbers of offspring or live offspring, the sex ratio, the live birth index, and the viability index or body weight. No abnormal findings ascribable to the compound were found for external features, clinical signs or necropsy of the offspring.

Therefore, the NOAEL for developmental toxicity is considered to be 1,000 mg/kg bw /day for offspring.

Studies in Humans

There is no information on humans available.

Conclusion

Triacetin did not produce any reproductive and developmental effects in rats. The NOAEL for reproductive and developmental toxicity by gavage is established at 1,000 mg/kg bw/day for parental animals and offspring.

3.2 Initial Assessment for Human Health

Triacetin is absorbed following ingestion and metabolised like other shorter-chain triglycerides. Several studies confirmed that triacetin is hydrolysed to glycerol and acetic acid by digestive enzymes, particularly lipases, liver or plasma carboxyesterases. Triacetin infused in dogs undergoes intravascular hydrolysis, and the majority of the resulting acetate is oxidized nearly quantitatively rather than reesterificated or elongated, as is the case with short- and medium-chain fatty acids.

In the oral acute toxicity study in rats (2,000 mg/kg bw, a limit dose level, OECD TG 401), no mortality occurred and no signs of systemic toxicity were observed during the 14-day observation period. Gross pathology revealed no treatment-related changes at the end of two weeks for both sexes. The LD_{50} of triacetin in rats by gavage is thus determined to be > 2,000 mg/kg bw. The LC_{50} in acute inhalation toxicity in rats is > 1.721mg/L (4h) for both sexes [OECD 403].

Most of the studies show that triacetin caused no irritation to rabbit skin [OECD TG 404] and to the rabbit eye [OECD TG 405]. Triacetin is not skin sensitising to guinea pigs.

In the tests using human volunteers, triacetin induced no skin irritation or skin sensitization. However, one case concerning allergic contact eczema caused by triacetin has so far been reported in a cigarette factory.

In an oral rat study according to the combined repeated dose and reproductive/developmental toxicity screening test [OECD TG 422], a dose of 1,000 mg/kg bw/day of triacetin exerted no effects on clinical signs, body weight, food consumption, and organ weight or necropsy findings. No histopathological changes ascribable to the compound were observed in either sex. The NOAEL for repeated dose toxicity is thus considered to be 1,000 mg/kg bw/day for both sexes.

Growing male rats were fed diets containing triacetin and/or glycerine (20 - 60 %) for 90 days. The animals well tolerated up to 20 % triacetin of the diet. The NOAEL for the feeding study is considered to be 10 g/kg bw/day for male rats.

An inhalation study was conducted in rats given triacetin for 90 days at dose of 249 ppm (2,220 mg/m3) under non-GLP condition. No toxic symptoms were noted during the exposure and all rats appeared to be normal. Haematological studies, urine analyses and autopsy showed no abnormal

observations attributable to the exposure. The NOAEL is considered to be 249 ppm (2,220 mg/m3) for 90 days, although the inhalation studies are considered to be useful, they do not fully comply with the current testing protocol.

In the combined repeated dose and reproductive/developmental oral toxicity study in rats [OECD TG 422], animals received gavage doses of 0, 40, 200 and 1,000 mg/kg bw/day. There were no statistically significant adverse effects on reproductive parameters including the mating index, fertility index, gestation length, numbers of corpora lutea and implantations, implantation index, gestation index, delivery index, parturition and maternal behavior at delivery and lactation. In addition, there were no significant differences in numbers of offspring or live offspring, the sex ratio, the live birth index, the viability index or body weight. No evidence of malformations at any doses ascribable to the compound was found for external features, clinical signs or necropsy of the offspring. Therefore, the NOAEL for reproductive and developmental toxicity by gavage is considered to be 1,000 mg/kg bw/day for parental animals and offspring.

For genotoxicity of triacetin, one non-bacterial in vitro and five bacterial reverse mutation tests are available. Triacetin did not induce gene mutation in bacteria at concentrations up to 5,000 ug /plate (OECD TG 471 and 472). Induction of chromosome aberrations, however, was observed in the Chinese hamster cultured cells only at the highest concentration (2.2 mg/mL, 10 mM) in the presence of an exogenous metabolic activation system (OECD TG 473). Because of high toxicity (75 %) and also low pH (4.9) at the end of treatment, the chromosomal aberration observed might not be biological relevant. Under un-physiological culture condition, such as low pH, it was reported that the frequency of chromosomal aberrations could be increased (Morita et al., 1990). Polyploidy was not induced under any of the conditions tested. Taking all data into consideration, triacetin could be considered to be non-genotoxic.

There is no information on human toxicity available. However, the Joint FAO/WHO Expert Committee on Food Additive (JECFA) considers it unnecessary to assign an acceptable daily intake (ADI) as triacetin is metabolized like other triglycerides in food. In an assessment of triacetin, JECFA concluded that based on the available data, and anticipated daily intake, triacetin did not represent a hazard to health (JECFA, 1975) and in a more recent evaluation, the EU's Scientific Committee for Food endorsed this position for triacetin (Commission, 1992, SCF, 1995). An estimate of additive intake in the UK suggests that an adult might ingest 7.8 mg triacetin/day as part of a total daily additive intake of 8.0 g (MAFF, 1993).

4. HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

Acute and Chronic Toxicity Test Results

Triacetin has been tested in a limited number of aquatic species. Results from acute and chronic tests on aquatic organisms are summarized in Table 5.

Table 5: Summary of Effects of Triacetin on Aquatic Organisms

Organism	Test duration	Result (mg/L)	Reference
Micro-organisms			
Green alga (*Selenastrum capricornutum*) §	0-72 h (cl, shaken)	(Growth inhibition) EC_{50} (G.rate) > 1,000 (nc*) NOEC = 556 (nc*) EC_{50} (Bms) > 1,000 (nc*) NOEC = 556 (nc*)	EA, Japan (1998)
Invertebrates			
Water flea (*Daphnia magna*)	24 h (op, s) 48 h (op, s)	EC_{50} (Imm) = 888 (nc*) EC_{50} (Imm) = 768 (nc*) EC_0 (Imm) = 309 (nc*)	EA, Japan (1998)
Water flea (*Daphnia magna*)	24 h (op, s) 48 h (op, s)	EC_{50} (Imm) > 974.4 (m) EC_{50} (Imm) = 810.9 (m) EC_0 (Imm) = 541.1 (m)	Lawrence (1995)[1]
Water flea (*Daphnia magna*)	48 h (op, s)	EC_{50} = 380 EC_0 = 65	Henkel KGaA
Water flea (*Daphnia magna*)	21 d (op, ss)	EC_{50} (Rep) > 100 (nc*) NOEC (Rep) = 100 (nc*)	EA, Japan (1998)
Fish			
Medaka (*Oryzias latipes*)	96 h (op, ss)	LC_{50}> 100 (nc*)	EA, Japan (1998)
Medaka (*Oryzias latipes*)	14 d (op, f)	LC_{50} >100 (nc*) LC_0 = 100 (nc*)	EA, Japan (1998)
Fathead minnow (*Pimephales promelas*)	96 h (op, s)	LC_{50} = 165.3 (m)	Lawrence (1995)[2]
Cyprinidae (Carp) (*Cyprinus carpio*)	48 h (op, s)	LC_{50} = 174	Unichema (1988)[1]
Golden orfe (*Leuciscus idus*)	48 h (op, s)	LC_{50} = 170	Henkel KGaA (1988)
Zebra-fish (*Brachydanio rerio*)	96 h (op, ss)	LC_{50} = 300	Henkel KGaA (1982)

cl = closed system m = measured concentration f = flow through
op = open system s = static ss = semi-static
nc = nominal concentration
nc* = calculated based on nominal concentrations, because measured concentrations were >80% of nominal concentrations.
Bms = biomass Imm = immobilization Rep = reproduction
G.rate = Growth rate

§ In the case of green alga, the pH decrease caused by the hydrolysis of triacetin was dependent on the concentration of triacetin and reached the plateau at 556mg/L at pH 5.3. Therefore, the NOEC of 556 mg/L was tentatively assigned for the toxicity of triacetin. It is, however, not clear whether the growth inhibition observed at 1,000 mg/L was due to the pH decrease or the chemical itself in this test.

4.2 Terrestrial Effects

There is no information available.

4.3 Other Environmental Effects

There is no information available.

4.4 Initial Assessment for the Environment

The Mackay level III fugacity model was employed to estimate the environmental distribution of triacetin in air, water, soil and sediment (Daicel, 2002). This was considered the key study and the results are shown below (For details, refer to Appendix in the SIDS Dossier). Table shows the estimated distribution of triacetin obtained from the solubility value (58 g/L) in parenthesis in addition to those obtained from 70 g/L for comparison.

Estimated Distribution Under Four Emission Scenarios

70 g/L (58 g/L)

Compartment	Release 100 % to air	Release 100 % to water	Release 100 % to soil	Equal emission scenario (1:1:1)
Air	0.9 (1.1) %	0.0 (0.0) %	0.0 (0.0) %	0.3 (0.4) %
Water	20.0 (19.9) %	99.7 (99.7) %	12.9 (12.9) %	30.1 (30.2) %
Soil	79.1 (79.0) %	0.0 (0.0) %	87.1 (87.1) %	69.5 (69.4) %
Sediment	0.1 (0.1) %	0.3 (0.3) %	0.0 (0.0) %	0.1 (0.1) %

Triacetin is readily biodegradable (77 % and 94 % based on BOD and TOC, respectively, Chemicals Evaluation and Research Institute, 1998) after 14 days. A half-life of 168 hrs (7 days) is thus derived from the biodegradation data. An estimated half-life of 168 hours is also obtained for water. Given slower transport rate and possible anaerobic change in microbes in soil and sediment, the calculation was made by using 168 hrs x 3 (504 hrs) for both compartments. The calculation revealed that in the case of 100 % release to water, more than 99 % of triacetin is expected to stay in water due to its high solubility and a low vapour pressure, but if it is released into air and/or soil, it is likely to be distributed in other compartments.

The results also show that approximately one third of triacetin will be distributed in water, whereas two third will stay in soil when applied to the equal emission scenario to water, soil and sediment (1:1:1). In addition, the fugacity model using 58 g/L reveals that there is little change in the distribution of triacetin between three compartments when compared to those obtained from 70 g/L.

Based on a water solubility of 58 g/L and a vapour pressure of 0.003306 hPa (0.00248 mmHg) at 25 °C, a Henry's law constant of 1.23 x 10^{-8} atm m^3/mol is estimated. This value indicates that triacetin is essentially non-volatile from water (Lyman, 1990).

Since triacetin is readily biodegradable in activated sludge (Chemicals Evaluation and Research Institute, 1998, Unichema Chemie B.V., 1990, Henkel KGaA, 2001 and Bayer AG), biologically

mediated hydrolysis is the predominant pathway in the primary degradation step when triacetin is discharged to the environment.

This compound is expected to have a low potential for bioaccumulation based on its low Log Pow (0.21, Chemicals Evaluation and Research Institute, 1998).

The BCF is estimated to be 1.3 from a recommended regression-derived equation using a water solubility of 58 g/L at 25 °C (Lyman, 1990), indicating that bioconcentration is of no environmental relevance.

The toxicity results of triacetin to aquatic plants (alga; *Selenastrum capricornutum*) are > 1,000 mg/L for EC_{50} and 556 mg/L for NOEC [growth inhibition, OECD TG 201] (EA, Japan, 1998). The acute (mortality or immobility, [OECD TG 202]) and chronic (reproduction, [OECD TG 211]) toxicity results for *Daphnia magna* are 888 mg/L (EC_{50}, 24 h), 768 mg/L (EC_{50}, 48 h) and 100 mg/L (21 d NOEC), based on nominal concentration (EA, Japan, 1998). The acute toxicity results to fish are > 100 mg/L (Medaka; *Oryzias latipes*) (EA, Japan, 1998) and 165.3 mg/L (Fathead minnow; *Pimephales promelas*) (Lawrence, 1995[2]) for 96 h LC_{50} [OECD TG 203]. In the prolonged toxicity test in fish (Medaka; *Oryzias latipes*), no mortality and any toxic symptom were observed [OECD TG 204]. The 14d LC_{50} and the 14d LC_0 for fish are reported as > 100 mg/L and 100 mg/L, respectively (EA, Japan, 1998).

Thus, triacetin can be regarded as being of low hazard to aquatic organisms.

Based on the acute and prolonged aquatic toxicity data on three trophic levels, a Predicted No Effect Concentration (PNEC) can be calculated. When an assessment factor of 100 was applied to the chronic toxicity for *Daphnia*, the lowest PNEC was determined to be 1.00 mg/L for the aquatic environment.

5. RECOMMENDATIONS

The chemical is currently of low priority for further work because of its low hazard potential.

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ANNEX

(Occupational exposure)

EHE values of 4.94 mg/kg bw/day (most likely case) and 49.43 mg/kg bw/day (worst case) for dermal absorption are defined in Section 2.2 for workers at the production site.

Using these EHE values and the NOAEL of 1,000 mg/kg bw/day, the margin of safety (MOS) for dermal route is calculated as 202 (most likely case) and 20 (worst case), respectively. Similarly, respiratory EHE values of 0.0244 mg/kg bw/day (most likely case) and 0.0379 mg/kg bw/day (worst case) are estimated for workers at the production site. For respiration, the MOS is calculated as 41,000 (most likely case) and 26,000 (worst case), respectively.

At working sites, absorption of triacetin via dermal and inhalation routes may occur simultaneously. Hence, the MOS combined for both routes is calculated as 202 (most likely case) and 20 (worst case), respectively. From these results, workers are not expected to be at risk of toxic health effects from occupational exposure to triacetin under regular conditions of the usage equipped with protective gears.

(Consumer exposure)

EHE values of 0.0429 mg/kg bw/day (most likely case) and 0.107 mg/kg bw/day (worst case) for dermal absorption are defined in Section 2.2 for consumers using products containing 0.3 % and 25 % of triacetin.

Using these EHE values and the NOAEL of 1,000 mg/kg bw/day, the MOS for dermal absorption is calculated as 23,000 (most likely case) and 9,000 (worst case).

The MOS for ingestion is calculated as 9,000 for most likely case.

(Environmental exposure)

EHE values of 0.00000514 mg/kg bw/day (most likely case) and 0.00714 mg/kg bw/day (worst case) are defined in Section 2.2 by assuming that individuals use untreated water as their sole source of drinking water (2 L/day for a 70 kg adult).

The MOS is calculated as 196,000,000 and 140,000 for most likely case and worst case, respectively. The results suggest that adverse effects by triacetin uptake via the environmental route could be negligibly small.

Potential exposure via consumption of fish is anticipated to be negligible because triacetin is expected to have a low potential for bioaccumulation and readily biodegradable.

SIDS DOSSIER

Triacetin

CAS No. 102-76-1

Sponsor Country: Japan

DATE: 9 August 2002

1. GENERAL INFORMATION

1.01 SUBSTANCE INFORMATION

A. CAS number 102 – 76 - 1

B. Name (IUPAC name) Triacetin

C. Name (OECD name) Triacetin

D. CAS Descriptor

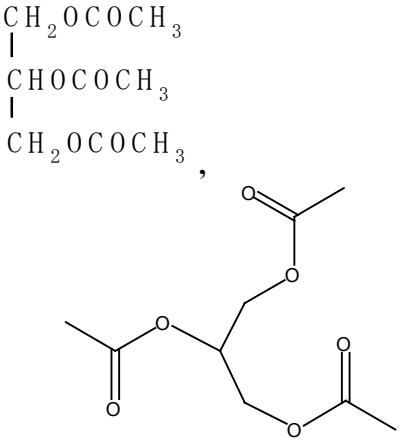
Not applicable in this case.

E. EINECS-Number 203 – 051 - 9

F. Molecular Formula $C_9H_{14}O_6$

G. Structural Formula

C_3H_5-$(OCOCH_3)_3$ or



SMILES Line Notation: CC(OC(C)=O)COCC.O=C.COC(C)=O

H. Substance Group

Not applicable.

I. Substance Remark

None

J. Molecular Weight 218.21

1.02 OECD INFORMATION

A. Sponsor Country: Japan

B. Lead Organisation:

Name of Lead Organisation: Daicel Chemical Industries, Ltd.

Contact person: Mr. Yasuhisa Kawamura, Director

Address: Ministry of Foreign Affairs
Economic Affairs Bureau
Second International Organizations Div.
2-2-1 Kasumigaseki, Chiyoda-ku
Tokyo 100

C. Name of responder

Name: The same as the contact person

Address: The same as the contact person

1.1 GENERAL SUBSTANCE INFORMATION

A. Type of Substance

element **[ ]**; inorganic **[ ]**; natural substance **[ ]**; organic **[X]**; organometallic **[ ]**; petroleum product **[ ]**

B. Physical State (at 20 °C and 1,013 hPa)

gaseous **[ ]**; liquid **[X]**; solid **[ ]**

C. Purity

99.5-99.8% weight/weight

1.2 SYNONYMS

(Chemical name)
1,2,3-Propanetriol, triacetate
1,2,3-Propanetriyl, triacetate
1,2,3-Triacetoxypropane
Acetic acid, glycerol triester
Acetic, 1,2,3-Propanetriyl ester
Acetin, Tri-
Glycerin triacetate
Glycerol triacatate
Glycerol, triester with acetic acid
Glyceryl triacetate
Propane-1,2,3-triyl triacetate
Triacetin
Triacetyl glycerin
Triacetyl glycerine
Triacetyl glycerol

(Trade name)
ENZACTIN

"ESTROBOND" B Plasticizer
FEMA NUMBER 2007
FUNGACETIN
GLYPED
KESSCOFLEX TRA

KODAFLEX TRIACETIN
VANAY

1.3 IMPURITIES

CAS No.:	26446-35-5
EINECS No.:	247-704-6
Name:	1,2,3-Propanetriol, monoacetate (Monoacetin)
Value:	< 0.01 %
Remarks:	None.
Reference:	Company data (Daicel Chemical, 2001).

CAS No.:	25395-31-7
EINECS No.:	246-941-2
Name:	1,2,3-Propanetriol, diacetate (Diacetin)
Value:	< 0.1 %
Remarks:	None.
Reference:	Company data (Daicel Chemical, 2001).

1.4 ADDITIVES

Not stated.

1.5 QUANTITY

Remarks:	In Japan, ca. 5,000 tonnes/year, produced by three Japanese companies. Estimated global production is 10,000-50,000 tonnes/year; Other major manufacturers are Eastman (USA), Cognis (Germany) and Uniqema (UK).
Reference:	Company data (Daicel Chemical, 2001).

1.6 LABELLING AND CLASSIFICATION (USE AND/OR TRANSPORTATION)

Labelling

Type:	As in Directive 67/548/EEC
Specific limits:	No
Symbols:	None
Nota:	
R-phrases:	None
Text of S-phrases:	
Remarks:	Not stated.

Classification

Type:	As in Directive 67/548/EEC
Category of danger:	None
Remarks:	EC Classification (Calculated).

Reference: Material safety data sheet, dated 26-1-1994; Unichema International.

1.7 USE PATTERN

A. General

Type of Use: **Category: Non dispersive**

(a) Main industrial use: Chemical industry: intermediate

Type of Use: **Category: Wide dispersive**

(b) Main industrial use:
(1) Metal extraction, refining and processing of metals
(2) Paints, lacquers, varnishes industry
(3) Paper pulp, and board industry
(4) Cigarette industry (Cellulose acetate plasticizer in cigarette filters)
(5) Food industry (Food/foodstuff additives)
(6) Photographic industry (Solvent in photographic films)
(7) Polymer industry
(8) Cosmetic industry (Fixative)

(c) Other: Solvents, adhesives, binding agents, flux agents for casting, impregnation agents, plasticizer for cellulose nitrate, absorbents and adsorbents.

Remarks: Not stated.
Reference: HSDB (2001), National Library of Medicine

B. Uses in Consumer Products

Function	Amount present (%)	Physical state
Soap	0.05-1.0	Solid
Detergent	0.005-0.1	Liquid
Cream, lotion	0.025-0.3	Liquid
Perfume	0.8-2.0	Liquid
Tobacco	3-5	Solid
Antifungal drug	15-25-33	Aerosol-Cream-Powder

Remarks: Not stated.
Reference: Opdyke D.L.J. (1978), Food Cosmet. Toxicol. 16 (Suppl. 1), 879-882. Permitted additives to Tobacco products, UK Department of Health, 1998.

1.8 OCCUPATIONAL EXPOSURE LIMIT

Exposure limit value
Type: Not stated.
Value: Not stated.
Remarks: No occupational exposure limits established.
Reference: MSDS-OHS, OHSN OHS10442 (2001), MDL Information Systems, Inc.

1.9 SOURCES OF EXPOSURE

A. Potential human exposure:

The production process consists of the batchwise controlled reaction of glycerol, acetic acid and acetic anhydride in a closed reaction system with adequate cooling facilities. This is followed by purification using vacuum distillation. The pungent nature of the raw materials demands a totally enclosed plant. Therefore, exposure can be negligible by applying protective measures as written below. The process is operated at three sites in Japan.

(a) At a production site: Exposure is possible when sampling, followed by analysing the product. Based on a calculation, the exposure time is estimated for 0.25 hours/day/person for both sampling

and analysis. During cleaning of the strainer for maintenance production line, the worker is also exposed to the substance and the exposure is estimated for 0.50 hours/day/person (Daicel Chemical Industries, 2001). The exposure time for drum filling is estimated 5.0 hours/day/person. The work place is provided with an air ventilator and workers are equipped with protective gear such as mask, rubber gloves and goggles to prevent exposure (MSDS Daicel Chemical, 2001). Spill is collected and incinerated.

(b) At user's facility: Material is used as a solvent in paints, metal processing and as a plasticizer in cigarette filters in addition to foodstuff additives and fixative cosmetics, etc., all of which are used in the industrial sector. Potential exposure is controlled by the use of efficient exhaust ventilation. Exposure is possible during dispensing the substance from drum or tank lorry into a container at user's facility. Workers may be exposed to the vapour or an intact liquid. They are recommended to put on protective gear such as mask, rubber gloves and goggles to prevent exposure (MSDS Daicel Chemical, 2001). Spill is collected and incinerated.

(c) At consumer's site: Due to its uses triacetin soon becomes diffused into small quantities and there is little possibility of large scale human contact or environmental effect after it leaves the manufacturer's production sites. Its use in adhesives may give skin contact. As foodstuff additives or soft drinks flavouring, ingestion of triacetin will occur. Very small amounts can be found in cigarette smoke drawn through a filter tip using triacetin as the plasticizer. (MSDS Daicel Chemical Industries, 2001).

B. Potential environmental exposure:

(a) At a production site:

Source:	Media release: Process wastewater
	Quantities per media: ca. 1,440 kg/year in a production site in Japan, in which ca. 2,000 t/year of the chemical was produced. (estimated by Daicel Chemical Industries, 2001)
Remarks:	Data used for the estimation:
	Waste water released: ca. 19,200 m^3/year
	Content of triacetin: 0.075 g/L
Reference:	Company data (Daicel Chemical Industries, 2001).

(b) At a user's facility:

	No substantial exposure is probable. Potential exposure is controlled by the use of efficient exhaust ventilation and protective gears.
Remarks:	Not stated.
Reference:	Company data (Daicel Chemical Industries, 2001).

1.10 ADDITIONAL REMARKS

A. Options for disposal

Remarks:	Dispose in accordance with all applicable regulations.
Reference:	MSDS-OHS (2001), MDL Information Systems, Inc.

B. Other remarks

Remarks:	CERCLA Sections 102a/103 Hazardous Substances (40 CFR 302.4): Not regulated. SARA TITLE III Section 302 Extremely Hazardous Substances(40 CFR 355.30): Not regulated. SARA TITLE III Section 304 Extremely Hazardous Substances (40 CFR 355.40): Not regulated. SARA TITLE III SARA Sections 311/312 Hazardous Categories (40 CFR 370.21): Acute: Yes Chronic: No Fire: No Reactive: No Sudden Release: No SARA TITLE III Section 313 (40 CFR 372.65): Not regulated. OSHA Process Safety (29CFR1910.119): Not regulated. State Regulations: California Proposition 65: Not regulated. Canadian Regulations: WHMIS classification: Not determined. German Regulations: Water Hazard Class (WGK): State of Classification: VwVwS, ID-Number 761 Classification under Hazard to Water: 1 (low hazard to waters) European Regulations: Refer to 1.6 LABELLING AND CLASSIFICATION (USE AND/OR TRANSPORTATION)
Reference:	MSDS-OHS (2001), MDL Information Systems, Inc.

2. PHYSICAL-CHEMICAL DATA

2.1 MELTING POINT

(a) **Preferred result**

Value:	3 °C
Decomposition:	Yes **[ ]** No **[ ]** Ambiguous **[ ]**
Sublimation:	Yes **[ ]** No **[ ]** Ambiguous **[ ]**
Method:	Not specified
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Remarks:	A thermodynamic melting point of crystalline triacetin.
Reference:	The Sigma-Aldrich Library of Regulatory and Safety Data, confirmed by Chemicals Evaluation and Research Institute (Kurume, Japan) (1998), Test No. 80919BK.

(b)

Value:	4.00 °C
Decomposition:	Yes **[ ]** No **[ ]** Ambiguous **[ ]**
Sublimation:	Yes **[ ]** No **[ ]** Ambiguous **[ ]**
Method:	Not specified
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Remarks:	A thermodynamic melting point of crystalline triacetin.
Reference:	Yumashev, N. V. et al. (1984), J. Gen. Chem. USSR (Engl. Transl.), 54 659-662.

(c)

Value:	4.1 °C
Decomposition:	Yes **[ ]** No **[ ]** Ambiguous **[ ]**
Sublimation:	Yes **[ ]** No **[ ]** Ambiguous **[ ]**
Method:	Not specified
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Remarks:	A thermodynamic melting point of crystalline triacetin.
Reference:	CRC Press Inc. (1975), 2 nd Ed, Cleveland Ohio.

(d)

Value:	3.20 °C
Decomposition:	Yes **[ ]** No **[ ]** Ambiguous **[ ]**
Sublimation:	Yes **[ ]** No **[ ]** Ambiguous **[ ]**
Method:	Not specified
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Remarks:	Ethanol as solvent. A thermodynamic melting point of crystalline triacetin.
Reference:	Hancock et al. (1948), J. Amer. Chem. Soc., 70 424.

(e)

Value:	4.10 °C
Decomposition:	Yes **[ ]** No **[ ]** Ambiguous **[ ]**
Sublimation:	Yes **[ ]** No **[ ]** Ambiguous **[ ]**
Method:	Not specified
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Remarks:	A thermodynamic melting point of crystalline triacetin.
Reference:	Baur (1945), J. Phys. Chem., 58 380.

(f)

Value:	< -78 °C
Decomposition:	Yes **[ ]** No **[ ]** Ambiguous **[ ]**
	Sublimation: Yes **[ ]** No **[X]** Ambiguous **[ ]**
Method:	Not stated.

GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: A glass transition temperature.
Reference: Hutchings, D. et al., (1993) Pharmaxie 48 (12) 912-914.

(g) Value: < -78 °C
Decomposition: Yes **[ ]** No **[ ]** Ambiguous **[ ]**
Sublimation: Yes **[ ]** No **[ ]** Ambiguous **[ ]**
Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: A glass transition temperature.
Reference: The Merck Index (1996), 12th edition, Merck & Co., Inc., p. 1636.

(h) Value: < -60 °C
Decomposition: Yes **[ ]** No **[ ]** Ambiguous **[ ]**
Sublimation: Yes **[ ]** No **[ ]** Ambiguous **[ ]**
Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: A glass transition temperature.
Reference: Timmermans (1922), Bull. Soc. Chim. Belg., 31 392.

2.2 BOILING POINT

(a) **Preferred result**
Value: 258 °C
Pressure: at 1,013 hPa
Decomposition: Yes **[ ]** No **[ ]** Ambiguous **[ ]**
Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: The Sigma-Aldrich Library of Regulatory and Safety Data.
Reference: Chemicals Evaluation and Research Institute (1998), Test No. 80919BK.

(b) Value: 258-259 °C
Pressure: at 1,013 hPa
Decomposition: Yes **[ ]** No **[ ]** Ambiguous **[ ]**
Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Not stated.
Reference: Prager, R. H. & Yurui Z. (1989) Aust. J. Chem., 6 1003-1005.

(c) Value: 258-259 °C
Pressure: at 1,013 hPa
Decomposition: Yes **[ ]** No **[ ]** Ambiguous **[ ]**
Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Not stated.
Reference: Perkin & Simonsen (1905), J. Chem. Soc., 87 859.

(d) Value: 258-260 °C
Pressure: at 1,013 hPa
Decomposition: Yes **[ ]** No **[ ]** Ambiguous **[ ]**
Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Not stated.

Reference: The Merck Index (1996), 12th edition, Merck & Co., Inc., p. 1636.

(e) Value: 258 °C
Pressure: at 1,013 hPa
Decomposition: Yes **[ ]** No **[ ]** Ambiguous **[ ]**
Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Not stated.
Reference: Jellum & Bjoernstad (1964), J. Lipid Res., 5 314-316.

(f) Value: 171-172 °C
Pressure: at 53 hPa
Decomposition: Yes **[ ]** No **[ ]** Ambiguous **[ ]**
Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Not stated.
Reference: Baur (1945), J. Phys. Chem. 58 380.

(g) Value: 170 °C
Pressure: at 53 hPa
Decomposition: Yes **[ ]** No **[ ]** Ambiguous **[ ]**
Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Not stated.
Reference: Togashi & Yamada (1969), Chem. Abstr., 71 101337m.

(h) Value: 135-137 °C
Pressure: at 9.3 hPa
Decomposition: Yes **[ ]** No **[ ]** Ambiguous **[ ]**
Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Not stated.
Reference: Nitrofanowa et al. (1966), J. Org. Chem. USSR (Engl. Transl.), 2 1748.

(i) Value: 130-131 °C
Pressure: at 5.3 hPa
Decomposition: Yes **[ ]** No **[ ]** Ambiguous **[ ]**
Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Not stated.
Reference: Golendee (1954), Chem. Abstr. 9914.

(j) Value: 123-124 °C
Pressure: at 9.3 hPa
Decomposition: Yes **[ ]** No **[ ]** Ambiguous **[ ]**
Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Not stated.
Reference: Umemura et al. (1966), Nippon Kagaku Zasshi, 87 986-990.

(k) Value: 101-113 °C
Pressure: at 2.7 hPa
Decomposition: Yes **[ ]** No **[ ]** Ambiguous **[ ]**

Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Not stated.
Reference: Umemura et al. (1966), Nippon Kagaku Zasshi, 87 986-990.

2.3 DENSITY

(a) **Preferred result**
Type: Bulk density **[ ]**; Density **[ ]**; Relative Density **[X]**
Value: 1.1562 g/cm^3
Temperature: 25 °C

Value: 1.1596 g/cm^3
Temperature: 20 °C

Value: 1.1630 g/cm^3
Temperature: 20 °C

Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: 4 °C and 20 °C (Reference Temperature)
Reference: The Merck Index (1996), 12th edition, Merck & Co., Inc., p. 1636.

(b) Type: Bulk density **[ ]**; Density **[ ]**; Relative Density **[X]**
Value: approx. 1.160 g/cm^3
Temperature: 20 °C
Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Not stated.
Reference: Cognis Deutschland GmbH (2000), Safety Data Sheet.

(c) Type: Bulk density **[ ]**; Density **[ ]**; Relative Density **[X]**
Value: 1.15620 g/cm^3
Temperature: 25 °C

Value: 1.07520 g/cm^3
Temperature: 100 °C

Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: 4 °C (Reference Temperature)
Reference: Jaeger (1917), Z. Anorg. Allg. Chem., 101 70.

(d) Type: Bulk density **[ ]**; Density **[ ]**; Relative Density **[X]**
Value: 1.15960 g/cm^3
Temperature: 20 °C
Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: 4 °C (Reference Temperature)
Reference: Dunbar, B. (1956), J. Org. Chem., 21 1041-1043.

(e) Type: Bulk density **[ ]**; Density **[ ]**; Relative Density **[X]**
Value: 1.16450 g/cm^3

Temperature: 20 °C

Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: 4 °C (Reference Temperature)
Reference: Nitrofanowa et al. (1966), J. Org. Chem. USSR (Engl. Transl.), 2 1748.

(f) Type: Bulk density **[ ]**; Density **[ ]**; Relative Density **[X]**
Value: 1.11100 g/cm^3
Temperature: 70 °C
Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: 4 °C (Reference Temperature)
Reference: Mohr, M. (1934), Milchwirtsch. Forsch., 16 193.

2.4 VAPOUR PRESSURE

(a) **Preferred result**
Value: 0.003306 hPa (0.00248 mmHg)
Temperature: 25 °C
Method: calculated **[ ]**; measured **[X]**
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: SRC recommended value.
Reference: Design Institute for Physical Property Data (1989).

(b) Value: 53.3 hPa
Temperature: 78 °C
Method: calculated **[ ]**; measured **[ ]**
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Not stated.
Reference: MSDS-OHS (2001), MDL Information Systems, Inc.

2.5 PARTITION COEFFICIENT $\log_{10}P_{ow}$

(a) **Preferred result**
Log Pow: 0.21
Temperature: 25 °C.
Method: calculated **[ ]**; measured **[X]**
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Remarks: OECD TG 107 (Shake Flask Method)
Reference: Chemicals Evaluation and Research Institute (1998), Test No. 80919BK.

(b) Log Pow: 0.25
Temperature: No data available.
Method: calculated **[ ]**; measured **[ ]**
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Not stated.
Reference: American Chemical Society (1995), 63.

(c) Log Pow: 0.1
Temperature: No data available
Method: calculated **[X]**; measured **[ ]**

GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: No information about method.
Reference: Chemical Safety Sheets (1991) Dutch Chemical Industry

Association.

(d) Log Pow: 0.368
Temperature: No data available
Method: calculated **[X]**; measured **[ ]**
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: version CLOGP 3.3.
Reference: ASTM Spec. Techn. Publ. 11 (1988) 468-489.

(e) Log Pow: 0.30
Temperature: No data available
Method: calculated **[X]**; measured **[ ]**
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Not stated.
Reference: Leo A. J. (1978), EPA files.

(f) Log Pow: 0.44
Temperature: No data available
Method: calculated **[X]**; measured **[ ]**
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Not stated.
Reference: Leo A. J. (1978), EPA files.

2.6 WATER SOLUBILITY

A. SOLUBILITY

(a) **Preferred result**
Value: 70 g/L
Temperature: 25°C.
Description: Miscible **[ ]**; Of very high solubility **[ ]**;
Of high solubility **[ ]**; Soluble **[X]**; Slightly soluble **[ ]**;
Of low solubility **[ ]**; Of very low solubility **[ ]**; Not soluble **[ ]**
Method: OECD TG 105.
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Remarks: No dissociation group.
Reference: Chemicals Evaluation and Research Institute (Kurume, Japan) (1998), Test No. 80919BK.

(b) **Preferred result**
Value: 58 g/L
Temperature: 25°C
Description: Miscible **[ ]**; Of very high solubility **[ ]**;
Of high solubility **[ ]**; Soluble **[X]**; Slightly soluble **[ ]**;
Of low solubility **[ ]**; Of very low solubility **[ ]**; Not soluble **[ ]**
Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Not stated.
Reference: Riddick J.A. et al. (1986), Techniques of Chemistry, 4th ed.

(c) Value: 80 g/L
Temperature: 20°C.
Description: Miscible **[ ]**; Of very high solubility **[ ]**;
Of high solubility **[ ]**; Soluble **[X]**; Slightly soluble **[ ]**;

Of low solubility **[ ]**; Of very low solubility **[ ]**; Not soluble **[ ]**
Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Not stated.
Reference: Cognis Deutschland GmbH (2000), Safety Data Sheet.

(d) Value: 7.17 vol%
Temperature: 15°C
Description: Miscible **[ ]**; Of very high solubility **[ ]**;
Of high solubility **[ ]**; Soluble **[ ]**; Slightly soluble **[ ]**;
Of low solubility **[ ]**; Of very low solubility **[ ]**; Not soluble **[ ]**
Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Not stated.
Reference: CHEMICAL DIVISION DI SISAS SPA CAVAGLIA.

(e) Value: 5.8 vol %
Temperature: Not specified.
Description: Miscible **[ ]**; Of very high solubility **[ ]**;
Of high solubility **[ ]**; Soluble **[X]**; Slightly soluble **[ ]**;
Of low solubility **[ ]**; Of very low solubility **[ ]**; Not soluble **[ ]**
Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Not stated.
Reference: Flick, Industrial Solvent Handbook, 3rd edition.

(f) Value: No data available.
Temperature: No data available.
Description: Miscible **[ ]**; Of very high solubility **[ ]**;
Of high solubility **[ ]**; Soluble **[ ]**; Slightly soluble **[X]**;
Of low solubility **[ ]**; Of very low solubility **[ ]**; Not soluble **[ ]**
Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Soluble in 14parts water.
Reference: The Merck Index (1996), 12th edition, Merck & Co., Inc., p. 1636.

B. pH VALUE, pKa VALUE

(a) pH Value: 7
Temperature: 20°C
Concentration: 10g/L
Method: Not specified
GLP: Yes **[ ]** No **[ ]** ? **[X]**
pKa value: No data available
Remarks: No dissociation group
Reference: Safety Data Sheet (2000), Cognis Deutschland GmbH.

2.7 FLASH POINT (liquids)

(a) **Preferred result**
Value: >145 °C
Type of test: Closed cup **[X]**; Open cup **[ ]**; Other **[ ]**
Method: DIN 51758/ISO 2719 (Pensky-Martens).
GLP: Yes **[ ]** No **[ ]** ? **[X]**

Remarks: Not stated.
Reference: Cognis Deutschland GmbH (2000), Safety Data Sheet.

(b) Value: 137.8 °C
Type of test: Closed cup **[ ]**; Open cup **[ ]**; Other **[X]**
Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Not stated.
Reference: Design Institute for Physical Property Data (1989), American Institute of Chemical Engineers.

(c) Value: 138 °C
Type of test: Closed cup **[X]**; Open cup **[ ]**; Other **[ ]**
Method: Not specified
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Not stated.
Reference: Database ECDIN; Commission of the EEC, Joint Research Centre Ispra, Italy.

(d) Value: 138 °C
Type of test: Closed cup **[ ]**; Open cup **[X]**; Other **[ ]**
Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Not stated.
Reference: Sax Dangerous Properties of Industrial Materials, 6th edition, p.2605.

(e) Value: 145 °C
Type of test: Closed cup **[ ]**; Open cup **[X]**; Other **[ ]**
Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Not stated.
Reference: Unichema International, Material Safety Data Sheet, dated 26-1-1994.

(f) Value: 149 °C
Type of test: Closed cup **[ ]**; Open cup **[ ]**; Other **[X]**
Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Not stated.
Reference: Sax, N.I. & Lewis, R.J. (eds.)(1987), Hawley's Condensed Chemical Dictionary, 11th edition.

(g) Value: 151 °C
Type of test: Closed cup **[X]**; Open cup **[ ]**; Other **[ ]**
Method: ASTM D 92.
GLP: Yes **[ ]** No **[X]** ? **[ ]**

Remarks: Not stated.
Reference: Eastman Kodak Company, Unpublished data.

(h) Value: 153 °C
Type of test: Closed cup **[ ]**; Open cup **[X]**; Other **[ ]**
Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**

Remarks: Not stated.
Reference: CHEMICAL DIVISION DI SISAS SPA CAVAGLIA.

2.8 AUTO FLAMMABILITY (solid/gases)

(a) **Preferred result**
Value: 432 °C
Pressure: No data available.
Method: ASTM D2155.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Not stated.
Reference: Eastman Kodak Company, Unpublished data.

(b) Value: 430 °C
Pressure: No data available.
Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Not stated.
Reference: Database ECDIN; Commission of the EEC, Joint Research Centre Ispra, Italy.

(c) Value: 433 °C
Pressure: No data available.
Method: Not specified..
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Not stated.
Reference: National Fire Protection Association (1991), Fire Protection Guide, on Hazardous Materials. 10th ed. Quincy, MA.

2.9 FLAMMABILITY

(a) Results: Extremely flammable **[ ]**; Extremely flammable - liquified gas **[ ]**; Highly Flammable **[ ]**; Flammable **[ ]**; Non flammable **[X]**; Spontaneously flammable in air **[ ]**; Contact with water liberates highly flammable gases **[ ]**; Other **[ ]**
Method: ASTM E681.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: Lower flammability limits of 1.05 % (vol./vol.) at 189 °C and upper flammability limits of 7.75 % (vol./vol.) at 215 °C in air.
Reference: Eastman Kodak Company, Unpublished data.

(b) Results: Extremely flammable **[ ]**; Extremely flammable - liquified gas **[ ]**; Highly Flammable **[ ]**; Flammable **[ ]**; Non flammable **[X]**;

Spontaneously flammable in air **[ ]**; Contact with water liberates highly flammable gases **[ ]**; Other **[ ]**
Method: Not specified.
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Remarks: Not stated.
Reference: National Fire Protection Association (1991), Fire Protection Guide, on Hazardous Materials. 10th ed. Quincy, MA.

2.10 EXPLOSIVE PROPERTIES

Results:	Explosive under influence of a flame **[ ]**; More sensitive to friction than m-dinitrobenzene **[ ]**; More sensitive to shock than m-dinitrobenzene **[ ]**; Not explosive **[X]**; Other **[ ]**
Method:	ASTM E537.
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Remarks:	No exothermic activity to boiling. Test type: Differential thermal analysis.
Reference:	Eastman Kodak Company, Unpublished data.

2.11 OXIDISING PROPERTIES

Remarks:	Stable at normal temperatures and pressure, even under fire exposure conditions.
Reference:	Hazardous Substances Databank (HSDB) (2001), The National Library of Medicine.

ADDITIONAL REMARKS

Remarks:	Sets to a glass at –37 °C
Reference:	Sax, N.I. & Lewis, R.J. (eds.)(1987), Hawley's Condensed Chemical Dictionary, 11th edition.
Remarks:	Solidification point: < -30 °C
Reference:	Cognis Deutschland GmbH (2000), Safety Data Sheet.
Remark:	Solubility: Soluble in acetone, ethanol, benzene and chloroform.
Reference:	Unichema Int. (1994), MSDS.
Remark:	Viscosity (25 °C) : ca. 17 mPa.s
Reference:	Unichema Int. (1994), MSDS.
Remark:	Not compatible with strong oxidizing agents. Stable in usual Industrial conditions. Polymerisation: Not occurring. Combustible liquid when exposed to flame or heat.
Reference:	CHEMICAL DIVISION DI SISAS SPA CAVAGLIA.
Remark:	Solubility: Soluble in acetone, ethanol, benzene and chloroform.
Reference:	Unichema Int. (1994), MSDS.
Remark:	Solubility: Soluble in acetone, ethanol, benzene and chloroform.
Reference:	Unichema Int. (1994), MSDS.
Remarks:	Solubility: Slightly soluble in carbon tetrachloride and carbon disulfide
Reference:	Hazardous Substances Databank (HSDB) (2001), The National Library of Medicine.
Remark:	Wt/Gal: 9.7 LB

Reference: Sax, N.I. & Lewis, R.J. (eds.)(1987), Hawley's Condensed Chemical Dictionary, 11th edition.

Remark: Crystals from alcohol, melting point 4.1 °C
Reference: Lide, D.R. (ed.), CRC Handbook of Chemistry and Physics (1991-1992).

2.12 OXIDATION: REDUCTION POTENTIAL

No studies located.

2.13 ADDITIONAL DATA

A. Partition co-efficient between soil/sediment and water (Kd)

Remark: Triacetin may leach readily in soil based upon an estimated Koc value of 10.5.

Reference: Lyman W.J. et al. (1990), Handbook of Chemical Property Estimation Methods Washington, DC: Amer Chem Soc p. 4-9.

B. Other data:

No studies located.

3. ENVIRONMENTAL FATE AND PATHWAYS

3.1 STABILITY

3.1.1 PHOTODEGRADATION

Type:	Air **[X]**; Water **[ ]**; Soil **[ ]**; Other **[ ]**
Indirect Photolysis:	
Type of sensitizer:	OH
Concentration of sensitizer:	500,000 molecule/cm^3
Rate constant (radical):	$7.810*10^{-12}$ cm^3/molecule*sec
Degradation:	ca. 50 % after 2 day
Method:	calculated **[X]**; measured **[ ]**
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Test substance:	No data available.
Remarks:	Temperature used in the calculation: 25 °C
Reference:	Atkinson, R (1987), J. Inter. Chem. Kinet., 19 799-828

3.1.2 STABILITY IN WATER

(a)	Type:	Abiotic (hydrolysis) **[X]**; biotic (sediment) **[ ]**;
	Half life:	60.4 days and 16.5 hours at pH 7 and 9 at 25 °C, respectively.
	Degradation:	No hydrolysis at pH 4 at 50 °C in 5 days Hydrolysis at pH 7 (50, 60, 70 °C) and 9 (30 and 40 °C).
	Method:	OECD TG111
	GLP:	Yes **[X]** No **[ ]** ? **[ ]**
	Test substance:	Tokyo Kasei, Lot No. GB 01, Purity: > 98 %, Impurity: not stated.
	Remarks:	Hydrolysis rates at pH 7 and 9 were determined at 50, 60, 70 and 30, 40 °C, respectively and they were extrapolated to 25 °C using Arrhenius relationship. Half life at 25 °C was calculated from the rate constant.
	Reference:	Chemicals Evaluation and Research Institute (Kurume, Japan) (1998), Test No. 80919BK.

(b)	Type:	Abiotic (hydrolysis) **[X]**; biotic (sediment) **[ ]**;
	Half life:	ca. 130 days at pH 7. ca. 13 days at pH 8. ca. 1.3 days at pH 9.
	Degradation:	Hydrolysis at pH 7, 8 and 9.
	Method:	Not specified.
	GLP:	Yes **[ ]** No **[ ]** ? **[X]**
	Test substance:	Not stated.
	Remarks:	Method: Estimation.
	Reference:	US EPA (1991), PCGEMS Graphical Exposure Modeling System PCHYDRO.

3.1.3 STABILITY IN SOIL

No studies located.

3.2 MONITORING DATA (ENVIRONMENTAL)

Type of Measurement: Background **[ ]**; At contaminated site **[ ]**; Other **[X]**
Media: Surface water
Method: Not specified.
Results: Triacetin was detected in a sample of Tennessee River water collected in April 1973.
Remarks: Concentration not reported.
Reference: Shackelford W. M. and Keith L. H (1976), US EPA-600/4-76-062, p.226.

3.3 TRANSPORT AND DISTRIBUTION BETWEEN ENVIRONMENTAL COMPARTMENTS INCLUDING ESTIMATED ENVIRONMENTAL CONCENTRATIONS AND DISTRIBUTION PATHWAYS

3.3.1 TRANSPORT

No studies located.

3.3.2 THEORETICAL DISTRIBUTION (FUGACITY CALCULATION)

(a) **Preferred result**
Media: Air-biota **[ ]**; Air-biota-sediment-soil-water **[X]**; Soil-biota **[ ]**; Water-air **[ ]**; Water-biota **[ ]**; Water-soil **[ ]**; Other **[ ]**
Method: Fugacity leve l I **[ ]**; Fugacity level II **[ ]**; Fugacity level III **[X]**; Fugacity level IV **[ ]**; Other (calculation) **[ ]**; Other (measurement) **[ ]**

Results:
Predicted distribution of triacetin using Fugacity level III under four emission scenarios
(1) Results from water solubility of 70 g/L

Compartment	Release 100 % to air	Release 100 % to water	Release 100 % to soil	Equal emission scenario (1:1:1)
Air	0.9 %	0.0 %	0.0 %	0.3 %
Water	20.0 %	99.7 %	12.9 %	30.1 %
Soil	79.1 %	0.0 %	87.1 %	69.5 %
Sediment	0.1 %	0.3 %	0.0 %	0.1 %

(2) Results from water solubility of 58 g/L

Compartment	Release 100 % to air	Release 100 % to water	Release 100 % to soil	Equal emission scenario (1:1:1)
Air	1.1 %	0.0 %	0.0 %	0.4 %
Water	19.9 %	99.7 %	12.9 %	30.2 %
Soil	79.0 %	0.0 %	87.1 %	69.4 %
Sediment	0.1 %	0.3 %	0.0 %	0.1 %

Remarks: Refer to Appendix.
Reference: Daicel Chemical Industries (2002), Predicted distribution of triacetin using Fugacity level III, unpublished report.

(b) Media: Air-biota **[ ]**; Air-biota-sediment-soil-water **[ ]**; Soil-biota **[ ]**; Water-air **[X]**; Water-biota **[ ]**; Water-soil **[ ]**; Other **[ ]**
Method: Fugacity level I **[ ]**; Fugacity level II **[ ]**; Fugacity level III **[ ]**; Fugacity level IV **[ ]**; Other (calculation) **[X]**; Other (measurement) **[ ]**
Results: Based on a water solubility of 58 g/L and a vapour pressure of 0.00248 mm Hg (at 25 degree C), a Henry's law constant of $1.23 * 10^{-8}$ atm*m^3/mol is estimated. This value indicates that the compound is essentially non-volatile from water.
Remarks: Not stated.
Reference: Lyman W. J. (1990), Amer. Chem. Soc., p.15-29.

(c) Media: Air-biota **[ ]**; Air-biota-sediment-soil-water **[ ]**; Soil-biota **[ ]**; Water-air **[ ]**; Water-biota **[ ]**; Water-soil **[X]**; Other **[ ]**
Method: Fugacity level I **[ ]**; Fugacity level II **[ ]**; Fugacity level III **[ ]**; Fugacity level IV **[ ]**; Other (calculation) **[X]**; Other (measurement) **[ ]**
Results: Based upon a measured water solubility of 58 g/L at 25 °C, the Koc-value can be estimated to be 10.5 from a regression derived equation. This Koc-value indicates very high soil mobility (Chemical Safety Sheets (1991), Dutch Chemical Industry Association).
Remarks: Not stated.
Reference: Lyman W. J. (1990), Amer. Chem. Soc., p.4-9.
Swann R.L.(1983), Res. Rev., 85 p.23.

3.4 IDENTIFICATION OF MAIN MODE OF DEGRADABILITY IN ACTUAL USE

No studies located.

3.5 BIODEGRADATION

(a) **Preferred result**
Type: aerobic **[X]**; anaerobic **[ ]**
Inoculum: adapted **[ ]**; non-adapted **[X]**; other **[ ]**: sewage treatment plant effluent (biological stage)
Concentration of the chemical: 100 mg/L, related to COD **[ ]**; DOC **[ ]**; test substance **[X]**
Medium: water **[X]**; water-sediment **[ ]**; soil **[ ]**; sewage treatment **[ ]**
Degradation: (1) 77 % after 14 day based on BOD.
(2) 94 % after 14 day based on TOC.
Results: readily biodeg. **[X]**; inherently biodeg. **[ ]**;
under test condition no biodegradation observed **[ ]**, other **[ ]**
Kinetic: Not stated.
Method: OECD Guideline 301 C, Modified MITI Test (I)
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Test substance: As prescribed by 1.1-1.4.
Remarks: Domestic activated sludge was used as inoculum..
Reference: Chemicals Evaluation and Research Institute (Kurume, Japan) (1998), Test No. 20919B.

(b) Type: aerobic **[X]**; anaerobic **[ ]**
Inoculum: adapted **[ ]**; non-adapted **[X]**; other **[ ]**: sewage treatment plant effluent (biological stage)
Concentration of the chemical: (1) 10mg/L, (2) 20mg/L, related to COD **[ ]**; DOC **[ ]**;

Test substance **[X]**
Medium: water **[X];** water-sediment **[ ];** soil **[ ];** sewage treatment **[ ]**
Degradation: (1) 64 % after 28 day based on $ThCO_2$ (10mg/L).
(2) 93 % after 28 day based on $ThCO_2$ (20mg/L).
Results: readily biodeg. **[X];** inherently biodeg. **[ ]**;
under test condition no biodegradation observed **[ ]**, other **[ ]**
Kinetic: Not stated.
Method: OECD TG 301B, Directive 84/449/EEC, C.5 "Biotic degradation-modified Sturm test"
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Test substance: As prescribed by 1.1-1.4.
Remarks: The study was also in accordance with OECD Guideline 301 B. Domestic activated sludge was used as inoculum.
Reference: Chemie B.V. (1990), unpublished data, RCC NOTOX Project 005164.

(c) Type: aerobic **[X]**; anaerobic **[ ]**
Inoculum: adapted **[ ]**; non-adapted **[X]**; other **[ ]**: sewage treatment plant effluent (biological stage)
Concentration of the chemical: 2, 5 mg/L. related to COD **[ ]**; DOC **[ ]**; test substance **[X]**
Medium: water **[X];** water-sediment **[ ];** soil **[ ];** sewage treatment **[ ]**
Degradation: 69 % (2 mg/L) and 79 % (5 mg/L) after 30 days by BOD.
Results: readily biodeg. **[X];** inherently biodeg. **[ ]**;
under test condition no biodegradation observed **[ ]**, other **[ ]**
Kinetic: 2 mg/L: 5% (5 d); 62% (15 d); 69% (30 d)
5 mg/L: 4% (5 d); 57% (15 d); 79% (30 d)
Method: OECD Guideline 301 D
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: As prescribed by 1.1-1.4.
Remarks: Municipal sewage treatment plant effluent was used as inoculum.
Reference: Henkel KGaA (2001), unpublished data (R0100896).

(d) Type: aerobic **[X]**; anaerobic **[ ]**
Inoculum: adapted **[ ]**; non-adapted **[X]**; other **[ ]**: sewage treatment plant effluent (biological stage)
Concentration of the chemical: 3 mg/L. related to COD **[ ]**; DOC **[ ]**; test substance **[X]**
Medium: water **[X];** water-sediment **[ ];** soil **[ ];** sewage treatment **[ ]**
Degradation: 70 % after 30 day.
Results: readily biodeg. **[X];** inherently biodeg. **[ ]**;
under test condition, no biodegradation observed **[ ]**, other **[ ]**
Kinetic: Not stated.
Method: DEV: H5 modif.
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: No data available.
Remarks: Domestic sewage was predominantly used as inoculum.
Reference: Bayer AG, unpublished data.

3.6 BOD_5, COD OR RATIO BOD_5/COD

No studies located.

3.7 BIOACCUMULATION

Species: Fish
Exposure period: No data available.
Temperature: 20 °C

Concentration:	No data available.
BCF:	ca. 1.3.
Elimination:	Yes **[ ]** No **[ ]** ? **[X]**
Method:	Other.
Type of test:	calculated **[X]**; measured **[ ]** static **[ ]**; semi-static **[ ]**; flow-through **[ ]**; other **[ ]**
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Test substance:	No data available.
Remarks:	The BCF was estimated from a recommended regression-derived equation using a water solubility of 58 g/L at 25 °C. This estimated BCF indicates that bioconcentration potential in fish will not be significant.
Reference:	Lyman W.J. et al. (1990), Amer. Chem. Soc., p.5-10.

3.8 ADDITIONAL REMARKS

A. Sewage treatment

Remarks: No additional remarks.

B. Other information

Remarks: No additional remarks.

4. ECOTOXICITY

4.1 ACUTE/PROLONGED TOXICITY TO FISH

A. ACUTE TOXICITY TO FISH

(a) **Preferred result**

Type of test:	static **[ ]**; semi-static **[X]**; flow-through **[ ]**; other **[ ]** open-system **[ ]**; closed-system **[ ]**
Species:	Oryzias latipes (Medaka, fresh water)
Exposure period:	96 hour(s)
Results:	LC_{50} (96 h) > 100.0 mg/L based on nominal concentrations.
Analytical monitoring:	Yes **[X]** No **[ ]** ? **[ ]**
Method:	OECD TG 203 (1992).
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	As prescribed by 1.1-1.4.
Remarks:	Drinking water was used after dechlorination by passing through activated carbon filter. No vehicle was used. Test was conducted at the nominal concentrations of 0 and 100 mg/L. Test solutions were replaced every 24 hours by newly prepared ones. When test solutions were analysed after 24 hours, the measured concentrations showed more than 80 % of the nominal concentrations. At the nominal concentrations of 0 mg/L, 100 % of fish survived until 96 h; At 100 mg/L, 100 % of fish survived until 96 h; at both doses, no fish showed abnormal swimming behaviour.
Reference:	Environment Agency of Japan (1998).

(b) Type of test: static **[X]**; semi-static **[ ]**; flow-through **[ ]**; other (e.g. field test) **[ ]**; open-system **[ ]**; closed-system **[ ]**

Species:	Pimephales promelas (Fathead minnow, fresh water)
Exposure period:	96 hour(s)
Results:	LC_{50} (96h) = 165.3 mg/L (178.3, 165.3 mg/L)
Analytical monitoring:	Yes **[X]** No **[ ]** ? **[ ]**
Method:	OECD TG 203 and EEC/Annex V C.1.
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	As prescribed by 1.1-1.4,Sample ID No.: 3045932, Purity: > 99.5 %.
Remarks:	During the test, 77 - 98.1 % of the initial analysed concentrations was maintained throughout the test. The exposure solutions did not appear to exceed the aqueous solubility of the test article as no particulates or surface slicks were observed in the exposure vessels containing the test article.
Reference:	Lawrence, D.L. and Hirsch, M.P. (1995), Eastman Kodak Company, Environmental Sciences Section, Corporate Health and Environment Laboratories, An acute aquatic effects test with the fathead minnow, Study No.: EN-430-900256-1, Unpublished data.

(c) Type of test: static **[X]**; semi-static **[ ]**; flow-through **[ ]**; other (e.g. field test) **[ ]**; open-system **[ ]**; closed-system **[ ]**

Species:	Cyprinus carpio (Cyprinidae, carp, fresh water)
Exposure period:	48 hour(s)
Results:	LC_{50} (48 h) = 174 mg/L
Analytical monitoring:	Yes **[ ]** No **[X]** ? **[ ]**
Method:	Other.
GLP:	Yes **[X]** No **[ ]** ? **[ ]**

	Test substance:	As prescribed by 1.1-1.4.
	Remarks:	Method used was Bewertung wassergefährdender Stoffe, Bestimmung der akuten Fischtoxizität, Ad-hoc-Arbeitsgruppe 1 (Obmann Dr. Niemitz), LTwS, Nr. 10, September 1979.
	Reference:	Unichema Chemie B.V. (1988), unpublished data, RCC NOTOX 0831/PA45.
(d)	Type of test:	static **[ ]**; semi-static **[X]**; flow-through **[ ]**; other (e.g. field test) **[ ]** open-system **[ ]**; closed-system **[ ]**
	Species:	Brachydanio rerio (Zebra-fish, fresh water)
	Exposure period:	96 hour(s)
	Results:	LC_{50} (96 h) = 300 mg/L
	Analytical monitoring:	Yes **[ ]** No **[X]** ? **[ ]**
	Method:	ISO-Guideline 7346/2 which conforms to OECD TG 203.
	GLP:	Yes **[ ]** No **[X]** ? **[ ]**
	Test substance:	As prescribed by 1.1 - 1.4.
	Remarks:	Test was conducted at a concentration of 0, 90, 130, 180, 250, 360 and 500 mg/L. Mortalities are recorded at 0, 6, 24, 48, 72 and 96 hr. The study was carried out before 1990, at a time when GLP was not implemented. However, the study adhered to GLP comparable conditions.
	Reference:	Henkel KGaA (1982), unpublished data (R-0100930).
(e)	Type of test:	static **[X]**; semi-static **[ ]**; flow-through **[ ]**; other (e.g. field test) **[ ]** open-system **[ ]**; closed-system **[ ]**
	Species:	Leuciscus idus (Golden orfe, fresh water)
	Exposure period:	48 hour(s)
	Results:	LC_{50} (48 h) = 170 mg/L
	Analytical monitoring:	Yes **[ ]** No **[X]** ? **[ ]**
	Method:	Bestimmung der Wirkung von Wasserinhaltsstoffen auf Fische, DIN38412 Teil15.
	GLP:	Yes **[ ]** No **[X]** ? **[ ]**
	Test substance:	As prescribed by 1.1 - 1.4.
	Remarks:	Test substance directly weighed into test vessel followed by treatment with Ultraturrax. Test was conducted at a concentration of 0, 100, 300 and 1,000 mg/L. Fish did not show any abnormal behaviour. LC_0 (48 h) and LC_{100} (48 h) were 100 mg/L and 300 mg/L, respectively. The study was carried out before 1990, at a time when GLP was not implemented. However, the study adhered to GLP comparable conditions.
	Reference:	Henkel KGaA (1988), unpublished data (R-0100933).
(f)	Type of test:	static **[ ]**; semi-static **[ ]**; flow-through **[ ]**; other (e.g. field test) **[ ]**; open-system **[ ]**; closed-system **[ ]**
	Species:	Cyprinus carpio (Cyprinidae, carp, fresh water)
	Exposure period:	66 hour(s)
	Results:	LC_{50} (Not stated)
	Analytical monitoring:	Yes **[ ]** No **[X]** ? **[ ]**
	Method:	Not stated.
	GLP:	Yes **[ ]** No **[ ]** ? **[X]**
	Test substance:	As prescribed by 1.1 - 1.4.
	Remarks:	Carp (Cyprinus carpio) force-fed with triacetin were killed at concentrations between 122 mg/kg bw (minimum) and 184 mg/kg bw (maximum). Alkalinity, Water temperature and pH were 10 mg/L $CaCO_3$, 18.3 °C and 6.7, respectively.
	Reference:	Loeb, H.A. & Kelly, W.H (1963), US Fish Wildl. Serv., Sp. Sci. Rep.-Fish No. 471.

B. PROLONGED TOXICITY TO FISH

Type of test:	static **[ ]**; semi-static **[ ]**; flow-through **[X]**; other (e.g. field test) **[ ]**; open-system **[ ]**; closed-system **[ ]**
Species:	Oryzias latipes (Medaka, fresh water)
Exposure period:	14 days.
Results:	LC_{50} (7 days) > 100.0 mg/L (nominal concentration) LC_{50} (14 days) > 100.0 mg/L (nominal concentration)
Analytical monitoring:	Yes **[X]** No **[ ]** ? **[ ]**
Method:	OECD TG 204.
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	As prescribed by 1.1-1.4.
Remarks:	Test was conducted at the nominal concentrations of 0, 30.9 (27.7), and 55.6 (51.6), 100 (97.0) mg/L (measured mean concentration of test chemical during test period). No reduction of food intake and no abnormal behaviours were observed at all doses tested during 14-day exposure period. There was no significant difference in fish body weight between all treated groups and in control.
Reference:	Environment Agency of Japan (1998).

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

A. Daphnia

(a) **Preferred result**

Type of test:	static **[X]**; semi-static **[ ]**; flow-through **[ ]**; other **[ ]** open-system **[ ]**; closed-system **[ ]**
Species:	Daphnia magna (Crustacea)
Exposure period:	48 hour(s)
Results:	EC_{50} (24 h) = 888 mg/L EC_{50} (48 h) = 768 mg/L EC_0 (48 h) = 309 mg/L
Analytical monitoring:	Yes **[X]** No **[ ]** ? **[ ]**
Method:	OECD TG 202
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	As prescribed by 1.1-1.4.
Remarks:	Test concentration: 95, 171, 309, 556, 1,000 mg/L. All the test solutions showed more than 90 % of the nominal concentrations after 48 hours.
Reference:	Environment Agency of Japan (1998).

(b)

Type of test:	static **[X]**; semi-static **[ ]**; flow-through **[ ]**; other **[ ]** open-system **[ ]**; closed-system **[ ]**
Species:	Daphnia magna (Crustacea)
Exposure period:	48 hour(s)
Results:	EC_{50} (24 h) > 974.4 mg/L (974.4, 1006.7 mg/L) EC_{50} (48 h) = 810.9 mg/ L (810.9, 904.2 mg/L) EC_0 (24 h) = 974.4 mg/L (974.4, 1006.7 mg/L) EC_0 (48 h) = 541.1 mg/L (541.1, 558.5 mg/L)
Analytical monitoring:	Yes **[X]** No **[ ]** ? **[ ]**
Method:	OECD TG 202 and EEC/Annex V C.2.
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	As prescribed by 1.1-1.4,Sample ID No.: 3045932, Purity: > 99.5 %.

Remarks:	The exposure solutions (nominally 95.0, 171.5, 308.5, 555.5, and 1,000.0 mg/L) were prepared by direct addition of the appropriate amounts of the test article to tanks of water. The exposure solutions did not appear to exceed the aqueous solubility of the test article, as throughout the test, there were no particulates, surface slicks or precipitates observed within the exposure solutions containing the test article.
Reference:	Lawrence, D.L. and Hirsch, M.P. (1995), Eastman Kodak Company, Environmental Sciences Section, Corporate Health and Environment Laboratories, An acute aquatic effects test with the daphnid, Study No.: EN-431-900256-1, Unpublished data.

(c) Type of test:	static **[X]**; semi-static **[ ]**; flow-through **[ ]**; other **[ ]** open-system **[ ]**; closed-system **[ ]**
Species:	Daphnia magna (Crustacea)
Exposure period:	48 hour(s)
Results:	EC_0 (48 h) = 65 mg/L EC_{50} (48 h) = 380 mg/L EC_{100} (48 h) = 1000 mg/L
Analytical monitoring:	Yes **[ ]** No **[ ]** ? **[X]**
Method:	Daphnien-Kurzzeittest, DIN 38412 Teil 11, Bestimmung der Wirkung von Wasserinhaltsstoffen auf Kleinkrebse
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	As prescribed by 1.1 - 1.4.
Remarks:	Test method conforms to OECD Guideline 202A.
Reference:	Henkel KGaA, unpublished data. (Report-No. R 9400102).

B. Other aquatic organisms

No studies located.

4.3 TOXICITY TO AQUATIC PLANTS, e.g. algae

Species:	Selenastrum capricornutum ATCC 22662
Endpoint:	Biomass **[X]**; Growth rate **[X]**; Other **[ ]**
Exposure period:	72 h.
Results:	EC_{50} (0-72 h) > 1,000 mg/L (Growth inhibition: growth rate & biomass) NOEC (0-72 h) = 556 mg/L (Growth inhibition: growth rate & biomass)
Analytical monitoring:	Yes **[X]** No **[ ]** ? **[ ]**
Method:	OECD TG 201(1984) open-system **[ ]**; closed-system **[X]**
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	As prescribed by 1.1-1.4.
Remarks:	All the test groups (95, 171, 309, 556 except 1,000 mg/L) showed normal and similar growth (170-224 fold increase after 72 hr) to control (207-fold increase after 72 hr).
Reference:	Environment Agency of Japan (1998).

4.4 TOXICITY TO BACTERIA

(a) Type:	Aquatic **[X]**; Field **[ ]**; Soil **[ ]**; Other **[ ]**
Species:	Pseudomonas putida (Bacteria)
Exposure Period:	18 hour(s)
Results:	EC_0 (18 h) > 541.6 mg/L

Analytical monitoring:	Yes **[ ]** No **[X]** ? **[ ]**
Method:	Not stated.
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	As prescribed by 1.1 - 1.4.
Remarks:	Bacteriotoxicity was determined according to Bewertung Wassergefährdender Stoffe, III Bestimmung der akuten Bakterientoxizität Ad-hoc-Arbeitsgruppe 1 (Obmann Dr. Niemitz), LTWS, Nr. 10 September 1979.
Reference:	Unichema Chemie B.V. (1988), unpublished data , RCC NOTOX B.V. 0831/PS9.

(b) Type:	Aquatic **[ ]**; Field **[ ]**; Soil **[ ]**; Other **[ ]**
Species:	Pseudomonas putida MIGULA (Bacteria)
Exposure Period:	30 min
Results:	EC_0 (30 min) = 10,000 mg/L
Analytical monitoring:	Yes **[ ]** No **[X]** ? **[ ]**
Method:	Pseudomonas oxygen consumption inhibition test, German standard method DIN 38412 Part 27
GLP:	Yes **[ ]** No **[X]** ? **[ ]**
Test substance:	As prescribed by 1.1 - 1.4.
Remarks:	Pseudomonas oxygen consumption inhibition test. Test was conducted at a concentration of 0 and 10,000 mg/L. The study was carried out before 1990, at a time when GLP was not implemented. However, the study adhered to GLP comparable conditions.
Reference:	Henkel KGaA (1988), unpublished data (R-0100931).

(c) Type:	Aquatic **[ ]**; Field **[ ]**; Soil **[ ]**; Other **[ ]**
Species:	Pseudomonas putida MIGULA (Bacteria)
Exposure Period:	16 hour(s)
Results:	NOEC (16 h) = 3,000 mg/L FOEC (16 h) = 10,000 mg/L NOEC: First Observed Effect Concentration, the highest measured substance concentration with an effect below 10 %. FOEC: First Observed Effect Concentration, the lowest measured substance concentration with an effect above 10 %.
Analytical monitoring:	Yes **[ ]** No **[X]** ? **[ ]**
Method:	Pseudomonas cell multiplication inhibition test in accordance to EU-Guideline EN ISO 10712 of December 1995
GLP:	Yes **[ ]** No **[X]** ? **[ ]**
Test substance:	As prescribed by 1.1 - 1.4.
Remarks:	Pseudomonas oxygen consumption inhibition test. Test was conducted at a concentration of 0, 3,000 and 10,000 mg/L. The study was carried out before 1990, at a time when GLP was not implemented. However, the study adhered to GLP comparable conditions.
Reference:	Henkel KGaA (1988), unpublished data (R-0100932).

4.5 CHRONIC TOXICITY TO AQUATIC ORGANISMS

4.5.1 CHRONIC TOXICITY TO FISH

No studies located.

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

INVERTEBRATES

Type of test:	static **[ ]**; semi-static **[X]**; flow-through **[ ]**; other (e.g. field test) **[ ]**; open-system **[ ]**; closed-system **[ ]**
Species:	Daphnia magna
Endpoint:	Mortality **[ ]**; Reproduction rate **[X]**; Other **[ ]**
Exposure period:	21 days.
Results:	EC50 (14-d, reproduction) > 100 mg/L EC50 (21-d, reproduction) > 100 mg/L NOEC (21-d, reproduction) = 100 mg/L (Calculated based based on nominal concentration)
Analytical monitoring:	Yes **[X]** No **[ ]** ? **[ ]**
Method:	OECD TG 211 (1997)
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	As prescribed by 1.1-1.4.
Remarks:	A single exposure group (100 mg/L) against control group was studied. Mean cumulative numbers of juveniles produced per adult alive for 21 days: Control: 93.8, 100 mg/L: 91.8. Time-weighted means of measured concentration of test chemical (100 mg/L) during 21-d exposure: 94 mg/L. LC50 for parental Daphnia (14-d) > 100 mg/L LC50 for parental Daphnia (21-d) > 100 mg/L (Calculated based on nominal concentrations)
Reference:	Environment Agency of Japan (1998).

4.6 TOXICITY TO TERRESTRIAL ORGANISMS

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

No studies located.

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

No studies located.

4.6.3 TOXICITY TO OTHER NON MAMMALIAN TERRESTRIAL SPECIES (INCLUDING AVIAN)

No studies located.

4.7 BIOLOGICAL EFFECTS MONITORING (INCLUDING BIOMAGNIFICATION)

No studies located.

4.8 BIOTRANSFORMATION AND KINETICS

No studies located.

4.9 ADDITIONAL REMARKS

Remarks:	Toxicity towards tadpoles (Rana temporaria): Threshold concentration for complete narcosis at 5000 mg/L.
Reference:	Lipnick, R.L.(1988), ASTM Spec. Techn. Publ. 11, 468-489.

5. TOXICITY

5.1 ACUTE TOXICITY

5.1.1 ACUTE ORAL TOXICITY

(a) Type:	LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain:	Rat
Value:	> 2,000 mg/kg bw.
Discriminating dose:	2,000 mg/kg bw (a limit dose level).
Method:	Referred to Remarks.
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	As prescribed by 1.1 - 1.4.
Remarks:	Method: OECD TG 401, EEC Directive 84/449/EEC, Annex V of the EEC Directive 67/548/EEC and Bewertung Wassergefährdender Stoffe, II Bestimmung der akuten oralen Saugetiertoxizität, Ad-hoc-Arbeitsgruppe I (Obmann: Dr. Niemitz), LTWS, Nr. 10 September 1979.
Reference:	Unichema Chemie B.V. (1988), unpublished data , RCC NOTOX 0831/1056.

(b) Type:	LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain:	Rat
Value:	6,400 – 12,800mg/kg bw.
Discriminating dose:	No data available.
Method:	Not specified.
GLP:	Yes **[ ]** No **[ ]** ? **[ ]**
Test substance:	As prescribed by 1.1 - 1.4.
Remarks:	Eastman Kodak Company, Laboratory of Industrial Medicine Protocol, 5 dose levels (800-12,800 mg/kg bw), 5 animal per dose level, 14 day observation, no necropsy. Time to death was 37min. Weakness and ataxia were observed.
Reference:	Fassett, D.W. (1955), Eastman Kodak Company, Corporate Health and Environment Laboratories, Unpublished data.

(c) Type:	LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain:	Rat
Value:	12,700 (11 mL) mg/kg bw (as $d^{20} = 1.1562$)
Discriminating dose:	580 (0.5 mL), 2,500 (2.2 mL), 5,500 (4.8 mL), 10,500 (9.1 mL), 14,600 (12.6 mL), 27,200 (23.5 mL), 52,800 (44.8 mL) mg/kg bw (as $d^{20} = 1.1562$)
Method:	Not specified.
GLP:	Yes **[ ]** No **[X]** ? **[ ]**
Test substance:	As prescribed by 1.1 - 1.4.
Remarks:	Eastman Kodak Company, Laboratory of Industrial Medicine Protocol, 7 dose levels (580-52,800 mg/kg bw), 5 animal per dose level, 24 day observation, no necropsy.
Reference:	Fassett, D.W. (1948), Eastman Kodak Company, Corporate Health And Environment Laboratories, Report No. 900256006, Unpublished data.

(d) Type:	LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain:	Rat
Value:	3,000 mg/kg bw
Discriminating dose:	No data available.
Method:	No data available.

GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Test substance:	As prescribed by 1.1 - 1.4.
Remarks:	Not stated.
Reference:	AMA Arch Ind. Health, 21 (1960), 28. Sax, Dangerous Properties of Industrial Materials, 6th ed. p. 2605

(e)

Type:	LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain:	Mouse
Value:	ca. 9,300 mg/kg bw
Discriminating dose:	No data available.
Method:	Refer to Remarks.
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	Triacetin supplied by Matheson..
Remarks:	The LD50 value was calculated from the given literature value of 8.0 mL/kg bw and the density of 1.16 g/cm^3. 7-Day observation period. Triacetin was administered at fixed level of 0.5, 1.0, 2.0, 4.0, 8.0 and 16 mL/kg bw.
Reference:	Lawrence, W.H., Malik, M, Autian, J. (1974), J. Biomed. Mater. Res. 8, 11.

(f)

Type:	LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain:	Mouse/Swiss
Value:	1,800 mg/kg bw (male) 1,100 mg/kg bw (female)
Discriminating dose:	No data available.
Method:	No data available.
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Test substance:	As prescribed by 1.1 - 1.4.
Remarks:	Triacetin in 50 % ethylalcohol was administerd.
Reference:	Gast, J.H. (1963), Fed. Proc. Fed. AM. Soc. Exp. Biol, 22 368.

(g)

Type:	LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain:	Mouse
Value:	3,200 – 6,400 mg/kg bw
Discriminating dose:	No data available.
Method:	No data available.
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Test substance:	As prescribed by 1.1 - 1.4.
Remarks:	Eastman Kodak Company, Laboratory of Industrial Medicine Protocol, 5 dose levels (1,600-25,600 mg/kg bw), 5 animal per dose level, 14 day observation period, no necropsy. Time to death was 6 min-1 hr. Weakness and ataxia were observed. Test was done in 1955.
Reference:	Fassett, D.W. (1955), Eastman Kodak Company, Corporate Health and Environment Laboratories, Unpublished data.

(h)

Type:	LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain:	Mouse
Value:	3,200 – 6,100 mg/kg bw
Discriminating dose:	No data available.
Method:	No data available.
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Test substance:	As prescribed by 1.1 - 1.4.
Remarks:	Not stated.
Reference:	Patty's Industrial Hygiene and Toxicology, 1983, Vol. 2A, p. 2321.

(i) Type: LD_0 [ ]; LD_{100} [ ]; LD_{50} [**X**]; LDL_0 [ ]; Other [ ]
Species/strain: Mouse
Value: 3,000 mg/kg bw
Discriminating dose: No data available.
Method: No data available.
GLP: Yes [ ] No [ ] ? [**X**]
Test substance: No data available.
Remarks: Not stated.
Reference: CHEMIAL DIVISIONE DI SISAS SPA CAVAGLIA".

(j) Type: LD_0 [ ]; LD_{100} [ ]; LD_{50} [**X**]; LDL_0 [ ]; Other [ ]
Species/strain: Rabbit
Value: > 2,000 mg/kg bw
Discriminating dose: No data available.
Method: No data available.
GLP: Yes [ ] No [ ] ? [**X**]
Test substance: As prescribed by 1.1 - 1.4.
Remarks: Not stated.
Reference: Material safety data sheet, dated 26-1-1994, Unichema International.

(k) Type: LD_0 [ ]; LD_{100} [ ]; LD_{50} [ ]; LDL_0 [**X**]; Other [ ]
Species/strain: Frog
Value: 150 mg/kg bw
Discriminating dose: No data available.
Method: No data available.
GLP: Yes [ ] No [ ] ? [**X**]
Test substance: As prescribed by 1.1 - 1.4.
Remarks: Not stated.
Reference: National Institute for Occupational Safety and Health (1976) cited in Food Cosmet. Toxicol. 16 (Suppl. 1), 879-882.

5.1.2 ACUTE INHALATION TOXICITY

(a) Type: LC_0 [ ]; LC_{100} [ ]; LC_{50} [**X**]; LCL_0 [ ]; Other [ ]
Species/strain: Rat/Wistar SPF-Cpb
Exposure time: 4 hours
Value: > 1.721 mg/L (analytical concentration)
Method: OECD 403.
GLP: Yes [ ] No [**X**] ? [ ]
Test substance: No data available.
Remarks: An aerosol of triacetin was tested. No vehicle was used. 100 % of particles < 5 um-diameter. Head only exposure. Five male and 5 female rats were tested in treated and control groups.
Effect: 0/5 males died, 0/5 females died.
No clinical symptoms were observed. No necropsy findings.
Reference: Bayer AG data. Report No. 13888 (P), 1985.

5.1.3 ACUTE DERMAL TOXICITY

(a) Type: LD_0 [ ]; LD_{100} [ ]; LD_{50} [**X**]; LDL_0 [ ]; Other [ ]
Species/strain: Rabbit
Value: > 5,000mg/kg bw
Method: Not specified.
GLP: Yes [ ] No [ ] ? [**X**]
Test substance: As prescribed by 1.1 - 1.4.

Remarks: Not stated
Reference: Bailey D.E. (1976); Report to RIFM, 21 May; cited in Opdyke D.L.J. (1978), Food Cosmet. Toxicol. 16 (Suppl. 1), 879-882.

(b) Type: LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain: Rabbit
Value: > 2,000 mg/kg bw
Method: No data available.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: As prescribed by 1.1 - 1.4.
Remarks: Not stated.
Reference: Material safety data sheet, dated 26-1-1994; Unichema International.

(c) Type: LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain: Guinea pig
Value: > 20 mL/kg bw
Method: No data available.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: As prescribed by 1.1 - 1.4.
Remarks: Eastman Kodak Company, Laboratory of Industrial Medicine Protocol, 3 dose groups (0, 5 - 20 mL/kg bw), resp. 3, 3 and 3 animals per group, 14 days observation. Unit : mL/kg bw. Slight Oedema and erythema. No dead animal was observed. No evidence of skin absorption.
Reference: Fassett, D.W. (1967), Eastman Kodak Company. Unpublished data, Corporate Health and Environment Laboratories.

(d) Type: LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain: Guinea pig
Value: > 20 mL/kg bw
Method: No data available.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: As prescribed by 1.1 - 1.4.
Remarks: Eastman Kodak Company, Laboratory of Industrial Medicine Protocol, 3 dose groups (0, 5 - 20 mL/kg bw), resp. 3, 3 and 3 animals per group, 14 days observation. Unit : mL/kg bw. Slight erythema and 1 - 3 erythema. Sparse hair and slight desquamation on high dose at one week. Sparse hair at 2 weeks. No evidence of absorption.
Reference: Fassett, D.W. (1959), Eastman Kodak Company. Unpublished data, Corporate Health and Environment Laboratories.

(e) Type: LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain: Guinea pig
Value: > 10 mL/kg bw
Method: No data available.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: As prescribed by 1.1 - 1.4.
Remarks: Eastman Kodak Company, Laboratory of Industrial Medicine Protocol, 3 dose groups (0, 5, 10 mL/kg bw), resp. 3, 3 and 2 animals per group, 14 days observation. Unit : mL/kg bw. No edema and slight redness.
Reference: Fassett, D.W. (1955), Eastman Kodak Company. Unpublished data, Corporate Health and Environment Laboratories.

5.1.4 ACUTE TOXICITY, OTHER ROUTES OF ADMINISTRATION

(a) Type: LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain: Rat
Route of Administration: i.m. **[ ]**; i.p. **[X]**; i.v. **[ ]**; infusion **[ ]**; s.c. **[ ]**; other **[ ]**
Exposure time: No data available.
Value: 800 – 1,600 mg/kg bw.
Method: No data available.
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: As prescribed by 1.1 - 1.4.
Remarks: Eastman Kodak Company, Laboratory of Industrial Medicine Protocol, 5 dose groups (400-6,400 mg/kg bw), 5 animal per group, 14 days observation, no necropsy. Weakness, incoordination, gasping and unconsciousness were observed. Time to death was 6 –13 min. Test was done in 1955.
Reference: Fassett, D.W. (1955), Eastman Kodak Company, Corporate Health and Environment Laboratories, Unpublished data.

(b) Type: LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain: Rat
Route of Administration: i.m. **[ ]**; i.p. **[X]**; i.v. **[ ]**; infusion **[ ]**; s.c. **[ ]**; other **[ ]**
Exposure time: No data available.
Value: 800 – 1,600 mg/kg bw.
Method: No data available.
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: As prescribed by 1.1 - 1.4.
Remarks: Eastman Kodak Company, Laboratory of Industrial Medicine Protocol, 5 dose groups (200-6,400 mg/kg bw), 12 animals per group, 14 days observation, no necropsy. Immediate squirming and gasping with cardiac arrest-death within 15min in high levels-others normal to moderately Weak-some initial gasping-no irritation at autopsy-testes normal. Test was done in 1967.
Reference: Fassett, D.W. (1967), Eastman Kodak Company, Unpublished data, Corporate Health and Environment Laboratories.

(c) Type: LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain: Rat
Route of Administration: i.m. **[ ]**; i.p. **[X]**; i.v. **[ ]**; infusion **[ ]**; s.c. **[ ]**; other **[ ]**
Exposure time: No data available.
Value: 1,600 mg/kg bw.
Method: No data available.
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: As prescribed by 1.1 - 1.4.
Remarks: Eastman Kodak Company, Laboratory of Industrial Medicine Protocol, 5 dose groups (200 - 3,200 mg/kg bw), 2 animals per group, 14 days observation, necropsy at termination. Time to death was 1 - 4 hr.
Reference: Fassett, D.W. (1968), Eastman Kodak Company, Unpublished data, Corporate Health and Environment Laboratories.

(d) Type: LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain: Rat
Route of Administration: i.m. **[ ]**; i.p. **[X]**; i.v. **[ ]**; infusion **[ ]**; s.c. **[ ]**; other **[ ]**
Exposure time: No data available.
Value: 2,100 mg/kg bw.

Method: No data available.
GLP: Yes [ ] No [ ] ? [X]
Test substance: Not stated.
Remarks: A limited number of adult rats was employed.
Reference: Gast, J.H. (1963), Fed. Proc. Fed. AM. Soc. Exp. Biol, 22 368.

(e) Type: LD_0 [ ]; LD_{100} [ ]; LD_{50} [X]; LDL_0 [ ]; Other [ ]
Species/strain: Rat
Route of Administration: i.m. [ ]; i.p. [ ]; i.v. [ ]; infusion [ ]; s.c. [X]; other [ ]
Exposure time: 15 Days after a single injection.
Value: 2.8 mL/kg bw.
Method: Refer to Remarks.
GLP: Yes [ ] No [ ] ? [X]
Test substance: Not stated.
Remarks: Inbred albino rats weighing 200-300 g were used. At least 10 animals were used at each dose level (2.0, 3.0 4-10 mL/kg bw). Not more than 1 mL was given at one site. Animals receiving fatal doses usually died from 20 min to 3 or 4 hours after injection. Symptoms of marked depression, weakness, prostration, and labored respiration just before death were noted. Triacetin was slightly haemolytic and relatively incompatible with blood stream.
Reference: Li, R.C. et al.(1941) Proc. Soc. Exp. Biol. Med., 46 26-28.

(f) Type: LD_0 [ ]; LD_{100} [ ]; LD_{50} [X]; LDL_0 [ ]; Other [ ]
Species/strain: Mouse/Swiss
Route of Administration: i.m. [ ]; i.p. [X]; i.v. [ ]; infusion [ ]; s.c. [ ]; other [ ]
Exposure time: No data available.
Value: 1,700 mg/kg bw (male).
1,400 mg/kg bw (female).
Method: No data available.
GLP: Yes [ ] No [ ] ? [X]
Test substance: Not stated.
Remarks: Peripheral nerve and sensation (Spastic paralysis 13), with/without sensory change. Behavioural (Altered sleeptime; stiffness).
Reference: Gast, J.H. (1963), Fed. Proc. Fed. AM. Soc. Exp. Biol, 22 368.

(g) Type: LD_0 [ ]; LD_{100} [ ]; LD_{50} [X]; LDL_0 [ ]; Other [ ]
Species/strain: Mouse/ICR
Route of Administration: i.m. [ ]; i.p. [X]; i.v. [ ]; infusion [ ]; s.c. [ ]; other [ ]
Exposure time: No data available.
Value: ca. 1.52 mL/kg bw (male).
Method: Refer to Remarks.
GLP: Yes [ ] No [ ] ? [X]
Test substance: Triacetin supplied by Matheson..
Remarks: 7-Day observation period. Triacetin was administered at fixed level of 0.5, 1.0, 2.0, 4.0, 8.0 and 16 mL/kg bw.
Reference: Lawrence W.H. et al. (1974), J. Biomed. Mater. Res., 8 11-34

(h) Type: LD_0 [ ]; LD_{100} [ ]; LD_{50} [X]; LDL_0 [ ]; Other [ ]
Species/strain: Mouse
Route of Administration: i.m. [ ]; i.p. [ ]; i.v. [ ]; infusion [ ]; s.c. [X]; other [ ]
Exposure time: No data available.
Value: 2.3 mL/kg bw.
Method: Refer to Remarks.
GLP: Yes [ ] No [ ] ? [X]

Test substance: Not stated.
Remarks: Inbred white mice weighing 17-21 g were used. At least 10 animals were used at each dose level (1.0, 2.0, 2.5, 3.0 mL/kg bw). Not more than 1 mL was given at one site. Animals receiving fatal doses usually died in from 20 min to 3 or 4 hours after injection. Symptoms of marked depression, weakness, prostration, and laboured respiration just before death were noted. Triacetin was slightly haemolytic and relatively incompatible with blood stream.
Reference: Li, R.C. et al.(1941) Proc. Soc. Exp. Biol. Med., 46 26-28.

(i) Type: LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[ ]**; LDL_0 **[X]**; Other **[ ]**
Species/strain: Guinea pig
Route of Administration: i.m. **[X]**; i.p. **[ ]**; i.v. **[ ]**; infusion **[ ]**; s.c. **[ ]**; other **[ ]**
Exposure time: One week.
Value: 1.5 mL (1,740 mg)/kg bw.
Method: Refer to Remarks.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Data not available.
Remarks: Triacetin (0.5 or 1.0 mL) was injected into the upper part of the leg of the test animal. Lungs, thorax or respiration (dyspnoea) were affected.
Reference: Lipschitz, W.L. et al. (1942), J. Pharmacol. Exp. Ther. 76 189.

(j) Type: LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain: Mouse
Route of Administration: i.m. **[ ]**; i.p. **[ ]**; i.v. **[X]**; infusion **[ ]**; s.c. **[ ]**; other **[ ]**
Exposure time: No data available.
Value: 1,600 mg/kg bw.
Method: Refer to Remarks.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Synthetically prepared by esterification of glycerin and acetic acid.
Remarks: Ten mice at each dose were used. Triacetin was administered in volumes between 2 and 40 mL/kg bw as 25% emulsion in 5% glucose. Injection of triacetin caused almost immediate convulsions, failure of the righting reflexes and respiratory arrest.
Reference: Wretlind, A. (1957), Acta Physiol. Scand., 40 338.

(k) Type: LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain: Rabbit
Route of Administration: i.m. **[ ]**; i.p. **[ ]**; i.v. **[X]**; infusion **[ ]**; s.c. **[ ]**; other **[ ]**
Exposure time: No data available.
Value: 750 mL/kg bw.
Method: No data available.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: No data available.
Remarks: Not stated.
Reference: Fassett, D.W. (1963), Eastman Kodak Company, Corporate Health and Environment Laboratories, Unpublished data.

(l) Type: LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain: Dog
Route of Administration: i.m. **[ ]**; i.p. **[ ]**; i.v. **[X]**; infusion **[ ]**; s.c. **[ ]**; other **[ ]**
Exposure time: No data available.
Value: 1.5-2.0 mL/kg bw.

Method: No data available.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: No data available.
Remarks: Not stated.
Reference: Fassett, D.W. (1963), Eastman Kodak Company, Corporate Health and Environment Laboratories, Unpublished data.

5.2 CORROSIVENESS/IRRITATION

5.2.1 SKIN IRRITATION/CORROSION

(a) Species/strain: Rabbit
Results: Highly corrosive **[ ]**; Corrosive **[ ]**; Highly irritating **[ ]**; Irritating **[ ]**; Moderate irritating **[ ]**; Slightly irritating **[ ]**; Not irritating **[X]**
Classification: Highly corrosive (causes severe burns) **[ ]**; Corrosive (causes burns) **[ ]**; Irritating **[ ]**; Not irritating **[X]**
Method: OECD Guide-line 404 "Acute Dermal Irritation/Corrosion" and Off. J. Europ. Commun. 27, L251 (1984)
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Test substance: As prescribed by 1.1 - 1.4.
Remarks: Triacetin was tested for its primary skin irritation under occlusive conditions on the shaved back skin of 4 rabbits. After a contact time of 4 hours, the skin reactions were evaluated. Only one animal showed slight skin redness one hour after the application. The other animals had no skin reactions at all.
Reference: Kaestner, W. (1988) Unpublished data Henkel KGaA. Rep. No. 880236.

(b) Species/strain: Guinea pig
Results: Highly corrosive **[ ]**; Corrosive **[ ]**; Highly irritating **[ ]**; Irritating **[ ]**; Moderate irritating **[ ]**; Slightly irritating **[X]**; Not irritating **[ ]**
Classification: Highly corrosive (causes severe burns) **[ ]**; Corrosive (causes burns) **[ ]**; Irritating **[X]**; Not irritating **[ ]**
Method: Other (referred to Remarks).
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: As prescribed by 1.1 - 1.4.
Remarks: Eastman Kodak Company, Laboratory of Industrial Medicine Protocol, 3 dose groups, resp. 3, 3 and 2 animals per dose group, and 14 days observation for signs of irritation. Findings erythema, slight oedema, alopecia and desquamation under the conditions of the test. Test was done in 1967.
Reference: Fassett, D.W. (1967), Corporate Health and Environment Laboratories, Eastman Kodak Company Unpublished data.

(c) Species/strain: Chicken/Hubbard Crossbred broiler (male)
Results: Highly corrosive **[ ]**; Corrosive **[ ]**; Highly irritating **[ ]**; Irritating **[ ]**; Moderate irritating **[ ]**; Slightly irritating **[ ]**; Not irritating **[X]**
Classification: Irritating **[ ]**; Not irritating **[X]**; Risk of serious damage to eyes **[ ]**
Method: Other (referred to Remarks).
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: As prescribed by 1.1 - 1.4.
Remarks: Tissue irritation evaluation was conducted by injecting 0.5 mL

of triacetin 1/2" deep in the right and left pectoral muscle of 7-8 week old chickens (six). Tissue irritation was evaluated at the injection sites at 1, 3, 7 days post injection. Triacetin caused very little irritation and was totally free of irritation by the 7th day after injection.

Reference: Hem S.L. et al. (1974-1975), Drug Dev Commun, 1,471-477.

(d) Species/strain: Human
Results: Highly corrosive **[ ]**; Corrosive **[ ]**; Highly irritating **[ ]**; Irritating **[ ]**; Moderate irritating **[ ]**; Slightly irritating **[ ]**; Not irritating **[X]**
Classification: Highly corrosive (causes severe burns) **[ ]**; Corrosive (causes burns) **[ ]**; Irritating **[ ]**; Not irritating **[X]**
Method: Other: Patch Test (geschlossener Epicutan-Test).
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: As prescribed by 1.1 - 1.4.
Remarks: Not stated.
Reference: Epstein W. L. (1976), Report to RIFM, 27 May, cited in Opdyke D.L.J. (1978), Food Cosmet. Toxicol. 16 (Suppl. 1), 879-882.

5.2.2 EYE IRRITATION/CORROSION

(a) Species/strain: Rabbit
Results: Highly corrosive **[ ]**; Corrosive **[ ]**; Highly irritating **[ ]**; Irritating **[ ]**; Moderate irritating **[ ]**; Slightly irritating **[ ]**; Not irritating **[X]**
Classification: Irritating **[ ]**; Not irritating **[X]**; Risk of serious damage to eyes **[ ]**
Method: OECD Guide-line 405 "Acute Eye Irritation/Corrosion"
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Test substance: As prescribed by 1.1 - 1.4.
Remarks: The conjunctival reactions were mild and disappeared totally within 6 to 24 hours after the application. According to the criteria in Off. J. Europ. Commun. 26 (L 257) 1983, the test substance doesn't need to be classified regarding its eye irritation potential. Reactions on the cornea and iris were not observed. As prescribed by 1.1 - 1.4.
Reference: Kaestner, W. (1988) Unpublished data Henkel KGaA. Rep. No. 880228.

(b) Species/strain: Rabbit (male and female albino rabbit)
Results: Highly corrosive **[ ]**; Corrosive **[ ]**; Highly irritating **[ ]**; Irritating **[ ]**; Moderate irritating **[ ]**; Slightly irritating **[ ]**; Not irritating **[X]**
Classification: Irritating **[ ]**; Not irritating **[X]**; Risk of serious damage to eyes **[ ]**
Method: Draize procedure recommended by FDA (1965) and Other (referred to Remarks).
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Triacetin, Eastman Ref. No.256: Eastman Organic Chemicals, Rochester, New York 14650.
Remarks: This study compared the subjective Draize score to several objective procedures, namely, corneal thickness measurement, evaluation of corneal and conjunctival water content, and conjunctival and aqueous humour concentration of a dye bound to plasma proteins after intravenous injection. After a single instillation of 100 uL of undiluted triacetin in the rabbit eye, evaluation of the above parameter was made at 2 and 24 hr. Draize score and corneal thickness were further determined daily for additional days. A linear correlation was found between Draize total score and tissue changes. There was a significant correlation between Draize

corneal score corneal oedema or thickness only on Day one. Therefore, in addition to the standard Draize method, corneal thickness measurements should be performed.

Reference: Conquet, Ph. et al. (1977), Toxic. Appl. Pharmac., 39 129-139.

(c) Species/strain: Rabbit/Rsk:NZW
Results: Highly corrosive **[ ]**; Corrosive **[ ]**; Highly irritating **[ ]**; Irritating **[ ]**; Moderate irritating **[ ]**; Slightly irritating **[ ]**; Not irritating **[X]**
Classification: Irritating **[ ]**; Not irritating **[X]**; Risk of serious damage to eyes **[ ]**
Method: Annex V, Part B of Directive 79/831/EEC and Annex VI, Part IID of Directive 83/467/EEC.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Purity: > 99 % (Fluca A.G., Buchs, Switzerland).
Remarks: The undiluted test substance (100 uL) was placed into one healthy eye of each animal. The other eye served as a blank. The eyes were not washed following instillation of triacetin. The eyes were examined and the grade of ocular reaction was recorded at 4, 24, 48, 72, 96, and 168 hr. Corneal swelling was determined by the ultrasonic pachometer technique. Good correlations were found between the mean percentage corneal swelling after 24, 48 and 72 hr and the mean corneal opacity (r=0.94) and erythema scores (r=0.93) after the same observation times.
Reference: Jacobs, G.A. and Martens, M.A. (1989), Fd Chem. Toxic., 27,255-258.

(d) Species/strain: Rabbit
Results: Highly corrosive **[ ]**; Corrosive **[ ]**; Highly irritating **[ ]**; Irritating **[ ]**; Moderate irritating **[ ]**; Slightly irritating **[X]**; Not irritating **[ ]**
Classification: Irritating **[ ]**; Not irritating **[ ]**; Risk of serious damage to eyes **[ ]**
Method: Other (referred to Remarks).
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: As prescribed by 1.1 - 1.4.
Remarks: Method: Eastman Kodak Company, Laboratory of Industrial Medicine Protocol, 2 rabbits received 1 drop of test substance in one eye. The eye of 1 rabbit was washed. Signs of irritation were evaluated 1, 24 and 48 hours after administration of the test substance.
Reference: Fassett, D.W. (1967), Corporate Health and Environment Laboratories, Eastman Kodak Company Unpublished data.

(e) Species/strain: Rabbit
Results: Highly corrosive **[ ]**; Corrosive **[ ]**; Highly irritating **[ ]**; Irritating **[ ]**; Moderate irritating **[ ]**; Slightly irritating **[ ]**; Not irritating **[X]**
Classification: Irritating **[ ]**; Not irritating **[X]**; Risk of serious damage to eyes **[ ]**
Method: Other (referred to Remarks).
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: Purity: ca. 98%.
Remarks: Triacetin was applied topically to both eyes of albino rabbits (2 males and 2 females). Triacetin was applied 1, 3, 6, 7 and 13 times over the following periods: 2, 4, 7, 26 and 50 hours. The instilled volume (0.1m) was delivered with a micropipette. Evaluation was conducted in terms of corneal and conjunctival oedema, serum extravasion in conjunctivae and blood/aqueous humour barrier disruption. No effects were reported except a possible reduction in corneal dry weight. However, injection of the neat liquid into the rabbit cornea (0.1 mL) resulted in some irritation.
Reference: Lailer J. et al. (1976), Proc. Eur. Soc. Toxic., 17 336-350.

(f) Species/strain: Rabbit
Results: Highly corrosive **[ ]**; Corrosive **[ ]**; Highly irritating **[ ]**; Irritating **[ ]**; Moderate irritating **[ ]**; Slightly irritating **[ ]**; Not irritating **[X]**
Classification: Irritating **[ ]**; Not irritating **[X]**; Risk of serious damage to eyes **[ ]**
Method: Other (referred to Remarks).
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: Data not available.
Remarks: No irritation occurred when one drop (ca. 0.05 mL) of neat triacetin was applied to rabbit eyes every 2 seconds for 6 min. The ocular reaction was observed over a period of 7-14 days.
Reference: Hughes W. F. Jr. (1976), Bull. Johns Hopkins Hosp., 82 338-353.

(g) Species/strain: Rabbit
Results: Highly corrosive **[ ]**; Corrosive **[ ]**; Highly irritating **[ ]**; Irritating **[ ]**; Moderate irritating **[ ]**; Slightly irritating **[ ]**; Not irritating **[ ]**
Classification: Irritating **[ ]**; Not irritating **[ ]**; Risk of serious damage to eyes **[ ]**
Method: Other (referred to Remarks).
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: No data available.
Remarks: No injury when tested on rabbits eyes.
Reference: Grant W.M. (1986), Toxicology of the Eye, 3rd ed. Springfield, IL: Charles C. Thomas Publisher, p 931.

(h) Species/strain: Data not available.
Results: Highly corrosive **[ ]**; Corrosive **[ ]**; Highly irritating **[ ]**; Irritating **[ ]**; Moderate irritating **[ ]**; Slightly irritating **[X]**; Not irritating **[ ]**
Classification: Irritating **[X]**; Not irritating **[ ]**; Risk of serious damage to eyes **[ ]**
Method: Other (referred to Remarks).
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Data not available.
Remarks: Not stated.
Reference: CHEMICAL DIVISION DI SISAS SPA CAVAGLIA".

5.3 SKIN SENSITISATION

(a) Type: Other.
Species/strain: Human.
Results: Sensitizing **[ ]**; Not sensitizing **[X]**; Ambiguous **[ ]**
Classification: Sensitizing **[ ]**; Not sensitizing **[ ]**
Method: Maximization test.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: As prescribed by 1.1 - 1.4.
Remarks: Substance concentration: 20 % in petrolatum; group size: 33 volunteers.
Reference: Epstein, WL (1976), Report to RIFM, cited in Opdyke D.L.J. (1978), Food Cosmet. Toxicol. 16 (Suppl. 1), 879-882.

(b) Type: Other.
Species/strain: Guinea pig.
Results: Sensitizing **[ ]**; Not sensitizing **[X]**; Ambiguous **[ ]**
Classification: Sensitizing **[ ]**; Not sensitizing **[X]**
Method: Not stated.
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: As prescribed by 1.1 - 1.4.

Remarks: Method: Eastman Kodak Company, Laboratory of Industrial MedicineProtocol, 0.05 ml of 0.1M solution of test material in solvent composed of acetone, dioxane and guinea pig fat (7:2:1), dosing 3 times in 5 days, challenges at 1, 2 or 3 weeks after initial exposure. Vehicle control and a positive control (phenyl hydrazine) included. Test was conducted in 1955.
Reference: Eastman Kodak Company (1955). Unpublished data, Corporate Health and Environment Laboratories.

(c) Type: Other.
Species/strain: Human.
Results: Sensitizing **[ ]**; Not sensitizing **[ ]**; Ambiguous **[ ]**
Classification: Sensitizing **[ ]**; Not sensitizing **[ ]**
Method: Not specified.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: As prescribed by 1.1 - 1.4.
Remarks: A contact eczema in humans caused by triacetin is reported.
Reference: Unna, P.J., Schulz (1963), K.H. Hautarzt 14, 423-25.

(d) Type: No data available.
Species/strain: Guinea pig.
Results: Sensitizing **[ ]**; Not sensitizing **[X]**; Ambiguous **[ ]**
Classification: Sensitizing **[ ]**; Not sensitizing **[X]**
Method: No data available.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: As prescribed by 1.1 - 1.4.
Remarks: Not stated.
Reference: Patty's Industrial Hygiene and Toxicology, 1983, Vol. 2A, p.2321
Opdyke D.L.J. (1978), Food Cosmet. Toxicol. 16 (Suppl. 1), 879-882.

5.4 REPEATED DOSE TOXICITY

(a) Species/strain: Rat / Crj:CD (SD) IGS
Sex: Female **[ ]**; Male **[ ]**; Male/Female **[X]**; No data **[ ]**
Route of Administration: Oral (gavage)
Exposure period: (male) 44 days
(female) From 14 days before mating to day 3 of lactation (41-48days)
Frequency of treatment: One administration/day
Post exposure observation period: None.
Dose: 0, 40, 200, 1,000 mg/kg bw/day
Control group: Yes **[X]**; No **[ ]**; No data **[ ]**;
Concurrent no treatment **[ ]**; Concurrent vehicle **[X]**; Historical **[ ]**
NOAEL: 1,000 mg/kg bw/day (male)
1,000 mg/kg bw/day (female)
LOAEL: Not determined under the conditions studied.
Method: OECD combined repeat dose and reproductive/developmental toxicity screening test (OECD TG 422).
Results: Triacetin had no effects on clinical signs, body weight, and food consumption, and organ weight or necropsy findings. No histopathological changes ascribable to the compound were observed in either sex. There were no haematological or blood chemical parameters in males. The NOAEL for repeat dose toxicity is thus considered to be 1,000 mg/kg bw/day for both sexes.
GLP: Yes **[X]** No **[ ]** ? **[ ]**

Test substance: Daihachi Chemical Industries Co. Ltd., purity: >98.2 wt %
Remarks: None
Reference: Ministry of Health & Welfare (MHW), Japan (1998), Toxicity Testing Reports of Environmental Chemicals vol.6 127-147.

(b) Species/strain: Rat
Sex: Female **[ ]**; Male **[X]**; Male/Female **[ ]**; No data **[ ]**
Route of Administration: Inhalation
Exposure period: 90 Days.
Frequency of treatment: Six hours per day for 5 days per week.
Post exposure observation period: 2 weeks.
Dose: 249 ppm (measured average concentration), 3 rats.
Control group: Yes **[ ]**; No **[X]**; No data **[ ]**;
Concurrent no treatment **[ ]**; Concurrent vehicle **[ ]**; Historical **[ ]**
NOAEL: 249 ppm (2,220 mg/m^3)/3 rats
LOAEL: Not stated.
Results: Average daily weight gain was 2.2 g/rat. No symptoms were noted at any time during the exposure, and all rats appeared to be normal. Haematological studies and urine analyses were done at intervals without finding anything abnormal in any of the animals. At the time of autopsy, no abnormalities attributable to the exposure were found. The weight of both liver and kidney when calculated as per cent of total body weight were found to be within the normal range. Under the conditions of the study no toxic effects caused by the inhalation of triacetin could be found.
Method: Not stated.
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: Plasticizer 88, Eastman Kodak Company.
Remark: Method: Eastman Kodak Company, Laboratory of Industrial Medicine Protocol, whole body exposure to vaporized (heated at 150 °C) test substance. The range of exposure was 14 to 918 ppm (130 to 8190 mg/m^3).
Reference: Fassett, D.W. (1955), Corporate Health and Environment Laboratories, Eastman Kodak Company Unpublished data.

(c) Species/strain: Rat
Sex: Female **[ ]**; Male **[X]**; Male/Female **[ ]**; No data **[ ]**
Route of Administration: Inhalation
Exposure period: Five days.
Frequency of treatment: Six hours per day for 5 days per week.
Post exposure observation period: One week.
Dose: 73.72 ppm (660 mg/m^3), 8271 ppm (73,700 mg/m^3, saturated concentration) (measured average concentration)/3 rats
Control group: Yes **[ ]**; No **[X]**; No data **[ ]**;
Concurrent no treatment **[ ]**; Concurrent vehicle **[ ]**; Historical **[ ]**
NOAEL: 8271 ppm
LOAEL: Not available.
Results: No damage to the rats was caused in five days exposure to saturated vapours of triacetin.
Method: Other.
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: Plasticizer 88, Eastman Kodak Company.
Remark: Method: Eastman Kodak Company, Laboratory of Industrial

Medicine Protocol, whole body exposure to vaporized (heated) test substance.
Triacetin was heated at 315 °C and the animals were exposed to saturated vapours at the temperature (28 °C) of the animal chamber. After the 90 days tests on rats inhaling the vapours of triacetin, an exposure to saturated vapours for one week was done to determine the effect on rats. Autopsy was done for 1 rat only.

Reference: Fassett, D.W. (1955), Corporate Health and Environment Laboratories, Eastman Kodak Company Unpublished data.

(d) Species/strain: Rat
Sex: Female **[ ]**; Male **[ ]**; Male/Female **[ ]**; No data **[X]**
Route of Administration: Inhalation
Exposure period: Five days.
Frequency of treatment: Six hours per day.
Post exposure observation period: Data not available.

Dose: Saturated vapour (plus some mist).
Control group: Yes **[ ]**; No **[ ]**; No data **[X]**;
Concurrent no treatment **[ ]**; Concurrent vehicle **[ ]**; Historical **[ ]**
NOAEL: Not stated.
LOAEL: Not stated.
Results: No symtoms or histopathology.
Method: Not stated.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Data not available.
Remark: Not stated.
Reference: Patty's Industrial Hygiene and Toxicology, 1983, vol 2A, 2321.

(e) Species/strain: Rat/ Sprague-Dawley (weanling)
Sex: Female **[ ]**; Male **[X]**; Male/Female **[ ]**; No data **[ ]**
Route of Administration: Oral feed.
Exposure period: 90 days
Frequency of treatment: Daily.
Post exposure observation period: Data not available.
Dose: The diet containing 20 %, 60 % of triacetin by weight or a mixture of triacetin and glycerol.
Control group: Yes **[X]**; No **[ ]**; No data **[ ]**;
Concurrent no treatment **[ ]**; Concurrent vehicle **[X]**; Historical **[ ]**
NOAEL: 20 % of the diet (10 g/kg bw/day).
LOAEL: Not stated.
Results: The animals tolerated up to 20 % triacetin.
Greater percentage caused a decrease in weight gain. A large loss in weight and considerable mortality was associated with diets containing either glycerol or triacetin as 60% (31 g/kg bw/day) of the diet. A diet containing a mixture of 40% glycerol and 20 % triacetin was tolerated fairly well.
Thus, the toxicity of these two compounds was not additive.
Method: Data not available.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: No data available.
Remark: Not stated.
Reference: Shapira, J. et al. (1969), Life Sci. Space Res. 7 123-129.

(f) Species/strain: Rat/ Sprague-Dawley

Sex: Female **[ ]**; Male **[X]**; Male/Female **[ ]**; No data **[ ]**
Route of Administration: Oral feed.
Exposure period: 13 weeks
Frequency of treatment: Daily.
Post exposure observation period: Data not available.
Dose: Total 60 % of the diet by weight with a mixture of triacetin (20 % or 30 %) and glycerol (40 % or 30 %) or propylene glycol (30 %).
Control group: Yes **[X]**; No **[ ]**; No data **[ ]**;
Concurrent no treatment **[ ]**; Concurrent vehicle **[X]**; Historical **[ ]**
NOAEL: Not stated.
LOAEL: Not stated.
Results: Eight male rats were used with each diet. Growth occurred with all diets but relative to starch control it was best in diet containing glycerol (30 % or 40 %) and propylene glycol (30 % or 20 %). With triacetin present (20 % or 40 %) in the diets, growth was relatively poor. Compared to the control diet, liver enlargement occurred in all animals on experimental diets.
Method: Data not available.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: No data available.
Remark: Not stated.
Reference: Shapira, J. et al. (1975), Proc. West. Pharm. Soc. 18 339-343.

(g) Species/strain: Rat/(weanling)
Sex: Female **[ ]**; Male **[ ]**; Male/Female **[X]**; No data **[ ]**
Route of Administration: Oral feed.
Exposure period: 60 days
Frequency of treatment: Daily.
Post exposure observation period: Not stated.
Dose: 55 % of the diet by weight (77 % of the calories).
Control group: Yes **[X]**; No **[ ]**; No data **[ ]**;
Concurrent no treatment **[ ]**; Concurrent vehicle **[X]**; Historical **[ ]**
NOAEL: Not stated.
LOAEL: Not stated.
Results: Triacetin allowed fair growth when compared to the control diet (coconut oil control).
Method: Four rats, two males and two females, weighing approximately 50 g at the age of weaning, were placed in wire bottom screen cages, and allowed to eat of the diet ad libitum. The food cups were weighed, cleaned, and refilled daily, and record kept of the food consumed.
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: Eastman Kodak Company, Purity: No data available.
Remark: Not stated.
Reference: Cox, W. M. Jr. (1933), J. Biol. Chem. 103 777-790.

(h) Species/strain: Mouse/Swiss
Sex: Female **[ ]**; Male **[ ]**; Male/Female **[ ]**; No data **[X]**
Route of Administration: Oral gavage.
Exposure period: Three to five weeks.
Frequency of treatment: Not stated.
Post exposure observation period: Data not available.
Dose: Data not available.
Control group: Yes **[ ]**; No **[ ]**; No data **[X]**;

Concurrent no treatment **[ ]**; Concurrent vehicle **[ ]**; Historical **[ ]**
NOAEL: Not stated.
LOAEL: Not stated.
Results: No symptoms or histopathology.
Method: Preliminary studies showed growth depression, unkempt appearance but no effect on activity over the test period.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Commercial preparations were used in 50 % ethanol.
Remark: Not stated.
Reference: Gast, J.H. (1963), Fed. Proc. Fed. AM. Soc. Exp. Biol, 22 368.

5.5 GENETIC TOXICITY IN VITRO

A BACTERIAL TEST

(a) **Preferred result**

Type: Bacterial reverse mutation assay
System of testing: Salmonella typhimurium strains TA98, TA100, TA1535, TA1537, Escherichia coli WP2 uvr A
Concentration: 0, 313, 625, 1,250, 2,500, 5,000 ug/plate (with and without S 9)
Metabolic activation: With **[ ]**; Without **[ ]**; With and Without **[X]**; No data **[ ]**
Results: Negative.
Cytotoxicity conc: With metabolic activation: Not observed up to 5,000 ug/plate (five strains)
Without metabolic activation: Not observed up to 5,000 ug/plate (five strains)
Precipitation conc: Not stated.
Genotoxic effects: Negative.

	+	?	-
With metabolic activation:	**[ ]**	**[ ]**	**[X]**
Without metabolic activation:	**[ ]**	**[ ]**	**[X]**

Method: OECD Guidelines No.471 and 472 Guidelines for Screening Toxicity Testing of Chemicals (Japan)
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Test substance: Daihachi Chemical Industries Co. Ltd., purity: >98.2 wt %
Remarks: For metabolic activation, mammalian metabolic preparations were used (pre-incubation assay).
Reference: Ministry of Health & Welfare (MHW), Japan (1998), Toxicity Testing Reports of Environmental Chemicals vol.6 127-147.

(b) Type: Bacterial reverse mutation assay
System of testing: Salmonella typhimurium strains TA98, TA100, TA1535, TA1537,
Concentration: 0, 50, 150, 500, 1,500, 5,000 ug/plate (with and without S 9)
Metabolic activation: With **[ ]**; Without **[ ]**; With and Without **[X]**; No data **[ ]**
Results: Negative.
Cytotoxicity conc: With metabolic activation: Not observed up to 5,000 ug/plate (four strains).
Without metabolic activation: Not observed up to 5,000 ug/plate (four strains).
Precipitation conc: Not stated.
Genotoxic effects: Negative.

	+	?	-
With metabolic activation:	**[ ]**	**[ ]**	**[X]**
Without metabolic activation:	**[ ]**	**[ ]**	**[X]**

Method: Other (Referred to Remarks).

GLP: Yes **[X]** No **[ ]** ? **[ ]**
Test substance: As prescribed by 1.1 - 1.4.
Remarks: Method: According Ames et al. (1975), Mutation Research, 31 347-364, and modifications according Maron et al. (1981), Mutation Research, 88 343-350 and Maron et al. (1983), Mutation Research, 113 173-215.
Reference: Uniqema unpublished data (1988), ESL Sample No.S 16674 TO1 .

(c) Type: Bacterial reverse mutation assay
System of testing: Salmonella typhimurium strains TA98, TA100, TA1535, TA1537, TA1538.
Concentration: 0, 4, 20,100, 500, 2,500 ug/plate (with and without S 9).
Metabolic activation: With **[ ]**; Without **[ ]**; With and Without **[X]**; No data **[ ]**
Results: Negative.
Cytotoxicity conc: With metabolic activation: No data available.
Without metabolic activation: No data available.
Precipitation conc: Data not available.
Genotoxic effects: Negative.

	+	?	-
With metabolic activation:	**[ ]**	**[ ]**	**[X]**
Without metabolic activation:	**[ ]**	**[ ]**	**[X]**

Method: Ames test. Test conditions were not available.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: As prescribed by 1.1 - 1.4.
Remarks: Triacetin suspension in water was prepared with the help of Tween 80.
Reference: Wallat, S. (1982), Unpublished data Henkel KGaA. Rep. No. TBD 820113.

(d) Type: Bacterial and yeast reverse mutation assay
System of testing: Salmonella typhimurium strains TA1535, TA1537, TA1538
Saccaromyces cerevisiae strain D4
Concentration: 0, 0.000325, 0.000650, 0.001300 w/v (with and without S 9) (bacteria)
0, 1.25, 2.50, 5.00 w/v (with and without S 9) (yeast)
Metabolic activation: With **[ ]**; Without **[ ]**; With and Without **[X]**; No data **[ ]**
Results: Negative.
Cytotoxicity conc: Without metabolic activation: The 50% survival level was determined. (bacteria) 0.001300 w/v (yeast) 5.00 w/v
Precipitation conc: Not stated.
Genotoxic effects: Negative.

	+	?	-
With metabolic activation:	**[ ]**	**[ ]**	**[X]**
Without metabolic activation:	**[ ]**	**[ ]**	**[X]**

Method: Other (Referred to Remarks).
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: Triacetin (Kressco).
Remarks: LBI project No. 2468.
Reference: NTIS PB Report (1976), PB-257871.

(e) Type: Bacterial reverse mutation assay.
System of testing: Salmonella typhimurium strains TA1535.
Concentration: Data not available.
Metabolic activation: With **[ ]**; Without **[ ]**; With and Without **[X]**; No data **[ ]**
Results: Negative.
Cytotoxicity conc: With metabolic activation: No data available.
Without metabolic activation: No data available.

Precipitation conc: Data not available.
Genotoxic effects: Negative.

	+	?	-
With metabolic activation:	**[ ]**	**[ ]**	**[X]**
Without metabolic activation:	**[ ]**	**[ ]**	**[X]**

Method: Data not available.
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: As prescribed by 1.1 - 1.4.
Remarks: Not stated.
Reference: Inveresk Research International (1981), Musselburgh, EH21 7UB, Scotland, Project 705352.

B. NON-BACTERIAL IN VITRO TEST

(a) Type: In vitro Mammalian Chromosome aberration test
System of testing: Chinese hamster lung (CHL/IU) cells
Concentration: 0, 0.55, 1.1, 2.2 mg/mL
Metabolic activation: With **[ ]**; Without **[ ]**; With and Without **[X]**; No data **[ ]**
Results: Triacetin induced structural chromosome aberrations on short-term treatment with an exogenous metabolic activation system at the maximum concentration of 2.2 mg/mL (10 mM). However, triacetin decreased pH of the medium at 2.2 mg/mL on short-term treatment with an exogenous metabolic activation system. Therefore, chromosome aberrations induced with triacetin were likely to be caused by lowering pH of the medium rather than by damaging DNA per se. It is, however, recognized that changes in pH of the medium caused by triacetin can induce such artifacts in this assay. Polyploidy was not induced under any of the conditions on continuous and short-term treatment with and without an exogenous metabolic activation system.
Cytotoxicity conc: With metabolic activation: Not observed up to 1.2 mg/mL for 6-Hours exposure. The 50 % inhibition of cell proliferation was calculated to be 1.8 mg/mL.
Without metabolic activation: Not observed up to 2.2 mg/mL for 24- and 48- hours exposure.
Precipitation conc: Not observed.
Genotoxic effects: Equivocal.

	Clastogenicity			Polyploidy		
	+	?	-	+	?	-
With metabolic activation:	**[ ]**	**[ ]**	**[X]**	**[ ]**	**[ ]**	**[X]**
Without metabolic activation:	**[..]**	**[X]**	**[ ]**	**[ ]**	**[ ]**	**[X]**

Method: OECD Guidelines No.473 and Guidelines for Screening Toxicity Testing of Chemicals (Japan).

GLP: Yes **[X]** No **[ ]** ? **[ ]**
Test substance: Daihachi Chemical Industries Co. Ltd., purity: >98.2 wt %
Remarks: Lowest concentration producing cytogenetic effects in vitro was 2.2 mg/mL with metabolic activation for short-term treatment. For metabolic activation, mammalian metabolic preparations were used.
Reference: Ministry of Health & Welfare (MHW), Japan (1998), Toxicity Testing Reports of Environmental Chemicals vol.6 127-147.

5.6 GENETIC TOXICITY IN VIVO

No studies located.

5.7 CARCINOGENICITY

No studies located.

5.8 TOXICITY TO REPRODUCTION

Type:	Fertility **[ ]**; One-generation study **[ ]**; Two-generation study **[ ]**; Other **[X]**
Species/strain:	Rat / Crj: CD (SD) IGS
Sex:	Female **[ ]**; Male **[ ]**; Male/Female **[X]**; No data **[ ]**
Route of Administration:	Oral (gavage)
Exposure period:	(male) 44 days (female) from 14days before mating to day 3 of lactation (41-48days).
Post exposure observation period:	None.
Premating exposure period:	male: 14days, female: 14day
Duration of the test:	(male) 44 days (female) 41-48 days
Doses:	0, 40, 200, 1,000 mg/kg bw/day
Control group:	Yes **[X]**; No **[ ]**; No data **[ ]**; Concurrent no treatment **[ ]**; Concurrent vehicle **[X]**; Historical **[ ]**
NOAEL Parental:	1,000 mg/kg bw/day (male) 1,000 mg/kg bw/day (female)
NOAEL F1 Offspring:	1,000 mg/kg bw/day
Results:	Triacetin did not exert any toxic effects on reproductive parameters including the mating index, fertility index, gestation length, number of corpora lutea or implantations, implantation index, gestation index, delivery index and parturition or maternal behaviour at delivery and lactation. General parental toxicity: Triacetin had no effects on clinical signs, body weight, food consumption, and organ weight or necropsy findings. No histopathological changes ascribable to the compound were observed in either sex. There were no haematological or blood chemical parameters in males. The NOAEL for reproductive toxicity is thus considered to be 1,000 mg/kg bw/day for both sexes.
Method:	OECD 422, combined repeat dose and reproductive/developmental toxicity screening test..
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	Daihachi Chemical Industries Co. Ltd., purity: >98.2 wt %
Remarks:	Not stated.
Reference:	Ministry of Health & Welfare (MHW), Japan (1998), Toxicity Testing Reports of Environmental Chemicals vol.6 127-147.

5.9 DEVELOPMENTAL TOXICITY/ TERATOGENICITY

Species/strain:	Rat / Crj: CD (SD) IGS
Sex:	Female **[ ]**; Male **[ ]**; Male/Female **[X]**; No data **[ ]**
Route of Administration:	Oral (gavage)
Exposure period:	(male) 44 days

(female) from 14days before mating to day 3 of lactation(41-48days).
Frequency of treatment: One administration/day
Post exposure observation period: None.
Premating exposure period: male: 14days. , female: 14day
Duration of the test: (male) 44 days
(female) 41-48 days
Doses: 0, 40, 200, 1,000 mg/kg bw/day
Control group: Yes **[X]**; No **[ ]**; No data **[ ]**;
Concurrent no treatment **[ ]**; Concurrent vehicle **[X]**; Historical **[ ]**
NOAEL Maternal Toxicity: 1000 mg/kg bw/day
LOAEL Maternal Toxicity: Not determined under the conditions tested.
NOAEL Teratogenicity: 1000 mg/kg bw/day
Results: No teratological or other developmental effects were observed at any dose.
General parental toxicity: Triacetin had no effects on clinical signs, body weight, food consumption, and organ weight or necropsy findings. No histopathological changes ascribable to the compound were observed in either sex. There were no haematological or blood chemical parameters in males.
Pregnancy/litter data: Triacetin did not exert any toxic effects on reproductive parameters including the mating index, fertility index, gestation length, number of corpora lutea or implantations, implantation index, gestation index, delivery index and parturition or maternal behaviour at delivery and lactation
Toxicity to offspring: On examination of neonates, there were no significant differences in numbers of offspring or live offspring, the sex ratio, the live birth index, the viability index or body weight. No abnormal findings ascribable to the compound were found for external features, clinical signs or necropsy of the offspring.
The NOAEL for reproductive and developmental toxicity is considered to be 1,000 mg/kg bw/day for parental animals and offspring.
Method: OECD 422, combined repeat dose and reproductive/developmental toxicity screening test..
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Test substance: Daihachi Chemical Industries Co. Ltd., purity: >98.2 wt %
Remarks: Not stated.
Reference: Ministry of Health & Welfare (MHW), Japan (1998), Toxicity Testing Reports of Environmental Chemicals vol.6 127-147.

5.10 OTHER RELEVANT INFORMATION

A. Specific toxicities

(a) Type: Chemobiokinetics general studies.
Species/strain: Lamb / Southdown
Sex: Female **[ ]**; Male **[ ]**; Male/Female **[X]**; No data **[ ]**
Route of Administration: Oral (feed)
Exposure period: 175 days.
Number of animals: 24 Male (rams), 24 female (ewes).
Method: The feeding experiment was factorially designed with two basal diets x two additives (triacetin and glycerol) x two levels of energy input x two sexes x 3 replications. Two basal diets consisted of (a) pelleted, finely ground Cayuga alfalfa hay harvested on May 25 near Ithaca, N.Y.,

partially dried in the field and finished by heat drying without weather damage, and (b) a pelleted mixture containing 50 % of the same hay and 50 % of yellow corn meal. Triacetin, employed as a source of acetic acid, was added to the basal diets in sufficient quantity to comprise 10 % of the total dietary dry matter. An amount of glycerol equivalent to that in triglyceride, triacetin, was added to the other diets.
Urine and faeces were collected totally, but separately, from each of the 48 animals during 7-day periods of months 2, 4 and 6 of the 175-day feeding periods.
Aliquots of faeces were analysed for the proximate chemical constituents and heat of combustion, and samples of urine were analysed for nitrogen. Urinary energy was estimated from urinary nitrogen and the amount of energy represented by the methane loss was computed from the amount of digestible dry matter.

Results: Each of two basal diets (pelleted, ground hay (H), and a pelleted mixture of the same hay and corn meal (HC) was supplemented singly with triacetin (Ac^3) and glycerol (G). A given animal was fed continuously one of the four diets at one of two levels of intake (approximately, 1 or 2.2 times the maintenance level) during the 175-day feeding period. The mean rates with which the metabolizable energy (ME) ingested above the maintenance level of intake was utilized for body-energy gain, were: (in %) H + Ac^3, 59.9; HC + G, 59.5; HC + Ac^3, 63.7; and HC + G, 61.8($p > 0.3$). Ignoring the kind of basal diet, utilization rates were 62.0and 61.2 % for the ME provided by the diets containing triacetin and glycerol, respectively. The mean pooled net utilization of ME for body-energy gain by females (65.5%) was markedly greater ($P<0.01$) than that by males (57.6 %). In a series of respiration-calorimetric experiments, the net utilization of ME provided by the acetic acid moiety of triacetin was 76.4%, between days 50 and 70 of continuous feeding.

(Conclusion) In a 175 day feeding study with sheep, 62 % of metabolic energy was utilized. Concentration of triacetin in food was 10 %. No data on toxicity are reported.

Test substance: Distillation Products Industries (Rochester, N.Y.),
bp=152-154 °C /22mm,
purity: data not available.

Remark: The efficiency of utilization for growth-fattening, of the energy of diets resulting in high (5.4 : 1) and low (3.1 : 1) ratio of acetic acid to propionic acid in the ruminal ingesta was determined in intact 24 male and 24 female sheep by means of a slaughter-analysis experiment.

Reference: Bull, L.S. et al. J. Nutr. 100 (1970), 262-276.

(b) Type: Other.
Results: Triacetin added directly to human food is affirmed as generally recognized as safe (GRAS) and classified as GRAS-substance.
Remark: Not stated.
Reference: 21 CFR 184.1901 (4/1/90).

(c) Type: Other.
Results: Substances classified as plasticizers, when migrating from food packaging shall including triacetin.
Remark: Not stated.
Reference: 21 CFR 181.27 (4/1/90).

(d) Type: Other.
Results: Triacetin used as a general purpose food additive in animal drugs, feeds, and related products are generally recognized as safe when used in accordance with good manufacturing or feeding practice.
Remark: Not stated.
Reference: 21 CFR 582.1901 (4/1/90).

(e) Type: Other.
Results: Pharmacological effect: decrease in blood pressure after i.v. application in cats.
Remark: Not stated.
Reference: Oetting W.F. (1960), Archs Ind. Health 21, 28-65.

(f) Type: Other.
Results: i.v. Study in dogs, lowest lethal value 1.5-2.0 cm^3/kg bw
i.v. Study in rabbits, lowest lethal value 0.75 cm^3/kg bw,
No effect dose 0.5 cm^3/kg bw
Remark: Not stated.
Reference: Patty's Industrial Hygiene and Toxicology, 1983, Vol. 2A, 2321.

(g) Type: Other.
Results: Laboratory rats have tolerated diets consisting of 50% triacetin. If hydrolysed, systematic acidosis is a possible consequence.
Remark: Not stated.
Reference: Gosselin R.E., R.P. Smith, H.C. Hodge (1984), Clinical Toxicology of Commercial Products. 5th edition, Baltimore: Williams and Wilkins, p. II-203.

(h) Type: Other.
Results: Neurotoxic effects of triacetin include tremors and convulsions.
Remark: Not stated.
Reference: O'Donoghue, J.L. (ed) (1985), Neurotoxicity of Industrial and Commercial Chemicals. Vol. I, Boca Raton, FL, CRC Press, Inc., 136.

(i) Type Other.
Results: Minimal tissue irritation in chicken pectoral muscle.
Remark: Not stated.
Reference: Hem S.L., Bright D.R., Banker G.S., Pogue J.P. (1975), Drug Dev. Commun. Vol. I, ISS 5, 471-7.

(j) Type Other.
Results: Triacetin will produce slight haemolysis in vitro.
Remark: Not stated.
Reference: Patty's Industrial Hygiene and Toxicology (1963), Volume II: Toxicology, 2nd ed., p.1870.

B. Toxicodynamics, toxicokinetics

(a) Type: Toxicokinetics
Species/strain: Dog / (mongrel)
Sex: Female **[ ]**; Male **[ ]**; Male/Female **[ ]**; No data **[X]**
Method: Triacetin was administered intravenously to mongrel dogs (n=10) 2 weeks after surgical placement of blood-sampling catheters in the aorta and in the portal, hepatic, renal, and femoral veins. [1-^{14}C] Acetate was infused to

allow quantification of organ uptake of acetate as well as systemic turnover and oxidation. Systemic acetate turnover accounted for approximately 70 % of triacetin-derived acetate, assuming complete hydrolysis of the triglyceride.

Results: Approximately 80 % of systemic acetate uptake was rapidly oxidized. Significant acetate uptake was demonstrated in all tissues (liver, 559 ± 68; intestine, 342 ± 23; hindlimb, 89 ± 7; and kidney, 330 ± 37 umol/min). (Conclusion) During intravenous administration in dogs, the majority of infused triacetin undergoes intravascular hydrolysis, and the majority of the resulting acetate is oxidized. Thus, energy in the form of short-chain fatty acids can be delivered to a resting gut via intravenous infusion of a short-chain triglyceride.

Test substance: Data not available.

Remarks: Triacetin is a water-soluble short-chain triglyceride that may have a role as a parenteral nutrient.

Reference: Bleiberg, Batia et al., (1993), Am. J. Clin. Nutr. 58 908-911.

(b) Type: Toxicokinetics

Species/strain: Dog / (mongrel)

Sex: Female **[ ]**; Male **[ ]**; Male/Female **[ ]**; No data **[X]**

Method: Triacetin was infused at 47 umol·kg bw^{-1}·min^{-1} for 3 hr at an isocaloric rate in mongrel dogs (n=6) to test its effects on serum phosphorus, calcium, and magnesium metabolism. Arterial blood was sampled at 15-30 min intervals until the end of the study. Urine was collected during the equilibration period and again during triacetin infusion.

Results: There were no changes in serum P or Ca. The serum Mg concentration decreased from 0.7 ± 0.03 to 0.57 ± 0.03 mmol/L ($p < 0.001$) by 90 min and remained at this level for the remainder of the study.
The triacetin infusion did not influence fractional urinary Mg excretion; thus, the decrease in serum Mg was likely because of an increase in cellular transport of this cation.

(Conclusion) An isocaloric infusion of the short-chain triglyceride triacetin in dogs resulted in modest increases in plasma acetate but did not significantly affect serum Ca or P concentrations. Serum Mg decreased by approximately 20 %, probably because of cellular uptake rather than accelerated excretion.
Triacetin administered to dogs at a rate approximating resting energy expenditure
has no demonstrable adverse effects on mineral metabolism.

Test substance: Sigma (St. Louis, MO), purity: data not available.

Remarks: Triacetin is a water-soluble short-chain triglyceride that
may have a role as a parenteral nutrient.

Reference: Bailey, J.W. et al. (1989), Am. J. Clin. Nutr., 49 385-388.

(c) Type: Toxicokinetics

Species/strain: Rat / Sprague-Dawley

Sex: Female **[ ]**; Male **[X]**; Male/Female **[ ]**; No data **[ ]**

Method: Male Sprague-Dawley rats (n=22) were fed intravenously an isovolemic, isocaloric and isonitrogenous diet for 7 days. The lipid energy represented 30 % of the nonprotein energy with a short-chain triglyceride, triacetin representing 0 % (Lyposyn II; a long-chain triglyceride 20.1 g/L, Abbot Laboratories), 50 % (triacetin 15.2 g/L + Lyposyn II 10.0 g/L) or 90 % (triacetin 27.2 g/L + Lyposyn II 2.0 g/L) of the lipid energy. Plasma acetate concentration was determined as well as indicators of protein

metabolism: daily and cumulative nitrogen balance, whole body leucine kinetics and rectus muscle and liver fractional protein synthetic rates.

Results: Triacetin caused no overt toxic effects at any point during the study. As the proportion of triacetin in the diet increased from 0 to 50 or 90 % of the lipid energy, cumulative nitrogen balance increased 50 or 120 %, respectively ($p < 0.05$). Whole-body and tissue leucine kinetics (determined during the last 2.5 hr of the 7-day study) were unaffected by the lipid composition of the diet. Plasma acetate concentration was not significantly different among groups.
(Conclusion) These results indicate that incorporation of triacetin in nutritionally balanced total parenteral nutrition formulas improves nitrogen balance with no overt toxic effects.

Test substance: Data not available.

Remarks: Triacetin is a water-soluble short-chain triglyceride that may have a role as a parenteral nutrient.

Reference: Bailey, J.W. et al. (1992), J. Nutr., 122 1823-1829.

(d) Type: Toxicokinetics

Species/strain: Dog / (mongrel)

Sex: Female **[X]**; Male **[ ]**; Male/Female **[ ]**; No data **[ ]**

Method: Animals received infusions of triacetin at 1.0 x estimated resting energy expenditure (REE), hyperenergetic triacetin at 1.5 x REE, glycerol, or saline during infusion of [1-^{14}C]leucine.
(Group 1) Six dogs were infused with a 5 % (vol: vol) triacetin solution at a rate (47 umol·kg bw^{-1}·min^{-1}) providing energy (12.6 kJ·kg bw^{-1}·h^{-1}) equal to REE in dogs.
(Group 2) Seven dogs were studied under identical conditions as those outlined for group 1, except they received triacetin at a rate (70 umol·kg bw^{-1}·min^{-1}) providing energy 50 % above REE.
(Group 3) Four dogs were studied under identical conditions, except they were infused with glycerol alone at a rate of 70 umol·kg bw^{-1}·min^{-1}, which is comparable to the amount of glycerol derived from the complete hydrolysis of the triacetin infused in group 2.
(Group 4) To control for tracer recycling, five animals were infused with saline for the duration of the study. Blood and breath samples were collected at 15-30-min intervals between - 45 and 180 min.

Results: During both triacetin infusions, plasma alfa-ketoisocaproate concentrations increased ($p < 0.05$). During triacetin infusion at 1.5 REE, the plasma leucine concentration decreased ($p < 0.05$) and leucine rate of appearance decreased by approximately 19 % ($p < 0.05$); this was significantly greater than the changes that occurred during triacetin at 1.0 x REE and glycerol ($p < 0.05$).
There was no difference in leucine oxidation between the dogs given triacetin at 1.0 x REE and control groups, whereas leucine oxidation decreased by 53 % during triacetin infusion at 1.5 REE glycerol ($p < 0.05$). Nonoxidative leucine disappearance, an indicator of protein synthesis, did not change in any of the studies.

(Conclusion) These results indicate that triacetin has effects on leucine metabolism similar to those previously reported with long-chain triglyceride emulsions.

Test substance: Sigma (St. Louis, MO), purity: data not available.

Remarks: Triacetin is a water-soluble short-chain triglyceride that

may have a role as a parenteral nutrient because of lack of toxicity and favourable effects on protein metabolism.

Reference: Bailey, J.W. et al. (1993), Am. J. Clin. Nutr., 58 912-916.

(e) Type: Toxicokinetics
Species/strain: Rat / Sheffield
Sex: Female **[ ]**; Male **[X]**; Male/Female **[ ]**; No data **[ ]**
Method: The procedure used in most experiments followed closely that outlined by Parsons et al. (1958) (J. Physiol. 144 387-402). The sacs of the everted intestine, the middle fifth of the combined jejunum and ileum was used. The sacs contained initially 1 mL of bicarbonate saline and shaken for 1 hr at 37 °C. Acetins, glucose, acetate, or metabolic inhibitors were added to the saline. At the end of the incubation, fluid transfer was estimated by weighing the sac and its contents, and acetate determinations were made on samples of the mucosal and serosal fluids.

Results:
(1) When triacetin, mono- and diacetins were incubated with the sacs of rats everted intestine, they entered the epithelial cells and were completely hydrolyzed to free glycerol and acetic acid. The activity of the preparation, as measured by acetate release, increased with the number of acetic acid residues in the glyceride. There is no absolute positional specificity, and all three ester linkages can be split.
(2) The rate limiting step in the process was the entry of glyceride into the epithelial cell.
(3) The three acetins entered the epithelial cells at the same rate.
(4) The acetate released appeared in higher concentrations on the serosal sides.

Test substance: British Drug Houses, purity: data not available.
Remarks: Volatile fatty acids, which released from acetins could be transferred into the cells by the rat intestine against a concentration gradient.
Reference: Barry, R.J.C. et al. (1966), J. Physiol. 185 667-683.

(f) Type: Toxicokinetics
Species/strain: Dog / (Mongrel)
Sex: Female **[X]**; Male **[ ]**; Male/Female **[ ]**; No data **[ ]**
Method: Triacetin was infused in mongrel dogs at isocaloric (N=6) or hypercaloric (ca. 1.5 REE, N=7) rates for 3 hr. Ketone body and glucose production rates were quantified with [$^{13}C_2$]acetoacetate and [^{3}H]glucose, respectively. An additional animals (N=4) were infused with glycerol to serve as control for the hypercaloric triacetin infusion. Energy expenditure was determined in the isocaloric experiments.
Results: Plasma acetate concentrations increased from basal levels to ca. 1 and ca. 13 mmol/L in the isocaloric and hypercaloric experiments, respectively. Plasma lactate and pyruvate concentrations decreased dramatically after 30 min of both isocaloric and hypercaloric triacetin infusions. Glucose production rates did not increase in either group, but glucose clearance decreased significantly in both groups ($p < 0.05$) over the last hour of triacetin infusion. Plasma ketone body concentrations increased from 1.4 to 3.5 and 1,8 to 13.5 umol/kg bw·min, respectively, during isocaloric and hypercaloric triacetin infusions. Resting energy expenditure increased from 3.0 ± 0.3 to 4.0 ± 0.5 kcal/kg bw·hr during isocaloric and hypercaloric triacetin infusions ($p < 0.05$).
(Conclusion) No evidence of acute toxicity such as irritability, somnolence, myoclonic activity, vomiting, diarrhoea, etc. was observed

during the 3-hr infusion of triacetin at either infusion rate. These studies indicate that triacetin can be administered to dogs at high rates without overt toxicity. The decrease in glucose clearance may represent competion between carbohydrate (glucose) and lipid (acetate). Triacetin infusion resulted in significant increases in ketone body production and concentration.

Test substance: Sigma (St. Louis, MO), purity: data not available.

Remarks: Triacetin is a water-soluble short-chain triglyceride that may have a role as a parenteral nutrient.

Reference: Bailey, J.W. et al. (1991), JPEN, 15 32-36.

5.11 EXPERIENCE WITH HUMAN EXPOSURE

(a) Remark: Commercial triacetin may contain diacetin, as well as monoacetin, and when applied to human eyes causes severe burning, pain and much redness of the conjunctiva, but no injury. Diacetin causes considerably more discomfort than pure triacetin.

Reference: Grant W.M. (1986), Toxicology of the Eye, 3rd ed. Springfield, IL: Charles C. Thomas Publisher, p. 932.

(b) Remarks: Glycerol triacetate appears to be innocuous when swallowed, inhaled or in contact with the skin, but may cause slight irritation to sensitive individuals.

Reference: International Labour Office (1983), Encyclopedia of Occupational Health and Safety. Vols I & II, Geneva, Switzerland. International Labour Office, p. 973.

(c) Remarks: A case of allergic contact eczema in a 29 year-old patient in a cigarette factory is reported, which was based on sensitisation towards the triacetin used for the production of cigarette filters. The allergy was demonstrated in a patch test. In addition to triacetin, the di- and mono acetate of glycerol also produced positive tests. It seems reasonable to regard the reaction as an expression of a group sensitisation towards glycerol acetate.

Test substance: Purity: 99 %.

Reference: Unna, P.J. and Schulz, K. H. (1963), Der Hautarzt, 14 423-425.

(d) Remarks: A Duhring-chamber test was conducted on 20 healthy volunteers
The test substance was applied as 50% dilution for 24 hours.

Result: Only very mild skin reactions were observed. The substance has good skin compatibility.

Reference: Matthies, W. (1988), Henkel KGaA., unpublished data. Rep. No. 880716.

(e) Remarks: No skin reactions occurred in 33 volunteers treated with 20% triacetin in petrolatum in an attempt to induce skin sensitisation using the maximization test.

Reference: Klingman, A.M. (1966), J. Invest. Derm., 47 393 and Klingman, A.M. & Epstein W. (1975), Contact Dermatitis, 1231.

(f) Remarks: Triacetin (20 % in petrolatum) did not irritate the skin of 33 volunteers when tested in a 48-hr covered patch test.

Reference: Epstein, W.L. (1976), Report to RIFM, 27 May, unpublished data.

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Appendix : Parameters used in calculation of distribution by Mackay level III fugacity model.
(Part 1)

Physico-Chemical Properties
(water solubility : 70g/L)

Chemical		Triacetin	Method
Molecular weight		218.21	calculated
Melting point [℃]		3	unkown
Vapour pressure [Pa]		0.331	unkown
Water solubility [g/m^3]		70000	measured
log Kow		0.21	measured
Half life [h]	In air	48	estimated
	In water	168	measured
	In soil	504	estimated
	In sediment	504	estimated

Temp. [℃]	25

Emission Scenario

Scenario	emission rate [kg/h]		
case	b.air E_1	b.w. E_2	b.soil E_3
1	1000	0	0
2	0	1000	0
3	0	0	1000
4	600	300	100
5	333	333	333

Theoretical Distribution of Triacetin

Compartment	Scenario 1	Scenario 2	Scenario 3	Scenario 4	Scenario 5
	100% to air	100% to water	100% to soil	60% to air, 30% to	Equal emission
				water, 10% to soi	air:water:soil=1: 1: 1
Air	0.9%	0.0%	0.0%	0.6%	0.3%
Water	20.0%	99.7%	12.9%	31.6%	30.1%
Soil	79.1%	0.0%	87.1%	67.8%	69.5%
Sediment	0.1%	0.3%	0.0%	0.1%	0.1%

Environmental Parameter

		volume [m3]	depth [m]	area [m2]	organic carbon	lipid content [-]	density [kg/m3]	residense time [h]
Bulk Air	air	1E+13					1.2	100
	water	2E+03						
	total	1E+13	1000	1E+10				
Bulk Water	water	2E+10					1000	1000
	susp. particles	1E+06			0.0		1500	
	fish	2E+05				0.05	1000	
	total	2E+10	10	2E+09				
Bulk Soil	air	3.2E+08					1.2	
	water	4.8E+08					1000	
	solid	8E+08			0.04		2400	
	total	1.6E+09	0.2	8E+09				
Bulk Sediment	water	8E+07					1000	
	solid	2E+07			0.06		2400	50000
	total	1E+08	0.05	2E+09				

Scenario	emission rate [kg/h]			fugacity [Pa]				concentration [g/m^3]			
case	b.air E_1	b.wat. E_2	b.soil E_3	b.air f_1	b.w. f_2	b.soil f_3	b.sed. f_4	b.air C_1	b.wat. C_2	b.soilC_3	b.sed.C_4
1	1000	0	0	4.3E-06	2.0E-08	3.0E-06	1.3E-08	3.8E-07	4.3E-03	2.1E-01	2.2E-03
2	0	1000	0	1.7E-10	4.6E-08	1.2E-10	2.9E-08	1.5E-11	9.7E-03	8.6E-06	5.1E-03
3	0	0	1000	5.1E-08	1.6E-08	4.2E-06	1.0E-08	4.5E-09	3.5E-03	2.9E-01	1.8E-03
4	600	300	100	2.6E-06	2.8E-08	2.2E-06	1.8E-08	2.3E-07	5.8E-03	1.6E-01	3.0E-03
5	333	333	333	1.4E-06	2.8E-08	2.4E-06	1.8E-08	1.3E-07	5.8E-03	1.7E-01	3.0E-03

Scenario	amount [kg]				total	transformation rate by reaction [kg/h]				transformation rate by advection [kg/h]		
case	b.air m_1	b.wat. m_2	b.soil m_3	b.sed. m_4	[kg]	b.air	b.wat. R_2	b.soil R_3	b.sed. R_4	b.air A_1	b.wat. A_2	b.sed. A_4
1	3.8E+03	8.6E+04	3.4E+05	2.2E+02	4.3E+05	5.4E+01	3.5E+02	4.7E+02	3.1E-01	3.8E+01	8.6E+01	4.5E-03
2	1.5E-01	1.9E+05	1.4E+01	5.1E+02	2.0E+05	2.2E-03	8.0E+02	1.9E-02	7.0E-01	1.5E-03	1.9E+02	1.0E-02
3	4.5E+01	6.9E+04	4.7E+05	1.8E+02	5.4E+05	6.6E-01	2.9E+02	6.4E+02	2.5E-01	4.5E-01	6.9E+01	3.6E-03
4	2.3E+03	1.2E+05	2.5E+05	3.0E+02	3.7E+05	3.3E+01	4.8E+02	3.5E+02	4.2E-01	2.3E+01	1.2E+02	6.1E-03
5	1.3E+03	1.2E+05	2.7E+05	3.0E+02	3.9E+05	1.8E+01	4.8E+02	3.7E+02	4.2E-01	1.3E+01	1.2E+02	6.1E-03

Scenario	transport rate between spheres [kg/h]						
case	air→ water	water→ air	air→ soil	soil→ air	soil→ water	water→ sed.	sed.→ water
1	1.8E+02	1.8E-02	7.3E+02	8.8E+00	2.6E+02	8.6E-01	5.5E-01
2	7.5E-03	4.1E-02	3.0E-02	3.6E-04	1.0E-02	1.9E+00	1.2E+00
3	2.2E+00	1.4E-02	8.8E+00	1.2E+01	3.5E+02	6.9E-01	4.4E-01
4	1.1E+02	2.4E-02	4.4E+02	6.5E+00	1.9E+02	1.2E+00	7.4E-01
5	6.2E+01	2.4E-02	2.5E+02	7.0E+00	2.0E+02	1.2E+00	7.4E-01

Z and D values

	Z_B [mol/m^3·Pa]	D_R [mol/Pa·h]	D_A [mol/Pa·h]
Bulk Air (1)	4.0E-04	5.8E+07	4.0E+07
Bulk Water (2)	8.0E+02	6.6E+10	1.6E+10
Bulk Soil (3)	2.7E+02	5.9E+08	0.0E+00
Bulk Sediment (4	6.6E+02	9.0E+07	1.3E+06

D_{12} [mol/Pa·h]	D_{21} [mol/Pa·h]	D_{13} [mol/Pa·h]	D_{31} [mol/Pa·h]
1.6E+08	4.0E+06	6.6E+08	1.3E+07

D_{32} [mol/Pa·h]	D_{24} [mol/Pa·h]	D_{42} [mol/Pa·h]
3.2E+08	1.6E+08	1.6E+08

Appendix: Parameters used in calculation of distribution by Mackay level III fugacity model.
(Part 2)

Physico-Chemical Properties

(water solubility : 58g/L)

Chemical		Triacetin	Method
Molecular weight		218.21	calculated
Melting point [℃]		3	unkown
Vapour pressure [Pa]		0.331	unkown
Water solubility [g/m^3]		58000	measured
log Kow		0.21	measured
Half life [h]	In air	48	estimated
	In water	168	measured
	In soil	504	estimated
	In sediment	504	estimated

Temp. [℃]	25

Emission Scenario

Scenario	emission	rate [kg/h]	
case	b.air E_1	b.w. E_2	b.soil E_3
1	1000	0	0
2	0	1000	0
3	0	0	1000
4	600	300	100
5	333	333	333

Theoretical Distribution of Triacetin

Compartment	Scenario 1	Scenario 2	Scenario 3	Scenario 4	Scenario 5
	100% to air	100% to water	100% to soil	60% to air, 30% to water, 10% to soi	Equal emission air:water:soil=1: 1: 1
Air	1.1%	0.0%	0.0%	0.7%	0.4%
Water	19.9%	99.7%	12.9%	31.7%	30.2%
Soil	79.0%	0.0%	87.1%	67.5%	69.4%
Sediment	0.1%	0.3%	0.0%	0.1%	0.1%

Environmental Parameter

		volume [m^3]	depth [m]	area [m^2]	organic carbon content [-]	lipid content [-]	density [kg/m^3]	residense time [h]
Bulk Air	air	1E+13					1.2	100
	water	2E+03						
	total	1E+13	1000	1E+10				
Bulk Water	water	2E+10					1000	1000
	susp. particles	1E+06			0.0		1500	
	fish	2E+05				0.05	1000	
	total	2E+10	10	2E+09				
Bulk Soil	air	3.2E+08					1.2	
	water	4.8E+08					1000	
	solid	8E+08			0.04		2400	
	total	1.6E+09	0.2	8E+09				
Bulk Sediment	water	8E+07					1000	
	solid	2E+07			0.06		2400	50000
	total	1E+08	0.05	2E+09				

Scenario	emission rate [kg/h]			fugacity [Pa]				concentration [g/m^3]			
case	b.air E_1	b.wat. E_2	b.soil E_3	b.air f_1	b.w. f_2	b.soil f_3	b.sed. f_4	b.air C_1	b.wat. C_2	b.soilC_3	b.sed.C_4
1	1000	0	0	5.0E-06	2.4E-08	3.6E-06	1.5E-08	4.5E-07	4.2E-03	2.1E-01	2.2E-03
2	0	1000	0	2.5E-10	5.6E-08	1.8E-10	3.5E-08	2.2E-11	9.7E-03	1.0E-05	5.1E-03
3	0	0	1000	7.1E-08	2.0E-08	5.0E-06	1.3E-08	6.2E-09	3.5E-03	2.9E-01	1.8E-03
4	600	300	100	3.0E-06	3.3E-08	2.7E-06	2.1E-08	2.7E-07	5.8E-03	1.5E-01	3.0E-03
5	333	333	333	1.7E-06	3.3E-08	2.9E-06	2.1E-08	1.5E-07	5.8E-03	1.7E-01	3.0E-03

Scenario	amount [kg]				total	transformation rate by reaction [kg/h]				transformation rate by advection [kg/h]		
case	b.air m_1	b.wat. m_2	b.soil m_3	b.sed. m_4	[kg]	b.air	b.wat. R_2	b.soil R_3	b.sed. R_4	b.air A_1	b.wat. A_2	b.sed. A_4
1	4.5E+03	8.4E+04	3.3E+05	2.2E+02	4.2E+05	6.4E+01	3.5E+02	4.6E+02	3.0E-01	4.5E+01	8.4E+01	4.4E-03
2	2.2E-01	1.9E+05	1.6E+01	5.1E+02	2.0E+05	3.1E-03	8.0E+02	2.2E-02	7.0E-01	2.2E-03	1.9E+02	1.0E-02
3	6.2E+01	6.9E+04	4.7E+05	1.8E+02	5.4E+05	9.0E-01	2.9E+02	6.4E+02	2.5E-01	6.2E-01	6.9E+01	3.6E-03
4	2.7E+03	1.2E+05	2.5E+05	3.0E+02	3.7E+05	3.9E+01	4.8E+02	3.4E+02	4.2E-01	2.7E+01	1.2E+02	6.0E-03
5	1.5E+03	1.2E+05	2.7E+05	3.0E+02	3.8E+05	2.2E+01	4.8E+02	3.7E+02	4.2E-01	1.5E+01	1.2E+02	6.0E-03

Scenario	transport rate between spheres [kg/h]						
case	air→ water	water→ air	air→ soil	soil→ air	soil→ water	water→ sed.	sed.→ water
1	1.8E+02	2.1E-02	7.2E+02	1.0E+01	2.5E+02	8.4E-01	5.4E-01
2	8.9E-03	4.9E-02	3.5E-02	4.9E-04	1.2E-02	1.9E+00	1.2E+00
3	2.5E+00	1.7E-02	1.0E+01	1.4E+01	3.5E+02	6.9E-01	4.4E-01
4	1.1E+02	2.9E-02	4.3E+02	7.5E+00	1.9E+02	1.2E+00	7.4E-01
5	6.1E+01	2.9E-02	2.4E+02	8.1E+00	2.0E+02	1.2E+00	7.4E-01

Z and D Values

	Z_B [$mol/m^3 \cdot Pa$]	D_R [$mol/Pa \cdot h$]	D_A [$mol/Pa \cdot h$]
Bulk Air (1)	4.0E-04	5.8E+07	4.0E+07
Bulk Water (2)	8.0E+02	6.6E+10	1.6E+10
Bulk Soil (3)	2.7E+02	5.9E+08	0.0E+00
Bulk Sediment (4	6.6E+02	9.0E+07	1.3E+06

D_{12} [$mol/Pa \cdot h$]	D_{21} [$mol/Pa \cdot h$]	D_{13} [$mol/Pa \cdot h$]	D_{31} [$mol/Pa \cdot h$]
1.6E+08	4.0E+06	6.6E+08	1.3E+07

D_{32} [$mol/Pa \cdot h$]	D_{24} [$mol/Pa \cdot h$]	D_{42} [$mol/Pa \cdot h$]
3.2E+08	1.6E+08	1.6E+08

ROBUST STUDY SUMMARIES
Triacetin CAS No. 102–76–1

Sponsor Country: Japan

DATE: 9 August 2002

PHYSICAL/CHEMICAL ELEMENTS

MELTING POINT

TEST SUBSTANCE

- **Identity:** Triacetin (CAS No. 102-76-1)
- **Remarks:** Source: Eastman Chemical Company, Purity: 99 %, Impurity: Not stated.

METHOD

- **Method/guideline:** Not stated.
- **GLP:** Not stated.
- **Year:** Not stated.
- **Remarks:** Not stated.

RESULTS

- **Melting point value:** 3 °C (276 K).
- **Decomposition:** Not stated.
- **Sublimation:** Not stated.
- **Remarks:** The temperature of 3 °C is a true thermodynamic melting point of crystalline triacetin, whereas the temperatures of - 60 to - 78 °C, those described elsewhere are a glass transition temperature.

CONCLUSIONS

Melting point is 3 °C (276 K).

DATA QUALITY

- **Reliabilities:** Valid with restriction.
- **Remarks:** The Sigma-Aldrich Library of Regulatory and Safety Data. Data confirmed by Chemicals Evaluation and Research Institute (Kurume, Japan).

REFERENCES (Free Text)

Chemicals Evaluation and Research Institute (Kurume, Japan) (1998), Test No. 80919BK.

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

BOILING POINT

TEST SUBSTANCE

- **Identity:** Triacetin (CAS No. 102-76-1)
- **Remarks:** Source: Eastman Chemical Company, Purity: 99 %, Impurity: Not stated.

METHOD

- **Method:** Not stated.
- **GLP:** Not stated.
- **Year:** Not stated.
- **Remarks:** Not stated.

RESULTS

- **Boiling point value:** 258 °C
- **Pressure:** 1,013
- **Pressure unit:** hPa
- **Decomposition:** Not stated.
- **Remarks:** Not stated.

CONCLUSIONS

Boiling point is 258 °C at 1,013hPa.

DATA QUALITY

- **Reliabilities:** Valid with restriction.
- **Remarks:** The Sigma-Aldrich Library of Regulatory and Safety Data. Data Confirmed by Chemicals Evaluation and Research Institute (Kurume, Japan).

REFERENCES

Chemicals Evaluation and Research Institute (Kurume, Japan) (1998), Test No. 80919BK.

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

VAPOR PRESSURE

TEST SUBSTANCE

- **Identity:** Triacetin (CAS No. 102-76-1)
- **Remarks:** Source: Unavailable.

METHOD

- **Method:** Not stated.
- **GLP:** Not stated.
- **Year:** Not stated.
- **Remarks:** Not stated.

RESULTS

- **Vapor Pressure value:** 0.003306 hPa (0.00248 mmHg)
- **Temperature:** 25 °C
- **Decomposition:** Not stated.
- **Remarks:** Not stated.

CONCLUSIONS

Vapor pressure is 0.003306 hPa at 25 °C.

DATA QUALITY

- **Reliabilities:** Valid with restriction.
- **Remarks:** SRC recommended value.

REFERENCES

Design Institute for Physical Property Data (1989); American Institute of Chemical Engineers, Hemisphere Pub. New York, NY, Vol. 4.

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

PARTITION COEFFICIENT

TEST SUBSTANCE

- **Identity:** Triacetin (CAS No. 102-76-1)
- **Remarks:** Source: Tokyo Kasei, Lot No. GB 01(Class: TCI-GR), Purity: > 98 %, Impurity: Not stated. Stability during use confirmed by IR spectrometry. Kept at cold temperature until use.

METHOD

- **Method/guideline:** OECD TG 107 (Shake Flask Method).
- **GLP:** Yes.
- **Year:** 1998.
- **Remarks field for Test Conditions**
  Not stated.

RESULTS

- **Log P_{ow} :** 0.21
- **Temperature:** 25°C ±1°C
- **Remarks:** Test condition: Test was conducted in duplicate under the following three conditions. Test chemical was analyzed by HPLC.

Test condition	**Condition-1**	**Condition-2**	**Condition-3**
1-Octanol saturated with water	5 mL	10 mL	20 mL
Water saturated with 1-octanol	30 mL	25 mL	15 mL
Test chemical added to 1-octanol saturated with water			
	5.95 mg	5.95 mg	5.95 mg
Test results	**Log Pow**		
	a	**b**	**Mean ±SD**
Condition-1	0.22	0.21	
Condition-2	0.21	0.19	0.21
Condition-3	0.21	0.21	

CONCLUSIONS

Log P_{ow} is 0.21.

DATA QUALITY

- **Reliabilities:** Valid without restriction.
- **Remarks:** Well conducted study, carried out by Chemicals Evaluation and Research Institute (Kurume, Japan).

REFERENCES

Chemicals Evaluation and Research Institute (Kurume, Japan) (1998), Test No. 80919BK.

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

WATER SOLUBILITY (1)

TEST SUBSTANCE

- **Identity:** Triacetin (CAS No. 102-76-1)
- **Remarks**: Source: Tokyo Kasei, Lot No. GB 01(Class: TCI-GR), Purity: > 98 %, Impurity: Not stated. Stability during use confirmed by IR spectrometry. Kept at cold temperature until use.

METHOD

- **Method:** OECD TG 105 (flask method).
- **GLP:** No.
- **Year:** 1998.
- **Remarks:** Each test solution was shaken for 24, 48 and 72 hours at 30 °C and then allowed to stand for 24 hours at 25 °C.

RESULTS

- **Value:** 70 g/L at 25 °C±1°C
- **Description of solubility:** Soluble.
- **pH value:** No dissociation group.
- **pKa value:** There is no pertinent functional group.
- **Remarks:** Not stated.

Solubility Test results

Shaking time (hr)	Concentration (g/L)	Mean (each shaking time) (g/L)	Mean (24 –72 hr) (g/L)
24	72 68	70	70
48	73 68	70	
72	71 70	71	

CONCLUSIONS

This chemical is soluble in water.

DATA QUALITY

- **Reliabilities:** Valid without restriction.
- **Remarks:** Well conducted study except GLP, carried out by Chemicals Evaluation and Research Institute (Kurume, Japan).

REFERENCES

Chemicals Evaluation and Research Institute (Kurume, Japan), Test No. 80919BK (1998).

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

WATER SOLUBILITY (2)

TEST SUBSTANCE

- **Identity:** Triacetin (CAS No. 102-76-1)
- **Remarks**: Source: Data not available.

METHOD

- **Method:** Unknown.
- **GLP:** Unknown.
- **Year:** Unknown.
- **Remarks:** Not stated.

RESULTS

- **Value:** 58 g/L at 25 °C
- **Description of solubility:** Soluble.
- **pH value:** No dissociation group.
- **pKa value:** There is no pertinent functional group.
- **Remarks:** Not stated.

CONCLUSIONS

This chemical is soluble in water.

DATA QUALITY

- **Reliabilities:** Valid with restriction.
  Remarks: This value is quoted elsewhere to calculate a vapour pressure, a Henry's constant and BCF (Lyman, W.J. et al. (1990), Handbook of Chemical Property Estimation).

REFERENCES

Riddick J.A. et al. (1986), Techniques of Chemistry, 4th ed.

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

ENVIRONMENTAL FATE AND PATHWAYS ELEMENTS

STABILITY IN WATER

TEST SUBSTANCE

- **Identity:** Triacetin (CAS No. 102-76-1)
- **Remarks:** Source: Tokyo Kasei, Lot No. GB 01(Class: TCI-GR), Purity: > 98 %, Impurity: Not stated. Stability during use confirmed by IR spectrometry. Kept at cold temperature until use.

METHOD

- **Method/guideline:** OECD TG111
- **Type :** Hydrolysis as a function of pH
- **GLP:** Yes
- **Year:** 1998
- **Remarks:** No hydrolysis of test chemical was observed at pH 4 at 50°C ± 1°C for 5 days. Hydrolysis rates at pH 7 (50, 60, 70°C ± 1°C) and at pH 9 (30, 40 °C± 1°C) were determined, respectively. They were extrapolated to 25 °C using Arrhenius relationship. Half-life at 25 °C was calculated from the rate constant.

RESULTS

- **Nominal:** ca. 1,020 mg/L
- **Measured value:**

pH	Rate constant (hr^{-1})	Half-life
pH 7	4.72×10^{-4}	60.4 (day)
pH 9	4.21×10^{-2}	16.5 (hour)

- **Degradation:** No hydrolysis occurred in 5 days at 50 °C at pH 4. At pH 7 and 9, test chemical was hydrolysed at all temperatures studied.
- **Half-life ($t_{(1/2)}$):** At pH 7 and 9, the rate constants were calculated as 4.72×10^{-4} and 4.21×10^{-2}, respectively. By extrapolating against temperature, the half-lives at 25 °C were calculated to be 60.4 days and 16.5 hours, respectively.
- **Breakdown products:** Not stated.
- **Remarks:** Not stated.

CONCLUSIONS

This chemical is stable to chemical hydrolysis in aqueous water at pH 4 under the condition studied, although it is hydrolysed at pH 7 and 9 at 25 °C with half-life of 60.4 days and 16.5 hours, respectively.

DATA QUALITY

- **Reliabilities:** Valid without restriction.
- **Remarks:** Well conducted study, carried out by Chemicals Evaluation and Research Institute (Kurume, Japan).

REFERENCES

Chemicals Evaluation and Research Institute (Kurume, Japan) (1998), Test No. 80919BK.

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS (FUGACITY)

TEST SUBSTANCE

- **Identity:** Triacetin (CAS No. 102-76-1)
- **Remarks:** Source: Not applicable.

METHOD

- **Test :** Calculation
- **Method :** Mackay Level III Fugacity Model.
- **Year :** 2002
- **Remarks :** The parameters used are shown in Appendix.

RESULTS

- **Media :**
- **Estimated Distribution under three emission scenarios :**

Predicted distribution of triacetin using Fugacity level III under four emission scenarios

(1) Results from water solubility of 70 g/L

Compartment	Release 100 % to air	Release 100 % to water	Release 100 % to soil	Equal emission scenario (1:1:1)
Air	0.9 %	0.0 %	0.0 %	0.3 %
Water	20.0 %	99.7 %	12.9 %	30.1 %
Soil	79.1 %	0.0 %	87.1 %	69.5 %
Sediment	0.1 %	0.3 %	0.0 %	0.1 %

(2) Results from water solubility of 58 g/L

Compartment	Release 100 % to air	Release 100 % to water	Release 100 % to soil	Equal emission scenario (1:1:1)
Air	1.1 %	0.0 %	0.0 %	0.4 %
Water	19.9 %	99.7 %	12.9 %	30.2 %
Soil	79.0 %	0.0 %	87.1 %	69.4 %
Sediment	0.1 %	0.3 %	0.0 %	0.1 %

- **Remarks:** Hydrolysis may be a major degradation process for triacetin in alkaline waters and in moist alkaline soils. Triacetin is readily biodegradable and biodegraded to glycerol and acetic acid, which, in turn, is degraded to carbon dioxide. Based on a vapour pressure of 0.003306 hPa at 25 °C, triacetin is expected to exist almost entirely in the vapour-phase in the ambient atmosphere. Triacetin leach readily in soil based on an estimated K_{OC} value of 10.5.

CONCLUSIONS

The calculation revealed that in the case of 100 % release to water, more than 99 % of triacetin is expected to stay in water due to its high solubility and a low vapour pressure, but if it is released into air and/or soil, it is likely to be distributed in other compartments. The results also show that approximately one third of triacetin will be distributed in water, whereas two third will stay in soil when applied to the equal emission scenario to water, soil and sediment (1:1:1). In addition, the fugacity model using 70 g/L reveals that there is little change in the distribution of triacetin between three compartments when compared to those obtained from 58 g/L.

DATA QUALITY

- **Reliabilities:** Valid without restriction.
- **Remarks:** Not stated.

REFERENCES

Daicel Chemical Industries Ltd. (2002), unpublished report.

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

BIODEGRADATION

TEST SUBSTANCE

- **Identity:** Triacetin (CAS No. 102-76-1)
- **Remarks:** Source: Tokyo Kasei, Lot No. GB 01(Class: TCI-GR), Purity: > 98 %, Impurity: Not stated. Stability during use confirmed by IR spectrometry. Kept at cold temperature until use.

METHOD

- **Method/guideline:** OECD TG 301C, Modified MITI Test (I)
- **Test Type:** Aerobic
- **GLP:** Yes
- **Year:** 1998
- **Contact time:** 14 days
- **Inoculum:** Sludge samples were collected from the 10 sites such as sewage treatment works, industrial wastewater treatment works, rivers, lakes, and sea throughout Japan and mixed thoroughly. A filtrate (500 mL) of the supernatant of the mixed sludge was then mixed with 5 L of the filtered supernatant of an activated sludge in the present use.

  After the combined sludge solution (pH adjusted at 7.0 ± 1.0) was aerated for 30 min., the supernatant corresponding 1/3 of the whole volume was discarded. An equal volume of pure water was then added to the remaining portion and the supernatant (final concentration: 0.1%) of the resulting sludge solution was mixed with sterile mineral medium and continuously aerated at 25 ± 2°C to allow minimization of residual dissolved organic carbon according to the procedure outlined in the TG.

  The test was conducted in triplicate with triacetin in sterile mineral medium at 100 mg/mL and with a small volume of the activated sludge to give a final MLSS concentration of 30 mg/L in 300 mL.

- **Remarks:** A blank control (sterile mineral medium only), positive control (aniline as reference compound at 100 mg/L) and triacetin control (triacetin in pure water at 100 mg/L) in 300 mL were incubated simultaneously.

  Oxygen consumption resulting from biodegradation of the compounds was measured over 14-day test period using an Okura Electric Closed System Oxygen Consumption measuring apparatus (Coulometer). Removal of dissolved organic carbon (DOC) was determined at the termination of the test (14 days). Percentage biodegradation was calculated based on BOD, TOC and GC analysis.

  The test solutions were maintained in a darkened room at a temperature of 25 ±1°C and continuously stirred by magnetic stir bars over the 14-day test period.
  Percent degradation (%) was obtained from the following equations.

  (BOD)
  Degradation (%) = (BOD - B)/ThOD * 100
  BOD (mg): BOD in Sludge + Triacetin system

B (mg): BOD in Sludge blank
ThOD: theoretical oxygen demand required when triacetin was completely oxidized.

(TOC)
Degradation (%) = (DOC_W - DOC_S)/DOC_W * 100
DOC_W (mgC): Residual DOC in Water + Triacetin system
DOC_S (mgC): Residual DOC in Sludge + Triacetin system

(GC)
Degradation (%) = (S_W - S_S)/S_W * 100
S_W (mg): Residual amount of triacetin detected by GC in Water + Triacetin system
S_S (mg): Residual amount of triacetin detected by GC in Sludge + Triacetin system

RESULTS

- **Degradation:**

Removal of DOC and Mineralization to CO_2 in Biodegradation Test Reactions after 14 Days

		(Water + Triacetin)	(Sludge + Triacetin)				Theoretical amount
		n=1	n=1	n=2	n-3	Mean	
BOD*	(mg)	1.40	34.2	31.5	30.6	32.1	41.8
Residual DOC	(mgC)	14.8	1.10	0.90	0.80	0.93	14.9
	(%)	99.0	7.00	6.00	6.00	6.33	-
Residual Triacetin	(mg)	29.7	0.00	0.00	0.00	0.00	30.1
(by GC)	(%)	99.0	0.00	0.00	0.00	0.00	-

***: Results are corrected for corresponding blank values.**

Test and Reference Material Biodegradation after 7 and 14-day test period

	Percent degradation of Triacetin (%) (after 14 days)			
	n=1	n=2	n-3	Mean
BOD	82	75	73	77
TOC	93	94	94	94
GC	100	100	100	100

	Percent degradation of aniline (%)	
	After 7 days	After 14 days
BOD	45	72

- **Results:** Readily biodegradable.
- **Kinetic:** Not stated.
- **Breakdown products:** Not stated.
- **Remarks:** Not stated.

CONCLUSIONS

This chemical is readily biodegradable.

DATA QUALITY

- **Reliabilities:** Valid without restriction.
- **Remarks:** Well conducted study, carried out by Chemicals Evaluation and Research Institute (Kurume, Japan).

REFERENCES

- Chemicals Evaluation and Research Institute (Kurume, Japan) (1998), Test No. 20919B

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

ECOTOXICITY ELEMENTS

ACUTE TOXICITY TO FISH (1)

TEST SUBSTANCE

- **Identity:** Triacetin (CAS No. 102-76-1)
- **Remarks**: Source: Wako Pure Chemical Industries, Lot No. TPH 6237, Purity ≥ 98.0 %. Stability during use confirmed by NMR, IR and gas chromatography. Kept at room temperature in a dark place until use.

METHOD

- **Method/guideline followed:** OECD TG 203
- **Type:** Semi-static.
- **GLP :** Yes.
- **Year :** 1998.
- **Species/Strain/Supplier:** *Oryzias latipes* (Medaka): Obtained from commercial domestic hatcheries.
- **Analytical monitoring** Yes. Test solutions were measured using by gas chromatography before and after the first 24-hour exchange of solutions.
- **Exposure period (h):** 96 h.
- **Statistical methods:** Not applicable because a limit test was conducted.
- **Remarks field for Test Conditions:**

  – ***Test fish:***

  · Acclimated for more than 12 days before testing; any groups showing no mortality for 7 days before test started. Fish with 19.8 mm (18.8 - 21.3 mm) in length were selected at random (n=10). Average body weight of fish was 0.1134 g (n=10).

  – ***Test conditions:***

  · Details of test: Semi-static (water exchanged every 24 hours)
  · Dilution water source: Tap water after dechlorinated by passing through activated carbon filter.
  · Dilution water chemistry: Hardness: 25 mg/L as $CaCO_3$; pH: 6.7
  · Stock and test solution and how they are prepared: Pipette or pour the appropriate amount of the solution (0.3 wt% of test chemical) into the test waters.
  · Concentrations dosing rate, flow-through rate, in what medium: Concentrations of 0 and 100 mg/L were tested because no fatality was observed in the preliminary run at 100 mg/L.
  · Vehicle/solvent and concentrations: Not used.
  · Stability of the test chemical solutions: Stable and transparent, no precipitate and colour formed during 96-hour exposure period.
  · Exposure vessel type: 3 L glass beaker.
  · Number of replicates, fish per replicate: 1, 10 individuals/replicate.
  · Water chemistry in test (O_2, pH) in the control and one concentration where effects were observed: Dissolved oxygen readings and pH values were taken daily during 96-hour exposure period.
  · Dissolved oxygen concentration: 5.7 - 9.8 mg/L.
  · pH values: 6.5 - 6.9.

– ***Test temperature range:***
  · Water temperature at 23.5 - 23.8 °C during 96-hour exposure period.
– ***Method of calculating mean measured concentrations:***
  · Geometric mean.

RESULTS

- **Nominal concentrations :**
  0, 100 (mg/L)
- **Measured concentrations :**

Nominal concentration (mg/L)	Measured concentration (mg/L)			Percent of nominal	
	0 hour	24 hour	Geometric mean	0 hour	24 hour
Control (0)	< 1.0	< 1.0	---	---	---
100	88.0	94.0	91.0	88.0	94.0

- **Unit :** mg/L.
- **Element value:**
  Cumulative numbers of died or stressed fish.
- **Statistical results as appropriate:** Not applied.
- **Remarks field for Results:**

– ***Biological observations:*** See below.
– ***Table showing cumulative mortality:***

Percent mortality of Oryzias latipes exposed to the test chemical

Nominal concentration (mg/L)	Cumulative number of died fish (% mortality)			
	24 hour	48 hour	72 hour	96 hour
Control (0)	0 (0)	0 (0)	0 (0)	0 (0)
100	0 (0)	0 (0)	0 (0)	0 (0)

– ***Lowest test substance concentration causing 100% mortality:***
  Not obtained under the test conditions studied.
– ***Mortality of controls:*** No mortality observed during the test period.
– ***Abnormal responses:*** No symptom observed during the test period.
– ***Reference substances (if used) – results:***
  Copper (II) sulfate pentahydrate. 96 h LC_{50} was 0.43 mg/L.
– ***Any observations, such as precipitation that might cause a difference between measured and nominal values:*** No precipitates and colour formation by the test chemical.

CONCLUSIONS

LC_{50} for medaka was determined to be > 100.0 mg/L for 96 hours based on nominal concentrations.

Remarks field with the ability to identify source of comment, i.e. author and/or submitter:

DATA QUALITY

- **Reliabilities:** Valid without restriction.
- **Remarks field for Data Reliability:**
  Experimental design and analytical procedure were well documented.

REFERENCES

Environment Agency (EA) of Japan (1998).

OTHER

- **Last changed :**
- **Order number for sorting :**
- **Remarks field for General Remarks :**

ACUTE TOXICITY TO FISH (2)

TEST SUBSTANCE

- **Identity:** Triacetin (CAS No. 102-76-1)
- **Remarks**: Source: Eastman^{R} Triacetin, Sample Reference Identification No.: 43045932,
  Purity ≥ 99.5 %. Stability during use confirmed by GC/FID and mass spectrometry.

METHOD

- **Method/guideline followed:** OECD TG 203 and EEC/Annex V C.1.
- **Type:** Static.
- **GLP :** Yes.
- **Year :** 1995.
- **Species/Strain/Supplier:** *Pimephales promelas* (Fathead minnow, fresh water): Supplied by The Eco-Chem Testing Group, Kodak Park, Rochester, NY (USA).
- **Analytical monitoring** Yes. Measured by gas chromatography (at preparation and after 24 or 96 hours exposure period). Aliquots of the exposure solutions containing 95.0 and 171.5 mg/L (nominally) were analysed at times 0 and 96 hours. Aliquots of the exposure solutions containing 308.5, 555.5 and 1,000 mg/L (nominally) were analysed at times 0 and 24 hours.
- **Exposure period (h):** 96 h.
- **Statistical methods:** A program developed by Stephan (Aquatic Toxicology and Hazard Evaluation, Spec. Tech. Publ.No. 634, American Society for Testing and Materials, Philadelphia, PA, pp.65-84, 1977) and ASTM (Proposed New Standard Practice for Using Probit Analysis, ASTME-47.07, Draft #4, 1988).
- **Remarks field for Test Conditions:**

  – ***Test fish:***

  · Acclimated to the diluent water prior to the test for at least two weeks. Fish with 19.8 mm (18.8 ~ 21.3 mm) in length were selected at random (n=10). Average body weight of fish for set #1 and set #2 at the start of the test was 0.06 and 0.07 g (n=10/set), respectively. Mean body length of fish at the end of the test was 1.61 and 1.57 cm (n=10/set), respectively.

  – ***Test conditions:***

  · Details of test: Static.
  · Dilution water source: The water from Lake Ontario was passed through an activated carbon filter and a set of 3-micron polypropylene filter. The filtered water next received 150 ppb of $Na_2S_2O_3$ to reduce trace level of residual chlorine.
  · Dilution water chemistry: Hardness and total alkalinity: 120 mg/L and 95 mg/L (as $CaCO_3$). pH = 7.4-8.3. DO: 7.1-9.0 mg/L.
  · Lighting: 16 h: 8 h light-darkness cycle.
  · Feeding: Biological loading within test vessels was kept below 1.0 g wet weight/L of test solution.
  · Stock and test solution and how they are prepared:
  The exposure solutions were prepared by direct addition of the appropriate amounts of the triacetin to tanks of water (20 L).

- Concentrations (nominally): 95.0, 171.5, 308.5, 555.5, 1,000.0 mg/L.
- Vehicle/solvent and concentrations: No vehicle used.
- Stability of the test chemical solutions: During the test, 77 - 98.1 % of the initial analysed concentrations was maintained throughout the test.
- Exposure vessel type: Glass 30.5-cm cuboidal jar, each containing 20 L of exposure solution.
- Number of replicates, fish per replicate: 2, 10 individuals/replicate.

– ***Test temperature range:***
- Water temperature at 20 ± 2 °C during 96-hour exposure period.

– ***Method of calculating mean measured concentrations:***
- Geometric Mean.

RESULTS

- **Nominal concentrations :**
0, 95.0, 171.5, 308.5, 555.5, 1,000.0 (mg/L).
- **Measured concentrations :**

Measured concentration of triacetin during 96-hour exposure of *Pimephales promelas* under static test conditions

Nominal concentration (mg/L)	Concentration determination	Mean conc. (mg/L)	% of Nominal (Series A)	Mean conc. (mg/L)	% of Nominal (Series B)
95.0	**(0, 96-hour)**	78.6	82.7	75.9	80.0
171.5	**(0, 96-hour)**	141.7	82.6	151.4	88.3
308.5	**(0, 24-hour)**	294.2	95.4	302.9	98.2
555.5	**(0, 24-hour)**	547.0	98.5	543.7	97.9
1,000.0	**(0, 24-hour)**	997.2	99.7	1057.5	105.8

- **LC_{50} and LC_0:**

Calculated LC_{50} and LC_0 for *Pimephales promelas* exposed to triacetin under static test conditions

Series	LC_{50} (mg/L)				LC_0 (mg/L)			
	24-hour	48-hour	72-hour	96-hour	24-hour	48-hour	72-hour	96-hour
A	220.5	220.5	178.3	178.3	141.7	141.7	78.6	78.6
B	188.3	188.3	177.4	165.3	75.9	75.9	75.9	75.9
Final value				165.3				75.9

- **Unit :** mg/L.
- **Element value:**
Cumulative numbers of died or signs of stressed fish.
- **Statistical results as appropriate:** Nonlinear interpolation were used to calculate the 24-, 48-, 72- and 96-hour LC_{50} values for replicates A and B at a confidence level of 95 %.
- **Remarks field for Results:**

– ***Biological observations:*** Not described.
– ***Table showing cumulative mortality:*** Data not available.
– ***Lowest test substance concentration causing 100% mortality:***
Not applicable.
– ***Mortality of controls:*** The control mortality was not greater than 10 % when adverse effects

were noted. The minnows in the diluent water control exhibited normal behaviour and appearance throughout the test.

- ***Abnormal responses:*** No descriptions.
- ***Reference substances (if used) – results:***
  No descriptions.
- ***Any observations, such as precipitation that might cause a difference between measured and nominal values:*** Throughout the test, there were no particulates, surface slicks, or precipitates observed within the exposure solutions containing the test article.

CONCLUSIONS

LC_{50} (96-hour) =165.3 mg/L

LC_0 (96-hour) = 75.9 mg/L

Remarks field with the ability to identify source of comment, i.e. author and/or submitter:

DATA QUALITY

- **Reliabilities:** Valid without restriction.
- **Remarks field for Data Reliability:**
  Experimental design and analytical procedure were well documented.

REFERENCES

Lawrence, D.L. and Hirsch, M.P. (1995), Eastman Kodak Company, Environmental Sciences Section, Corporate Health and Environment Laboratories, An acute aquatic effects test with the fathead minnow, Study No.: EN-430-900256-1,Unpublished data.

OTHER

- **Last changed :**
- **Order number for sorting :**
- **Remarks field for General Remarks :**

PROLONGED TOXICITY TO FISH

TEST SUBSTANCE

- **Identity:** Triacetin (CAS No. 102-76-1)
- **Remarks**: Source: Wako Pure Chemical Industries, Lot No. TPH 6237, Purity ≥ 98.0 %. Stability during use confirmed by NMR, IR and gas chromatography. Kept at room temperature in a dark place until use.

METHOD

- **Method/guideline followed :** OECD TG 204
- **Type :** Flow-through.
- **GLP:** Yes.
- **Year :** 1998.
- **Species/Strain/Supplier:** *Oryzias latipes* (Medaka): Obtained from commercial domestic hatcheries.
- **Analytical monitoring:** Yes. Test solutions were measured by gas chromatography before and after 7 and 14days exposure period.
- **Exposure period :** 14 day.
- **Statistical methods:** Binomial method (TOXDAT MULTI-METHOD PROGRAM, USEPA) was not applied because of no mortality observed at all doses tested**.** Dunnet method was used for fish body weight difference.

- **Remarks field for Test Conditions:**

  – ***Test fish:***

  Acclimated for more than 12 days before testing; any groups showing no mortality for 7 days before test started. Fish with 22.8 mm (21.2 - 24.7 mm) (n=10) in length were selected at random. Average body weight of fish was 0.1638 g (0.1227 - 0.2446 g, n=10). Fish were starved for 24 hours before the test started.

  – ***Test conditions:***

  · Details of test: Flow-through.
  · Dilution water source: Tap water after dechlorinated by passing through an activated carbon filter.
  · Dilution water chemistry: Hardness: 25 mg/L as $CaCO_3$; pH: 6.7.
  · Stock and test solution and how they are prepared: The working solution (0.2 wt % of the test chemical) was prepared by diluting the stock solution (4.0 wt % of the test chemical) with the dilution water. The test solution was supplied continuously by mixing the working solution and the dilution water with the help of a mechanically operated quantitative water-pump.
  · Concentrations dosing rate, flow-through rate, in what medium: Nominal concentrations of 0, 30.9, 55.6 and 100 mg/L were tested.
  · Vehicle/solvent and concentrations: Not used.
  · Stability of the test chemical solutions: Stable, no precipitate and colour formed during the exposure period.
  · Exposure vessel type: 3L glass beaker.
  · Number of replicates, fish per replicate: 10 and one replicate was done.
  · Water chemistry in test (O_2, pH) in the control and one concentration where effects were observed: Dissolved oxygen readings and pH values

were taken every 2 - 3 days during the exposure period.
- Dissolved oxygen concentration: 5.9 - 7.8 mg/L.
- pH values: 6.6 - 6.8.
- Lighting: 16 h: 8 h light-darkness cycle.

– ***Test temperature range:***
- Water temperature ranged 23.6 - 24.5°C.

– ***Method of calculating mean measured concentrations:***
- Time-weighted mean.

RESULTS

- **Nominal concentrations :** 0, 30.9, 55.6, 100 (mg/L)

- **Measured concentrations :**

Measured concentration of the test chemical during a 14-day exposure of Medaka (Oryzias latipes) under flow-through test conditions

Nominal concentration (mg/L)	Measured concentration (mg/L)			(percent of nominal)
	0 day	7 day	14 day	Mean
Control (0)	< 1.0	< 1.0	< 1.0	-
30.9	25.8 (83.5)	26.3 (85.1)	31.1 (100.6)	27.7 (89.8)
55.6	49.7 (89.4)	49.2 (88.5)	56.0 (100.7)	51.6 (92.9)
100	90.2 (90.2)	99.2 (99.2)	101.5 (101.5)	97.0 (97.0)

- **Unit :** mg/L
- **Element value:**

LC_{50} (7 days) > 100.0 mg/L (nominal concentration)
LC_{50} (14 days) > 100.0 mg/L (nominal concentration)
LC_0 (14 days) = 100.0 mg/L (nominal concentration)

- **Statistical results as appropriate:**
The mean body weight of fish exposed to the concentrations at 30.9, 55.6 and 100.0 mg/mL (nominal concentration) of the test chemical was not significantly different from the control after 14-day exposure period (alfa=0.05, Dunnet).

– **Calculated LC_{50} values for fish exposed to the test chemical based on nominal concentration under flow-through test conditions:**

Exposure period (day)	LC_{50} (mg/L)	95 % Confidence limits	Statistical method
7	> 100.0	-	Not applied
14	> 100.0	-	Not applied

- **Remarks field for Results.:**

– **Biological observations*:* Not described.**
B. Cumulative mortality:

Percent mortality of Oryzias latipes exposed to the test chemical under flow-through test conditions

Nominal conc. (mg/L)	Cumulative number of died fish (% mortality)													
0	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14 (days)**
Control (0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
30.9	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
55.6	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
100.0	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)

* Threshold level of lethal effect: > 100.0 mg/L

– **Fish weight:**

Nominal conc. (mg/L)	Fish weight (g)										
	No.1	**No.2**	**No. 3**	**No.4**	**No.5**	**No.6**	**No.7**	**No.8**	**No.9**	**No.10**	**Average**
Control	0.1502	0.1302	0.2040	0.2224	0.1895	0.1686	0.2303	0.1789	0.0983	0.1233	0.1696
30.9	0.1220	0.1993	0.2370	0.1815	0.1073	0.0900	0.1572	0.1697	0.1364	0.1331	0.1534
55.6	0.2354	0.1440	0.1227	0.2291	0.1602	0.1892	0.2506	0.1768	0.1350	0.1733	0.1821
100.0	0.1792	0.1463	0.1375	0.1499	0.1176	0.1311	0.1983	0.1626	0.1860	0.1091	0.1518

No significant differences were observed among control and each exposure levels.

– ***Lowest test substance concentration causing 100% mortality:*** Not determined.
– ***Mortality of the control:*** No mortality was observed during the test period (14 days).
– ***Food intake:*** Fish were fed with TetraMin® fish food (2 % of fish body weight/day). No reduction of food intake was observed at all doses tested during 14-day exposure period.
– ***Abnormal responses:*** No abnormal behaviour was observed at all doses tested during 14-day exposure period.
– ***Reference substances (if used) – results:*** Copper (II) sulfate pentahydrate. LC_{50} at 96h was 0.43 mg/L.
– ***Any observations, such as precipitation that might cause a difference between measured and nominal values:*** No precipitates and colour formation by the test chemical.

CONCLUSIONS

LC_{50} (14 days) was determined to be >100.0 mg/L based on nominal concentrations. No fish showed abnormal swimming behaviour.

Remarks field with the ability to identify source of comment, i.e. author and/or submitter:

DATA QUALITY

- **Reliabilities:** Valid without restriction.
- **Remarks field for Data Reliability:** Experimental design and analytical procedure were well documented.

REFERENCES

Environment Agency (EA) of Japan (1998).

OTHER

- **Last changed :**
- **Order number for sorting :**
- **Remarks field for General Remarks :**

TOXICITY TO AQUATIC PLANTS (E.G., ALGAE)

TEST SUBSTANCE

- **Identity:** Triacetin (CAS No. 102-76-1)
- **Remarks:** Source: Wako Pure Chemical Industries, Lot No. TPH 6237, Purity ≥ 98.0 %. Stability during use confirmed by NMR, IR and gas chromatography. Kept at room temperature in a dark place until use.

METHOD

- **Method/guideline followed :** OECD TG 201
- **Test type :** Static.
- **GLP :** Yes
- **Year :** 1998
- **Species/strain # and source:** *Selenastrum capricornutum* ATCC22662 (purchased from ATCC)
- **Element basis:** Growth rate and area under the growth curve.
- **Exposure period:** 72 h.
- **Analytical monitoring:** Yes, measured by gas chromatography at 0 h and 72h.
- **Statistical methods:** Logit analysis for EC_{50} and an ANOVA for NOEC (Bartlett test for homogeneity in variances and One-way Anova (p=0.05), For each analysis, software of EcoTox-Statistics Ver.1.0 beta R1.4 was used.

Remarks field for Test Conditions :

– ***Test organisms:***

· The alga culture was obtained by incubating for 3 days before the exposure to triacetin under the same condition for the main test. The microscopic observation confirmed that there were no deformed or abnormal cells in the culture.
· Laboratory culture: OECD medium
· Method of cultivation: Shaking at 100 rpm
· Control: OECD medium. EC_{50} of potassium dichromate was 0.41 mg/L.

– ***Test Conditions:***

· Test temperature range: 23 ± 2 °C (22.0 - 22.2 °C)
· Growth/test medium: OECD medium.
· Shaking: 100 rpm
· Dilution water source: OECD medium.
· Exposure vessel type: A 300 mL Erlenmeyer flask with a silicon cap, which allows ventilation.
· Medium volume: 100 mL (OECD medium).
· Water chemistry in test (pH) in at least one replicate of each concentration (at start and end of the test): pH=7.5 - 7.6 at start and 5.3 - 8.5 at end of the test (72 h).
· Stock solutions preparation : Test chemical was diluted to 0.2 wt.% (2,000 mg/L) with OECD medium and sterilised with filter before use. Stock solution was not preserved.
· Light levels and quality during exposure: 4,000 - 5,000 lux, continuous illumination.

– ***Test design:***

· Number of replicates: Triplicate

· Concentrations: 0,95, 171, 309, 556 and 1,000 mg/L
· Initial cell number in cells/mL: $1x10^4$

– ***Method of calculating mean measured concentrations:***
· Geometric mean.

RESULTS

- **Nominal concentrations :** 0, 95, 171, 309, 556 and 1,000 (mg/L)

- **Measured concentrations :**

Nominal Concentration (mg/L)	**Measured Concentration (mg/L)**			
	0 hr (at start of the test)	**% of Nominal**	**72 hr (at end of the test)**	**% of Nominal**
Control	< 1.0	-	< 1.0	-
95	95.0	100.3	56.0	58.9
171	163	95.2	110	64.6
309	313	101.3	216	69.8
556	535	96.1	401	72.1
1,000	997	99.7	883	88.3

- **Unit :** Cell density (cells/mL)

- **Results:** (calculated based on nominal concentrations)

(1) Growth inhibition (comparison of the area under growth curve)
EC_{50} (0-72 h) > 1,000 mg/L
NOEC (0-72 h) = 556 mg/L

(2) Growth inhibition (comparison of the growth rates)
EC_{50} (0-72 h) > 1,000 mg/L
NOEC (24-48 h) = 1,000 mg/L
NOEC (24-72 h) = 556 mg/L

Cell density of *Selenastrum capricornutum* at each concentration at different measuring points

Nominal Concentration (mg/L)	**Cell Density ($x10^4$ cells/mL)**				**pH**	
	0 hr	**24 hr**	**48 hr**	**72 hr**	**0 hr**	**24 hr**
Control	1.0 ± 0.00	7.4 ± 0.55	35.6 ± 11.15	207.0 ± 40.96	7.5	8.5
95	1.0 ± 0.00	6.0 ± 0.54	35.9 ± 9.01	220.4 ± 61.00	7.6	7.4
171	1.0 ± 0.00	6.9 ± 0.63	41.4± 4.01	223.7 ± 16.07	7.6	6.8
309	1.0 ± 0.00	5.7 ± 0.97	32.4± 5.80	183.3 ± 28.35	7.6	5.9
556	1.0 ± 0.00	6.5 ±0.23	35.5 ± 11.43	170.4 ± 30.32	7.5	5.3
1,000	1.0 ± 0.00	6.6 ± 0.63	34.7± 6.28	80.0± 18.44	7.5	5.3

(Each value represents the mean of three sample counts ± SD.)

Growth Inhibition of *Selenastrum capricornutum* at each concentration at different intervals

Nominal Concentration (mg/L)	**Area $x10^4$ A(0-72h)**	**Inhibition (%) I_A(0-72h)**	**Rate u(24-48h)**	**Inhibition (%) I_m(24-48h)**	**Rate u (24-72h)**	**Inhibition (%) I_m (24-72h)**
Control	3455	-	0.0642	-	0.0691	-
95	3594	-4.02	0.0735	-14.58	0.0741	-7.17
171	3783	-9.48	0.0748	-16.49	0.0726	-4.96
309	3056	11.57	0.0720	-12.14	0.0722	-4.37
556	2992	13.41	0.0694	-8.21	0.0679	1.76
1,000	1893	45.21	0.0686	-6.88	0.0515	25.52

(Each value represents the mean of three values.)

A: Area under the growth curve
I_A = (Ac – At)/Ac
Ac: Area under the growth curve of control
At: Area under the growth curve at each concentration

u: Growth rate
$I_m = (u_c-u_t)/u_c$
u_c: Average growth rate of control
u_t: Average growth rate at each concentration

- **Was control response satisfactory:**
  Yes: Mean cell density increased to $2.07x10^6$ cells/mL (207-fold increase) after 72 hr (cell density at start = $1.00x10^4$ cells/mL).

- **Statistical results as appropriate:**
  Significant differences in the growth curves were not observed at nominal concentration of 95, 171, 309, and 556 mg/L when compared to that of the control. At such concentrations, 170 - 224 fold increase of cell density was observed.

Remarks field for Results:

– ***Biological observations:***
  · Growth curves: Logarithmic growth until end of the test (72 h).
  · Observations: All test groups (95-556 mg/L) except that of 1,000 mg/L showed normal and similar growth (170.4 - 223.7-fold increase during 72 hr) to that of control (207-fold increase during 72 hr). The 1000 mg/L-group showed only 80-fold increase (38.6 % of the control) after 72 hr, when compared to that of control.

CONCLUSIONS

All the test groups (95, 171, 309, 556 except 1,000 mg/L) showed normal and similar growth (170-224 fold increase after 72 hr) to control (207-fold increase after 72 hr).
EC_{50} (0-72 h) > 1,000 mg/L
NOEC (0-72 h) = 556 mg/L

Remarks field with the ability to identify source of comment, i.e. author and/or submitter:

DATA QUALITY

- **Reliabilities:** Valid without restriction.
- **Remarks field for Data Reliability:**
  Experimental design and analytical procedure were well documented.

REFERENCES

Environment Agency (EA) of Japan (1998).

OTHER

- **Last changed :**
- **Order number for sorting :**
- **Remarks field for General Remarks :**

ACUTE TOXICITY TO AQUATIC INVERTEBRATES (DAPHNIA) (1)

TEST SUBSTANCE

- **Identity:** Triacetin (CAS No. 102-76-1)
- **Remarks:** Source: Wako Pure Chemical Industries, Lot No. TPH 6237, Purity ≥ 98.0 %. Stability during use confirmed by NMR, IR and gas chromatography. Kept at room temperature in a dark place until use.

METHOD

- **Method/guideline:** OECD TG 202.
- **Test type:** Static.
- **GLP :** Yes.
- **Year :** 1998.
- **Analytical procedures:** Yes. Measured by gas chromatography (at preparation and after 48 hours exposure period).
- **Species/Strain:** *Daphnia magna*
- **Test details:** Static, open-system.
- **Statistical methods:** TOXDAT MULTI - METHOD PROGRAM (US EPA) Moving average method.

Remarks field for Test Conditions :

– ***Test organisms:***
  - Source, supplier, any pre-treatment, breeding method: Supplied by NIES (Japan).
  - Age at study initiation: Juveniles within 24h old.
  - Control group: Yes.

– ***Test conditions:***
  - Stock solutions preparation and stability: No solvent used. Test chemical was diluted to 1.0 wt.% with diluting mineral medium (Elendt M4) before use.
  - Test temperature range: 20.1 - 20.4 °C (average temperature within 21±1 °C).
  - Exposure vessel type: 100 mL test solution in a 100 ml glass beaker; 4 beakers per treatment.
  - Dilution water source: Elendt M4.
  - Dilution water chemistry: Hardness: 228 mg/L as $CaCO_3$.
  - Lighting: < 1,200 lx, 16h: 8h light-darkness cycle.
  - Water chemistry in test: DO= 7.6 - 8.7 mg/L, > 60 % of saturation (8.84 mg/L at 20 °C); pH=7.3 - 7.5.
  - Feeding: *Chlorella vulgaris*, 0.1 - 0.2 mgC/day/individual.

– ***Element (unit) basis:*** Cumulative numbers of died or immobilized juveniles.

– ***Test design:*** Number of replicates = 4; individuals per replicate = 5; concentrations: 0,95, 171, 309, 556 and 1,000 mg/L.

– ***Method of calculating mean measured concentrations:***
Geometric mean.

– ***Exposure period:*** 48 hours.

– ***Analytical monitoring:*** By GC analysis, 103.5 - 111.6 % of the nominal concentration at

preparation; 90.8 - 109.5 % after 48 hours exposure period.

Unit : mg/L (calculated based on the nominal concentrations).

RESULTS

- **Nominal concentrations:** 0, 95, 171, 309, 556 and 1,000 mg/L.
- **Measured concentrations:**
  - Triacetin concentration of the test solutions measured at preparation and after 48 hours exposure period.

Measured concentration of triacetin during 48-hour exposure of *Daphnia magna* under static test conditions

Nominal concentration (mg/L)	Measured concentration (mg/L)			Percent of Nominal	
	0-hour (new)	48-hour (old)	Geometric Mean	0-hour (new)	48-hour (old)
Control	< 1.0	< 1.0	-	-	-
95	106	104	105	111.6	109.5
171	178	172	175	103.9	100.7
309	324	323	323	104.8	104.6
556	576	566	571	103.5	101.8
1,000	1,086	908	993	108.6	90.8

new: Freshly prepared test solutions.
old: Test solutions after 48 hours exposure period.

Mortality or immobility of *Daphnia magna* exposed to triacetin under static test conditions.

Nominal concentration (mg/L)	Cumulative numbers of died or immobilized *Daphnia magna* (Percent mortality or immobility)	
Control	**24-hour**	**48-hour**
Control	0 (0)	0 (0)
95	0 (0)	0 (0)
171	0 (0)	0 (0)
309	0 (0)	0 (0)
556	3 (15)	5 (25)
1000	17 (85)	18 (90)
(Mortality: %)		

- **Statistical results as appropriate:**

Calculated EC_{50} values for *Daphnia magna* exposed to triacetin under static test conditions

Exposure period (hour) (hour)	EC_{50} (mg/L)	95% confidence limits (mg/L)	Statistical method
24	888	648-1,489	Moving average
48	768	582-1,176	Moving average

EC_0 and Lowest Concentration in 100 % mortality or immobility values

Exposure period (hour)	EC_0 (mg/L)	Lowest Concentration in 100 % mortality or immobility values (mg/L)
24	309	> 1,000
48	309	> 1,000

Remarks field for Results :

– ***Biological observations:***

· Was control response satisfactory: Yes.
Cumulative numbers of dead or immobilized *Daphnia* during observation period. 0 (mortality: 0%)

CONCLUSIONS

(Based on nominal concentration)

- EC_{50} (24-hour, mortality or immobility): 888 mg/L
- EC_{50} (48-hour, mortality or immobility): 768 mg/L
- EC_0 (48-hour, mortality or immobility): 309 mg/L

Remarks field with the ability to identify source of comment, i.e. author and/or submitter:

DATA QUALITY

- **Reliabilities:** Valid without restriction.
- **Remarks field for Data Reliability:**

Experimental design and analytical procedure were well documented.

REFERENCES

Environment Agency (EA) of Japan (1998).

OTHER

- **Last changed :**
- **Order number for sorting :**
- **Remarks field for General Remarks :**

ACUTE TOXICITY TO AQUATIC INVERTEBRATES (DAPHNIA) (2)

TEST SUBSTANCE

- **Identity:** Triacetin (CAS No. 102-76-1)
- **Remarks:** Source: Eastman^{R} Triacetin, Sample Reference Identification No.: 43045932,
  Purity ≥ 99.5 %. Stability during use confirmed by GC/FID and mass spectrometry.

METHOD

- **Method/guideline:** OECD TG 202 and EEC/Annex VC.2.
- **Test type:** Static.
- **GLP :** Yes.
- **Year :** 1995.
- **Analytical procedures:** Yes. Measured by gas chromatography (at preparation and after 48 hours exposure period).
- **Species/Strain:** *Daphnia magna*
- **Test details:** Static.
- **Statistical methods:** A program developed by Stephan (Aquatic Toxicology and Hazard Evaluation, Spec. Tech. Publ.No. 634, American Society for Testing and Materials, Philadelphia, PA, pp.65-84, 1977) and ASTM (Proposed New Standard Practice for Using Probit Analysis, ASTME-47.07, Draft #4, 1988).

Remarks field for Test Conditions :

– ***Test organisms:***

- Source, supplier, any pre-treatment, breeding method: Supplied by The Eco-Chem Testing Group, Kodak Park, Rochester, NY (USA).
- Age at study initiation: Juveniles between 6 and 24h old.
- Control group: Yes.

– ***Test conditions:***

- Stock solutions preparation and stability: No solvent used. The exposure solutions were prepared by direct addition of the appropriate amounts of the triacetin to tanks of water (20 L).
- Test temperature range: 20±2 °C.
- Exposure vessel type: 200 mL test solution in a 250 ml glass beaker; Two beakers per treatment.
- Dilution water source: The water from Lake Ontario was passed through an activated carbon filter and a set of 3-micron polypropylene filter. The filtered water next received 150 ppb of $Na_2S_2O_3$ to reduce trace level of residual chlorine.
- Dilution water chemistry: Hardness and total alkalinity: 120 mg/L and 95 mg/L (as $CaCO_3$).
- Lighting: 16 h: 8 h light-darkness cycle.
- Water chemistry in test: DO: 8.0 - 9.0 mg/L. pH of exposure solution was measured at times 0 and 48 hours (pH = 7.7 - 8.2).
- Feeding: 5 mL of food/1 L diluent water/100 gravid daphnids.

– ***Element (unit) basis:*** Cumulative numbers of dead or immobilized/stressed organisms.

– ***Test design:*** Number of replicates = 2; individuals per replicate = 10; nominal

concentrations: 0, 95.0, 171.5, 308.5, 555.5 and 1,000.0 mg/L.

– ***Method of calculating mean measured concentrations:***
Geometrical mean.
– ***Exposure period:*** 48 hours.
– ***Analytical monitoring:*** By GC analysis, the mean value of time 0 and 48 hours:
92.2 % (86.6 - 97.4 %) of the nominal concentration (Series A).
95.1 % (86.5 - 100.7 %) of the nominal concentration (Series B).

Unit: ***mg/L (calculated based on the nominal concentrations).***

RESULTS

- **Nominal concentrations:** 0, 95.0, 171.5, 308.5, 555.5 and 1,000.0 mg/L.
- **Measured concentrations:**
  · Triacetin concentration of the test solutions was measured at preparation and after 48 hours exposure period.
  · The analysed mean values of time 0 and 48 hours were calculated.

Measured concentration of triacetin during 48-hour exposure of *Daphnia magna* under static test conditions

Nominal concentration (mg/L)	Mean conc. (mg/L) Series A (0, 48-hour)	% of Nominal	Mean conc. (mg/L) Series B (0, 48-hour)	% of Nominal
95	83.5	87.9	82.2	86.5
171.5	148.5	86.6	156.6	91.3
308.5	283.4	91.9	297.3	96.4
555.5	541.1	97.4	558.5	100.5
1,000.0	974.4	97.4	1006.7	100.7

Calculated EC50 and No-Observed- Effect Concentration (NOEC) for *Daphnia magna* exposed to triacetin under static test conditions

Series	EC_{50} (mg/L)		EC_0 (mg/L)	
	24-hour	48-hour	24-hour	48-hour
A	> 974.4	810.9	974.4	541.1
B	> 1006.7	904.2	1006.7	558.5
Final value	> 974.4	810.9	974.4	541.1

- **Statistical results as appropriate:**
The binominal method and nonlinear interpolation were used to calculate all the EC50 values for replicates A and B at a confidence level of 95 %.

Remarks field for Results :

– ***Biological observations:***
· Was control response satisfactory: Yes.
The control immobility was not greater than 10 % when adverse effects were noted.

CONCLUSIONS

(Based on the measured concentration)

- EC_{50} (24-hour, mortality or immobility): > 974.4 mg/L
- EC_{50} (48-hour, mortality or immobility): 810.9 mg/L
- EC_0 (48-hour, mortality or immobility): 541.1 mg/L

Remarks field with the ability to identify source of comment, i.e. author and/or submitter:

DATA QUALITY

- **Reliabilities:** Valid without restriction.
- **Remarks field for Data Reliability:**

Experimental design and analytical procedure were well documented.

REFERENCES

Lawrence, D.L. and Hirsch, M.P. (1995), Eastman Kodak Company, Environmental Sciences Section, Corporate Health and Environment Laboratories, An acute aquatic effects test with the fathead minnow, Study No.: EN-430-900256-1,Unpublished data.

OTHER

- **Last changed :**
- **Order number for sorting :**
- **Remarks field for General Remarks :**

CHRONIC TOXICITY TO AQUATIC INVERTEBRATES (DAPHNIA)

TEST SUBSTANCE

- **Identity:** Triacetin (CAS No. 102-76-1)
- **Remarks:** Source: Wako Pure Chemical Industries, Lot No. TPH 6237, Purity ≥ 98.0 %. Stability during use confirmed by NMR, IR and gas chromatography. Kept at room temperature in a dark place until use.

METHOD

- **Method/guideline:** OECD TG 211 (revised edition of No.202).
- **Test type:** Semi-static.
- **GLP :** Yes.
- **Year :** 1998.
- **Analytical procedures:** Yes. Measured by gas chromatography 2 - 3 times a week (before and after the replacement of the test water.
- **Species/Strain:** *Daphnia magna*
- **Test details:** Semi-static (water renewal: 3 times a week), open-system.
- **Statistical methods:** F & t-test (Yukms StatLight #3).

Remarks field for Test Conditions :

– ***Test organisms:***
  - Source, supplier, any pre-treatment, breeding method: Supplied by NIES (Japan).
  - Age at study initiation: Juveniles within 24h old.
  - Control group: Yes.

– ***Test conditions:***
  - Stock solutions preparation and stability: No solvent used. Test chemical was diluted to 1.0 wt.% with diluting mineral medium (Elendt M4) before use.
  - Test temperature range: 19.4 - 20.7 °C (average temperature within 20±1 °C).
  - Exposure vessel type: 80 mL test solution in a 100 ml glass beaker;
  - Dilution water source: Elendt M4.
  - Dilution water chemistry: Hardness: 243 mg/L as $CaCO_3$
  - Lighting: <1,200 lx, 16 h: 8 h light-darkness cycle
  - Water chemistry in test: DO= 7.4 - 8.6 mg/L; pH=7.2.
  - Feeding: *Chlorella vulgaris*, 0.1 - 0.2 mgC/day/individual

– ***Element (unit) basis:*** Mean cumulative numbers of juveniles produced per adult (reproduction)

– ***Test design:*** Number of replicates=10; individuals per replicate=1; concentrations: 0 and 100 mg/L (limit test).

– ***Method of calculating mean measured concentrations:*** Time-weighted mean.

– ***Exposure period:*** 21 d

– ***Analytical monitoring:*** By GC analysis, 87.9 - 103.2 % of the nominal concentration at preparation; 75.8 - 100.7 % just before the renewal of the test water (after 2 days exposure).

Unit : ***mg/L (calculated based on measured concentrations)***

RESULTS

- **Nominal concentrations:** 0, 100 mg/L
- **Measured concentrations:**

Time-weighted means of measured concentration of the test chemical during 21-d exposure: 94 mg/L for the test solutions.

Measured concentration of the test chemical during 21-day exposure

Nominal concentration	Measured concentration (mg/L)					
(mg/L)	0 day (new)	2 day (old)	7 day(new)	9 day(old)	14day(new)	16day(old)
Control	< 1.0	< 1.0	< 1.0	< 1.0	< 1.0	< 1.0
100	87.9	75.8	99.4	100.7	103.2	97.4

new: Freshly prepared test solutions.
old: Test solution after 2 days.

Time-weighted means of measured concentration of the test chemical during 21-d exposure

Nominal concentration (mg/L)	Time-weighted mean (mg/L)	Percent of nominal concentration (%)
Control	-	-
100	94.0	94.0

Mean cumulative numbers of juveniles produced per adult during 21-d.

Nominal concentration	Days																				
(mg/L)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Control	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.5	4.8	11.8	17.1	25.8	36.8	44.4	50.5	65.9	73.5	76.9	90.4	91.0	93.8
100	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.9	3.4	8.3	10.5	21.7	33.9	41.0	50.1	68.2	69.9	74.9	90.8	91.3	91.8

Cumulative numbers of dead parental Daphnia during 21-d.

Nominal concentration	Days																				
(mg/L)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
100	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1(10)	1(10)	1(10)
(Mortality: %)																					

- **Statistical results as appropriate:**

There was no statistically significant difference between data from the control and 100 mg/L test groups.

Remarks field for Results :

– ***Biological observations:***

· Cumulative numbers of dead parental *Daphnia*:
Control: 0 (mortality: 0%)
100 mg/L: 1 (mortality: 10 %)

· Time of the first production of juveniles:
Control: 8 - 10 day (Mean: 8.7)
100 mg/L: 8 - 12 day (Mean: 9.1).

· Mean cumulative numbers of juveniles produced per adult alive for 21days:
Control: 93.8

100 mg/L: 91.8
- Was control response satisfactory: Yes.
  Mean cumulative numbers of juveniles produced per adult was 93.8 > 60.

CONCLUSIONS

(Based on nominal concentration)

- NOEC (21-d, reproduction) : = 100 mg/L
- EC50 (14-d, reproduction) : > 100 mg/L
- EC50 (21-d, reproduction) : > 100 mg/L
- LC50 for parental *Daphnia* (14-d) : > 100 mg/L
- LC50 for parental *Daphnia* (21-d) : > 100 mg/L;

Remarks field with the ability to identify source of comment, i.e. author and/or submitter:

DATA QUALITY

- **Reliabilities:** Valid without restriction.
- **Remarks field for Data Reliability:**

Experimental design and analytical procedure were well documented.

REFERENCES

Environment Agency (EA) of Japan (1998).

OTHER

- **Last changed :**
- **Order number for sorting :**
- **Remarks field for General Remarks :**

HEALTH ELEMENTS

(a) ACUTE ORAL TOXICITY

TEST SUBSTANCE

- **Identity:** Triacetin (CAS No. 102-76-1)
- **Remarks:** Source: Unichema Chemie B.V., The Netherlands. ESTOL 1579, Purity: approx. 100 %.

METHOD

- **Method/guideline:** OECD TG 401, EEC Directive 84/449/EEC, Annex V of the EEC Directive 67/548/EEC and Bewertung Wassergefährdender Stoffe, II Bestimmung der akuten oralen Saugetiertoxizität, Ad-hoc-Arbeitsgruppe I (Obmann: Dr. Niemitz), LTWS, Nr. 10 September 1979..
- **Test type:** Acute Oral Toxicity Test
- **GLP:** OECD GLP, US FDA (21 CFR 58) and US EPA (40 CFR 160 and 40 CFR 792).
- **Year:** 1988
- **Species:** Rat
- **Strain:** Wistar (SPF)
- **Route of administration:** Oral (by single-dose gavage)
- **Doses/concentration levels:**

  2,000 mg/kg bw/rat
- **Sex:** Male & Female
- **Control group and treatment:** No control and vehicle used.
- **Post exposure observation period:** Two weeks.
- **Statistical methods:** Not applied because of no mortality observed.

REMARKS FIELD FOR TEST CONDITIONS

– ***Test Subjects:***
  - ***Age at study initiation*:** Eight weeks old.
  - ***Weight at study initiation*:** No data available.
  - ***No. of animals per sex per dose*:** Five per sex per dose group.

– ***Study Design:***
  - ***Vehicle*:** No vehicle, undiluted.
  - ***Satellite groups and reasons they were added*:** None
  - ***Clinical observations performed and frequency*:**

Each rat was weighed immediately prior to treatment, the day after and weekly thereafter for two-week post-treatment observation period. Clinical observations were performed on the day of dosing (once every two hours) and once daily thereafter for two-week post-treatment observation period. Any signs of toxicity were recorded along with the time of onset and duration. At the end of the study (day 14), all animals were euthanized and subjected to necropsy.

RESULTS

- **LD_{50}:** ***Male*** **:** > 2,000 mg/kg bw.
  Female**:** > 2,000 mg/kg bw.

REMARKS FIELD FOR RESULTS.

– ***Body weight:*** All rats gained weight during the two-week observation period. No detailed body weight data available.
– ***Food/water consumption:*** No data available.
– ***Clinical signs :***
No mortality occurred and no signs of systemic toxicity were observed during the 14-day observation period.

Individual animal observations

Physical/Clinical		Animal Number/Sex									
Parameter		**4488**	**4490**	**4492**	**4494**	**4498**	**4219**	**4221**	**4223**	**4225**	**4229**
		Males					**Females**				
No effect of treatment	DPD	14	14	14	14	14	14	14	14	14	14
Dead	KIL	X	X	X	X	X	X	X	X	X	X
Necropsy findings	NGL	X	X	X	X	X	X	X	X	X	X

Glossary of terms for list of individual findings:
DPD=Days post dosing.
KIL=Killed at necropsy.
NGL=No gross lesions.
X=Positive.

– ***Haematology*****:** Not done.
– ***Biochem:*** Not done.
– ***Ophthalmologic findings:*** Not examined.
– ***Mortality and time to death:***

Mortality of male and female rats dosed orally with the undiluted test material

Dose level (mg/kg bw)	*# Dead / # Treated*		*Time of Death*	
	Males	**Females**	**Males**	**Females**
2,000	0/5	0/5	--	--

– ***Gross pathology incidence and severity:***
No treatment-related lesions were observed upon gross pathological examination of all animals at the end of two weeks for both sexes.

– ***Organ weight changes:*** Not done.

– ***Histopathology (incidence and severity):*** Not done.

CONCLUSIONS

Since no mortality occurred, the oral LD_{50} value for both males and females was noted as exceeding 2,000 mg/kg bw ("Bewertungszahl"1).

DATA QUALITY

- **Reliabilities:** Valid without restriction.

- **Remarks field for Data Reliability**
  Well conducted study, carried out by RCC NOTOX B.V., The Netherlands.

REFERENCES

Unichema Chemie B.V. (1988), "Acute Oral Toxicity of ESTOL 1579 in the Rat", unpublished data, RCC NOTOX 0831/1056.

GENERAL REMARKS

None.

(b) SKIN IRRITATION/CORROSION

TEST SUBSTANCE

- **Identity:** Triacetin (CAS No. 102-76-1)
- **Remarks:** Source: Data not available.
- **pH:** Not stated.

METHOD

- **Method/guideline:** OECD TG 404 and Off. J. Europ. Coimmun. 27, L251 106-108 (1984).
- **Test type:** *In vivo*
- **GLP:** Yes
- **Year:** 1988
- **Species:** Rabbit
- **Strain:** Chbb : HM
- **Sex:** Male
- **Number of animals per sex per dose:** Four.
- **Total dose:** 0.5 mL/animal.
- **Vehicle:** No vehicle used.
- **Exposure time period:** Four hours.

Grading scale: EC, L257/8 of the 16., September 1983 Corrosive action.

Method remarks: Not mentioned.

RESULTS

- **Primary irritation index:** Not applicable because of no irritation.

Results remarks: Triacetin was tested for its primary skin irritation under occlusive conditions on the shaved back skin of 4 rabbits. After a contact time of 4 hours, the skin reactions were evaluated. Only one animal showed slight skin redness one hour after the application. The other animals had no skin reactions at all.

CONCLUSIONS

According to the criteria in Off. J. Europ. Commun. 26, (L257) 1983, triacetin doesn't need to be classified regarding its skin irritation potential.

DATA QUALITY

- **Reliabilities:** Valid without restriction

Remarks field for Data Reliability

Well conducted study, carried out by Henkel Institut für Toxikologie (Düsseldorf).

REFERENCES

Kaestner, W. (1988), unpublished data Henkel KGaA. Rep. No. 880236.

GENERAL REMARKS

(c) EYE IRRITATION/CORROSION

TEST SUBSTANCE

- **Identity:** Triacetin (CAS No. 102-76-1)
- **Remarks:** Source: Data not available.
- **pH:** Not stated.

METHOD

- **Method/guideline:** OECD TG 405 and Off. J. Europ. Coimmun. L251, 27. Jg., 1984, S.109-112.
- **Test type:** *In vivo.*
- **GLP:** Yes.
- **Year:** 1988.
- **Methods Remarks:**
- **Species:** Rabbit.
- **Strain:** Chbb : HM
- **Sex:** Male.
- **Number of animals per sex per dose:** Four.
- **Doses used:** 0.1 mL/eye/animal.
- **Observation period:** Seventy two hours after the application.
- **Scoring Method used:** 79/831/EWG, Annex V, Part B.

RESULTS:

Reactions on the cornea and iris were not observed.
The conjunctival reactions were mild and disappeared totally within 6 to 24 hours after the application.

Conjunctivale reaktionen nach application der unverdünnten prüfsubstanz triacetin und dauerkontakt.

Tier-Nr.	Stunden nach der behandlung														
	1			6			24			48			72		
	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C
837	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
847	1	0	2	1	0	0	0	0	0	0	0	0	0	0	0
853	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0
854	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0
Mean A		0.25			0.25			0			0			0	
Mean B		0			0			0			0			0	
Mean C		1.75			0			0			0			0	

A=Rotung, B=Chemosis, C=exsudation

- **Corrosive:** Not applicable (see the results).
- **Irritation score (Cornea/Iris):** No irritation (see the results).
- **Irritation score (Conjunctivae): (Redness/Chemosis)** No irritation (see the results).
- **Overall Irritation Score:** 0.
- **Tool used to assess score:** Not stated.
- **Description of lesions (if seen):** Not stated.

Results remarks: Reactions on the cornea and iris were not observed. The conjunctival reactions were mild and disappeared totally within 6 to 24 hours after the application.

CONCLUSIONS

Triacetin is not eye irritant. According to the criteria in Off. J. Europ. Commun. 26 (L 257) 1983, the test substance doesn't need to be classified regarding its eye irritation potential.

DATA QUALITY

Valid without restriction

QUALITY CHECK

Well conducted study, carried out by Henkel Institut für Toxikologie (Düsseldorf).

REFERENCES

Kaestner, W. (1988), unpublished data Henkel KGaA. Rep. No. 880228.

GENERAL REMARKS

(d) SKIN SENSITIZATION (A HUMAN CASE REPORT)

TEST SUBSTANCE

- **Identity:** Triacetin (CAS No. 102-76-1)
- **Remarks:** Source: Eastman Kodak, purity: 99 %.
- **pH:** Not stated.

METHOD

- **Method/guideline:** Other.
- **Test type:** *In vivo* (Human patch test).
- **GLP:** No.
- **Year:** 1963
- **Species:** Human.
- **Strain:** Not applicable.
- **Sex:** Female.
- **Number of animals per sex per dose:** Not applicable.
- **Route of administration:** Skin patch test.
- **Induction concentration:** Not applicable.
- **Induction vehicle:** Not applicable.
- **Challenge concentration:** 0.1, 1, 10 and 50 %.
- **Challenge vehicle:** Ethanol.
- **Grading system used:** Not stated.

Method remarks: Not stated.

RESULTS

- **Case report:** The 29 year old female patient attended outpatients' clinic a few months ago with subacute eczema, which extended over both hands and the backs of the fingers as well as the lateral areas of the first three fingers of both hands. In addition on the right hand the ulnar and radial parts of the palm of the hand were affected. The skin was reddened and thickened in these areas, was covered in individual blisters, scales and crusts and displayed lichenification in part. Tonsillectomy in 1959 as a result of chronic recurrent tonsillitis and abscesses on tonsils. In the same year enucleation of a uterine myoma.

Results of the first patch test.

Test substance	Concentration Solvent	Result after 24 hrs	48 hrs	Comments
Potassium bichromate	0.6 % W	0	0	
	0.1 % W	0	0	
Nickel sulphate	5 % W	0	0	
Formalin	2 % W	0	0	
Terpentine	10 % O	0	0	
p-Phenylenediamine bis	1 % S	0	0	
p-Toluylenediamine bis	1 % S	0	0	
Ethyl p-aminobenzoate	2 % O	0	0	
p-aminomethyl-benzosulphoamide (Marfanil)	10 % W	0	0	
Procaine	2 % w	0	0	
Parobalsam	10 % S	0	0	
Tetramethyl-thiuramdisulphide	1 % S	0	0	
Mercaptobenzothiazole	1 % S	0	0	
Triacetin	50 % A	+++	+++	substance taken from
	10 % A	++	++	the Eastman Kodak patent
	1 % A	+	+	
Filter material (treated with triacetin)	pure	++	++	working substances taken from the Eastman Kodak patent
Filter material (not treated with triacetin)	pure	0	0	

W=dissolved in water, O=dissolved in peanut oil, S=incorporated in ointment, A=dissolved in ethanol, + to +++=positive test reaction of varying intensity, 0=negative reaction.

Results of the second patch test.

Test substance	Concentration Solvent	Result after 24 hrs	48 hrs	Comments
Triacetin	10 % A	++	+++	Haarmann u. Reimann, Holzminden
	1 % A	+	++	
	0.1 % A	+	+	
Diacetin	10 % W	+	+	Redistilled, pure
	1 % W	+	+	Chem. Fabrik Fluka AG, Buchs S,
	0.1 % W	0	0	Switzerland
Monoacetin	10 % W	+	+	Chem. Fabrik Fluka AG, Buchs S,
	1 % W	(+)	?	Switzerland
	0.1 % W	0	0	
Glycerol	pure	0	0	analytical grade
Acetic acid	10 % W	0	0	analytical grade
	1 % W	0	0	
Acetic anhydride	1 % W	0	0	analytical grade
Methyl acetate	10 % A	0	0	analytical grade
Ethyl acetate	10 % W	0	0	analytical grade
Sodium acetate	10 % W	0	0	analytical grade
Methyl glycol acetate	10 % W	0	0	analytical grade

W=dissolved in water, O=dissolved in peanut oil, S=incorporated in ointment, A=dissolved in ethanol, + to +++=positive test reaction of varying intensity, 0=negative reaction.

Grades: **0, +, ++, +++ (four grades)**

Results remarks: In the first and second challenge, control tests with 20 other patients who suffered from eczema with several concentration of triacetin as well as with the filter material had negative results.

CONCLUSIONS

A case of allergic eczema in a 29 year-old patient in a cigarette factory is reported, based on sensitization towards triacetin used for the

production of cigarette filters. The allergy was demonstrated in a patch test. In addition to triacetin, monoacetin and diacetin also produced positive results.

DATA QUALITY

- **Reliabilities:** Valid with restriction

Remarks field for Data Reliability

This is only a case report so far available, carried out by the University Skin Clinic Hamburg-Eppendorf (Germany) and published in detail.

REFERENCES

Unna, P.J., Schulz (1963), K.H. Hautarzt, 14 423-25.

GENERAL REMARKS

(e) REPEATED DOSE TOXICITY (ORAL BY GAVAGE)

TEST SUBSTANCE

- **Identity:** Triacetin (CAS No. 102-76-1)
- **Remarks:** Source: Daihachi Chemical Industry. Co., Ltd., Lot No. N-80302, Purity > 98.2 %. Stability during use confirmed by gas chromatography.

METHOD

- **Method/guideline:** OECD TG 422
- **Test type:** OECD Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test
- **GLP:** Yes
- **Year:** 1998
- **Species:** Rat
- **Strain:** Crj: CD (SD) IGS
- **Route of administration:** Oral (by gavage)
- **Doses/concentration levels:** 0, 40, 200, 1,000 mg/kg bw/day (5 mL/kg bw in 3 % gum arabic solution)
- **Sex:** Male & Female
- **Exposure period:** ***Males;*** for 44 days from 2 weeks prior to mating.
  Females**;** for 41 - 48 days from 14 days before mating to day 3 postpartum.
- **Frequency of treatment:** Once daily.
- **Control group and treatment:** Concurrent vehicle.
- **Post exposure observation period:** None.
- **Duration of test:** ***Male*****;** for 44 days
  Female**;** for 41 - 48 days
- **Statistical methods:** Kruskal-Wallis test for non-continuous data or Dunnett's or Scheffe's test for continuous data and Chi square test for quantal data.

REMARKS FIELD FOR TEST CONDITIONS

– ***Test Subjects:***

- ***Age at study initiation*****:** 9 week old for males and females
- ***Weight at study initiation*****:** 317 - 375 g for males, 203 - 240 g for females
- ***No. of animals per sex per dose*****:** 12 per sex per dose group

– ***Study Design:***

· ***Vehicle*:** 3 % gum arabic purified water
· ***Satellite groups and reasons they were added*:** None
· ***Clinical observations performed and frequency*:**
General condition was observed once a day and body wt. was determined on the first, day 3, 7 and 14, the last day of the administration, the day sacrificed and once a week during the administration period. For pregnant females, body wt. was determined on the day 0, 14 and 20 of gestation and on day 0 and 4 of lactation. Food consumption was determined on the same day when body wt. was measured for 24 hr. Haematology and biochemistry for males conducted only at time of necropsy after 44 days of chemical exposure. Urinalysis was not conducted.

· ***Organs examined at necropsy:***
Organ weight: for both sexes, brain, pituitary gland, thyroid gland, heart, liver, kidney, spleen, adrenal, thymus, and in addition for males, testes and epididymis.
Microscopic: all animals in control and 1,000 mg/kg bw group, and unfertilized animals in other groups: brain, spinal cord, pituitary gland, eyeball, thyroid gland (including parathyroid gland), thymus, heart, trachea, lung, liver, kidney, adrenal, spleen, stomach, small intestine, large intestine, pancreas, urinary bladder, bone marrow, sciatic nerve, lymph node, testes, epididymis, prostate, seminal vesicle, ovary, uterus, vagina, mammary gland and any organs, which might be expected to have histopathological changes and thymus and lung of dead animals.

RESULTS

- **NOAEL**

***Male*:** 1,000 mg/kg bw/day
***Female*:** 1,000 mg/kg bw/day

- **LOAEL**

Not determined under the conditions tested.

REMARKS FIELD FOR RESULTS.

– ***Body weight:***

For both sexes, no statistically significant difference from controls was observed in body weight and body weight gain during administration period.

– ***Food/water consumption:***

For both sexes, no statistically significant difference from controls was observed in food consumption during administration period.

– ***Clinical signs :***

Males **:** No dose-related changes in general clinical signs.
Females **:** No dose-related changes in general clinical signs.

– ***Haematology :***

Males **:** Decrease in differential leukocyte count (%) in neutrophils

(band) at 40 ($p<0.05$) and 1,000 mg/kg bw ($p<0.01$), but within physiological changes.

Dose level (mg/kg bw/day)	0	40	200	1,000
Differential leukocyte counts (%)				
Neutrophils (band)	0.7 ± 0.8	0.1 ± 0.3*	0.3 ± 0.6	0.0± 0.0**

Values are expressed as Mean ± SD
* Significant at $p \leq 0.05$.
** Significant at $p \leq 0.01$.

– ***Biochem:***

Males **:** Decrease in creatinine at 40 ($p<0.01$) and 1,000 mg/kg bw ($p<0.01$), but within physiological changes. Increase in inorganic phosphorus at 200 mg/kg bw ($p<0.05$), but with no dose-related changes.

Dose level (mg/kg bw/day)	0	40	200	1,000
Creatinine (mg/dL)	0.58 ± 0.06	0.51 ± 0.03**	0.56 ± 0.14	0.49± 0.03**
Inorganic phosphorus (mg/dL)	7.45 ± 0.46	7.72 ± 0.47	8.05 ± 0.60*	7.94± 0.40

Values are expressed as Mean ± SD
* Significant at $p \leq 0.05$.
** Significant at $p \leq 0.01$.

– ***Urinalysis:*** Not examined.
– ***Ophthalmologic findings:*** Not examined.
– ***Mortality and time to death:*** One male at 1,000 mg/kg bw was dead 32 days after the administration started.
– ***Gross pathology incidence and severity:***

No changes in gross pathology in both sexes.

– ***Organ weight changes:***

Male **:** No dose-related changes in organ weight.
Female **:** No dose-related changes in organ weight.

– ***Histopathology***

Tissue pathology revealed no alteration of tissues even in the highest dose groups for both sexes.

CONCLUSIONS

Triacetin had no effects on clinical signs, body weight, food consumption, and organ weight or necropsy findings. No histopathological changes ascribable to the compound were observed in both sexes. There were no effects on haematological or blood chemical parameters in males.
A NOAEL was thus established at 1,000 mg/kg bw/day for both sexes.

DATA QUALITY

- **Reliabilities:** Valid without restriction

Remarks field for Data Reliability

Well conducted study, carried out by Mitsubishi Chemical Safety Institute Ltd., Kashima Laboratory (Japan).

REFERENCES

Ministry of Health & Welfare (MHW), Japan (1998), Toxicity Testing Reports of Environmental Chemicals vol.6 127-147.

GENERAL REMARKS

This study was conducted to examine both repeated dose toxicity and reproductive/developmental toxicity as an OECD screening combined study. Therefore, biochemical and haematological analysis, and urinalysis in females were not performed. Functional observation, oestrous cycle length and pattern, and sperm examination were not performed because the test was conducted by the TG adopted in 1990.

(f) REPEATED DOSE TOXICITY (INHALATION)

TEST SUBSTANCE

- **Identity:** Triacetin (CAS No. 102-76-1)
- **Remarks:** Source: Plasticizer 88, Eastman Kodak Company, Purity: data not available. Stability and composition of the test material during use was confirmed by gas chromatography.

METHOD

- **Method/guideline:** Eastman Kodak Company, Laboratory of Industrial Medicine Protocol, whole body exposure to vaporized (heated at 150 °C) test substance.
- **Test type:** 90 Days vapour inhalation toxicity study.
- **GLP:** No
- **Year:** 1955.
- **Species:** Rat
- **Strain:** Data not available.
- **Route of administration:** Inhalation
- **Doses/concentration levels:**
  The measured average: 249 ppm (2,220 mg/m^3)
  Measured range of exposure: 14 - 918 ppm (130 – 8190 mg/m^3).
- **Sex:** Data not available.
- **Exposure period:** 90 Days.
- **Frequency of treatment:** Six hours each working day from March 7, 1955 to June 3, 1955.
- **Control group and treatment:** No data available.
- **Post exposure observation period:** None.
- **Duration of test:** 103 Days including the exposure period.
- **Statistical methods:** Data not available.

REMARKS FIELD FOR TEST CONDITIONS

– ***Test Subjects:***

  · ***Age at study initiation*:** Data not available.
  · ***Weight at study initiation*:** 209 g (average of three rats).
  · ***No. of animals per sex per dose*:** Three rats.

– ***Study Design:***

- ***Vehicle*:** None
- ***Satellite groups and reasons they were added*:** None
- ***Clinical observations performed and frequency*:**
  Body wt. for each animal was recorded prior to the first exposure and every 2-9 days interval during the test. The final body wt. of each animal was taken prior to the termination. Haematological studies (RBC, HGB, WBC) and urine analyses (albumin, sugar) were done at intervals (50, 64, 101 days, and 51, 65 days, respectively).

- ***Organs examined at necropsy:***
  Organ weight: liver, kidney.
  Microscopic: No data available except trachea, bronchi, lung, kidney, liver, and bladder

RESULTS

- **NOAEL**
  249 ppm (2,220 mg/m^3)

- **LOAEL**
  Not applicable.

REMARKS FIELD FOR RESULTS.

- ***Body weight:***
  The weights of the animals were followed closely on the graph of the average growth curve. The growth of all animals was normal under the conditions of the experiment. Average daily weight gain was 2.2 g/rat.

- ***Food/water consumption:*** Data not available.
- ***Clinical signs :***
  No symptoms were noted at any time during the exposure, and all rats appeared to be normal.
- ***Haematology :***
  Haematological studies revealed that there was nothing abnormal in any of the animals.
- ***Biochem :***
  Data not available.
- ***Urinalysis :***
  Urine revealed that there was nothing abnormal in any of the animals.

- ***Ophthalmologic findings:*** Not examined.
- ***Mortality and time to death:*** No deaths prior to scheduled termination.
- ***Gross pathology incidence and severity:*** No changes in gross pathology.
- ***Organ weight changes:***
  The weight of both liver and kidney when calculated as per cent of total body weight were found to be within the normal range.
- ***Histopathology :***
  At the time of autopsy, no abnormalities attributable to the exposure were found.

CONCLUSIONS

Histopathology, haematology and urine analyses revealed no changes in diagnostic of an adverse treatment-related effect. Under the conditions of the study, no toxic effects caused by the inhalation of triacetin could be found. Therefore, a NOAEL was established at 249 ppm (2,220 mg/m^3) for male rats.

DATA QUALITY

- **Reliabilities:** Valid with restriction because the studies do not fully comply with the current testing protocol.

Remarks field for Data Reliability

Insufficient data in terms of the current testing guideline, however, carefully conducted study, carried out by Corporate Health and Environment Laboratories, Eastman Kodak Company, Rochester, New York.

REFERENCES

Fassett, D.W. (1955), Corporate Health and Environment Laboratories, Eastman Kodak Company Unpublished data.

GENERAL REMARKS

The purpose of this study was to determine if the plasticiser, when used in acetate cigarette filters, would have any toxic effect on the individuals inhaling the compound.

GENETIC TOXICITY IN VITRO (BACTERIAL TEST)

TEST SUBSTANCE

- **Identity:** Triacetin (CAS No. 102-76-1)
- **Remarks:** Source: Daihachi Chemical Industry. Co., Ltd., Lot No. N-80302, Purity > 98.2 %. Stability during use confirmed by gas chromatography.

METHOD

- **Method/guideline**: Guideline for Screening Toxicity Testing of Chemicals (Japan) and OECD TG 471 and 472
- **Test type**: Reverse mutation assay
- **GLP**: Yes
- **Year**: 1998
- **Species/Strain:**

  Salmonella typhimurium TA100, TA1535, TA98, TA1537
  Escherichia coli WP2 *uvr*A
- **Metabolic activation:** With and without S9 from rat liver, induced with phenobarbital and 5,6-benzoflavone.
- **Statistical methods**: No statistical analysis was done.

REMARKS FIELD FOR TEST CONDITIONS

- **Study Design:**
  - ***Concentration*:**
    -S9: 0, 313, 625, 1,250, 2,500, 5,000 ug/plate (five strains)
    +S9: 0, 313, 625, 1,250, 2,500, 5,000 ug/plate (five strains)
  - ***Number of replicates*:** 2
  - ***Plates/test*:** 3
  - ***Procedure*:** Pre-incubation method
  - ***Positive controls*:**
    -S9 mix ; 2-(2-furyl)-3-(5-nitro-2-furyl)acrylamide (TA100, TA98, WP2 uvrA), sodium azide (TA1535) and 9-aminoacridine (TA1537)
    +S9 mix ; 2-aminoanthracene (five strains)

RESULTS

- **Cytotoxic concentration:**

  Toxicity was not observed up to 5,000ug/plate in five strains with and without metabolic activation (S9 mix).

- **Genotoxic effects:**

	+	?	-
– ***With metabolic activation:***	**[ ]**	**[ ]**	**[x]**
– ***Without metabolic activation:***	**[ ]**	**[ ]**	**[x]**

REMARKS FIELD FOR RESULTS.

CONCLUSIONS

Triacetin did not induce gene mutation in *S. typhimurium* and *E. coli* strains with and without metabolic activation.

DATA QUALITY

- **Reliabilities:** Valid without restriction.

Remarks field for Data Reliability

Well conducted study carried out by Hatano Research Institute, Food and Drug Safety Center (Hadano, Japan).

REFERENCES

Ministry of Health & Welfare (MHW), Japan (1998), Toxicity Testing Reports of Environmental Chemicals vol.6 127-147.

GENERAL REMARKS

None.

GENETIC TOXICITY IN VITRO (NON-BACTERIAL IN VITRO TEST)

TEST SUBSTANCE

- **Identity:** Triacetin (CAS No. 102-76-1)
- **Remarks:** Source: Daihachi Chemical Industry. Co., Ltd., Lot No. N-80302, Purity > 98.2 %. Stability during use confirmed by gas chromatography.

METHOD

- **Method/guideline**: OECD TG 473 and Guideline for Screening Toxicity Testing of Chemicals (Japan)
- **Test type**: Chromosomal aberration test
- **GLP**: Yes
- **Year**: 1998
- **Species/Strain:** CHL/IU cell
- **Metabolic activation:** With and without S9 from rat liver, induced with phenobarbital and 5,6-benzoflavone.
- **Statistical methods**: Fisher's exact analysis

REMARKS FIELD FOR TEST CONDITIONS

- **Study Design:**

For continuous treatment, cells were treated for 24 or 48 hrs without S9. For short-term treatment, cells were treated for 6 hrs with and without S9 and cultivated with fresh media for 18 hrs.

· ***Concentration*:**
-S9 (continuous treatment): 0, 0.55, 1.10, 2.20 mg/mL
-S9 (short-term treatment): 0, 0.55, 1.10, 2.20 mg/mL
+S9 (short-term treatment): 0, 0.55, 1.10, 2.20 mg/mL

· ***Plates/test*:** 2
· ***Positive controls*:**
Mitomycin C for continuous treatment
Cyclophosphamide for short-term treatment

RESULTS

- **Cytotoxic concentration:**

Toxicity was not observed up to 2.20 mg/mL in continuous and short-term treatment without S9 mix, although cell growth was retarded with S9 mix at this concentration under the both treatments. IC_{50} of the test chemical was calculated to be 1.80 mg/mL.

Chromosome analysis of Chinese hamster cells (CHL/IU) continuously treated with triacetin (Ta)**

without S9 mix

Group	Conc. (mg/mL)	Time of exposure (h)	No. of cells analysed	No. of structural aberrations gap	ctb	cte	csb	cse	mul[2]	total	others[3]	No. of cells with aberrations TAG(%)	TA(%)	Polyploid[4] (%)	Trend test[5] SA	NA	Concurrent cytotoxicity[6] (%)	Mitotic index[7] (%)
Non-treatment			200	0	0	0	0	0	0	0	1	0 (0.0)	0 (0.0)	0.25			-	-
Solvent[1]	0	24	200	0	1	0	0	0	0	1	0	1 (0.5)	1 (0.5)	0.50			100.0	-
Ta	0.55	24	200	0	0	2	0	0	0	2	1	2 (1.0)	2 (1.0)	0.00			100.0	-
Ta	1.10	24	200	0	1	2	0	0	0	3	1	3 (1.5)	3 (1.5)	0.25	-	-	92.5	-
Ta	2.20	24	200	0	0	0	0	0	0	0	0	0 (0.0)	0 (0.0)	0.00			90.5	8.6
MC	0.00005	24	200	2	8	26	0	0	0	36	0	33*(16.5)	31*(15.5)	0.13			-	-
Solvent[1]	0	48	200	0	0	0	0	0	0	0	0	0 (0.0)	0 (0.0)	0.25			100.0	-
TA	0.55	48	200	0	0	0	0	0	0	0	0	0 (0.0)	0 (0.0)	0.38			105.0	-
TA	1.10	48	200	0	0	0	0	0	0	0	1	0 (0.0)	0 (0.0)	0.38	-	-	104.0	-
TA	2.20	48	200	0	0	0	0	0	0	0	0	0 (0.0)	0 (0.0)	0.13			85.0	6.8
MC	0.00005	48	200	6	13	27	0	4	0	50	4	40*(20.0)	34*(17.0)	0.25			-	-

Abbreviations, gap: chromatid gap and chromosome gap, ctb: chromatid break, cte: chromatid exchange, ctb: chromosome break, cse: chromosome exchange (dicentric and ring), mul: multiple aberrations, TAG: total no. of cells with aberrations, TA: total no. of cells with aberrations except gap, SA: structural aberration, NA: numerical aberration, MC: mitomycin C.
1) DMSO was used as solvent. 2) More than nine aberrations in a cell were scored as 10. 3) Others, such as attenuation and premature chromosome condensation, were excluded from the no. of structural aberrations. 4) Eight hundred cells were analysed in each group. 5) Cochran-Armitage's trend test was done at $p<0.01$. 6) Cell confluency, representing cytotoxicity, was measured with Monocellater™. 7) Number of metaphase per 500 cells was scored in each dish in order to select the highest dose enable to analyse chromosomes.
*: Significantly different from solvent control at $p<0.01$ by Fisher's exact test. **: Purity was 98.2 wt%. Diacetin (0.9%) was contained as an impurity.

Chromosome analysis of Chinese hamster cells (CHL/IU) treated with triacetin (Ta)** with and without

S9 mix

Group	Conc. (mg/mL)	S9 mix	Time of exposure (h)	No. of cells analysed	No. of structural aberrations gap	ctb	cte	csb	cse	mul[2]	total	others[3]	No. of cells with aberrations TAG(%)	TA(%)	Polyploid[4] (%)	Trend test[5] SA	NA	Concurrent cytotoxicity[6] (%)	Mitotic index[7] (%)
Non-treatment				200	0	0	0	0	0	0	0	0	0 (0.0)	0 (0.0)	0.00			-	-
Solvent[1]	0	-	6-(18)	200	0	0	0	0	0	0	0	1	0 (0.0)	0 (0.0)	0.13			100.0	-
Ta	0.55	-	6-(18)	200	0	0	0	4	0	0	4	0	1 (0.5)	1 (0.5)	0.63			100.0	-
Ta	1.10	-	6-(18)	200	0	1	1	0	0	0	2	0	2 (1.0)	2 (1.0)	0.00	-	-	99.5	-
Ta	2.20	-	6-(18)	200	0	0	0	0	0	0	0	0	0 (0.0)	0 (0.0)	0.25			90.5	9.2
CPA	0.005	-	6-(18)	200	0	2	0	2	0	0	4	3	1 (0.5)	1(0.5)	0.50			-	-
Solvent[1]	0	+	6-(18)	200	0	0	0	0	0	0	0	0	0 (0.0)	0 (0.0)	0.25			100.0	-
Ta	0.55	+	6-(18)	200	0	0	0	0	0	0	0	0	0 (0.0)	0 (0.0)	0.50			109.0	-
Ta	1.10	+	6-(18)	200	0	0	1	0	0	0	1	0	1 (0.5)	1 (0.5)	0.25	+	-	104.5	-
Ta	2.20***	+	6-(18)	200	10	59	103	0	0	70	242	1	87*(43.5)	84*(42.0)	0.26			25.5	1.6
CPA	0.005	+	6-(18)	200	4	28	113	1	0	0	146	0	91*(45.5)	90*(45.0)	0.13			-	-

Abbreviations, gap: chromatid gap and chromosome gap, ctb: chromatid break, cte: chromatid exchange, ctb: chromosome break, cse: chromosome exchange (dicentric and ring), mul: multiple aberrations, TAG: total no. of cells with aberrations, TA: total no. of cells with aberrations except gap, SA: structural aberration, NA: numerical aberration, MC: mitomycin C.
1) DMSO was used as solvent. 2) More than nine aberrations in a cell were scored as 10. 3) Others, such as attenuation and premature chromosome condensation, were excluded from the no. of structural aberrations. 4) Eight hundred cells were analysed in each group. 5) Cochran-Armitage's trend test was done at $p<0.01$. 6) Cell confluency, representing cytotoxicity, was measured with Monocellater™. 7) Number of metaphase per 500 cells was scored in each dish in order to select the highest dose enable to analyse chromosomes. 8) Seven hundred and eighty cells were analysed.
*: Significantly different from solvent control at $p<0.01$ by Fisher's exact test. **: Purity was 98.2 wt%. Diacetin (0.9%) was contained as an impurity.
***: Medium colour was changed to yellow during the incubation and the pH adjusted to 6.93 at 0 hr lowered to 4.91 after the 6-hr incubation.

- **Genotoxic effects:**

	Clastogenicity			polyploidy		
	+	?	-	+	?	-
– ***Without metabolic activation:***	**[ ]**	**[ ]**	**[x]**	**[ ]**	**[ ]**	**[x]**
– ***With metabolic activation:***	**[ ]**	**[x]**	**[ ]**	**[ ]**	**[ ]**	**[x]**

REMARKS FIELD FOR RESULTS.

Structural chromosomal aberrations were induced on a short-term treatment with an exogenous metabolic activation system at the highest concentration of the test chemical (2.2 mg/mL or 10 mM). Under such conditions, pH of the test medium decreased to pH 4.91 in the presence of the chemical. It is recognised that changes in pH can induce artefacts in this assay. Therefore, it was suggested that chromosomal aberrations induced by the triacetin were due to the lowering pH effect of the chemical rather than DNA damage per se. Polyploidy were not induced under any conditions tested.

CONCLUSIONS

Triacetin induced chromosomal aberration in CHL/IU cells on a short-term treatment with metabolic activation system. It is, however, recognized that chromosomal aberration induced at 2.2 mg/mL can be artefacts in this assay.

DATA QUALITY

- **Reliabilities:** Valid without restriction.

Remarks field for Data Reliability

Well conducted study, carried out by Hatano Research Institute, Food and Drug Safety Center (Hadano, Japan).

REFERENCES

Ministry of Health & Welfare (MHW), Japan (1998), Toxicity Testing Reports of Environmental Chemicals vol.6 127-147.

GENERAL REMARKS

None.

TOXICITY TO REPRODUCTION/DEVELOPMENT

TEST SUBSTANCE

- **Identity:** Triacetin (CAS No. 102-76-1)
- **Remarks:** Source: Daihachi Chemical Industry. Co., Ltd., Lot No. N-80302, Purity > 98.2 %. Stability during use confirmed by gas chromatography.

METHOD

- **Method/guideline:** OECD TG 422
- **Test type:** OECD Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test
- **GLP:** Yes
- **Year:** 1998
- **Species:** Rat
- **Strain:** Crj:CD (SD)IGS
- **Route of administration:** Oral (by gavage)
- **Doses/concentration levels:**

  0, 40, 200, 1,000 mg/kg bw/day (5 mL/kg bw in 3 % gum arabic solution)
- **Sex:** Male & Female
- **Exposure period:** ***Males*****;** for 44 days from 2 weeks prior to mating
  Females**;** for 41 - 48 days from 14 days before mating to day 3 postpartum throughout mating and pregnancy.
- **Frequency of treatment:** Once daily.
- **Control group and treatment:** Concurrent vehicle (3 % gum arabic purified water).
- **Post exposure observation period:** None.
- **Duration of test:** ***Male*****;** for 44 days
  Female**;** for 41 - 48 days
- **Statistical methods:** Kruskal-Wallis test for non-continuous data or Dunnett's or Scheffe's test for continuous data and Chi square test for quantal data.

REMARKS FIELD FOR TEST CONDITIONS

– ***Test Subjects:***

  · ***Age at study initiation*****:** 9 week old for males and females
  · ***Weight at study initiation*****:** 317 - 375 g for males, 203 - 240 g for females

· ***No. of animals per sex per dose*:** 12 per sex per dose group

– ***Study Design:***

The animals were sacrificed on the day 4 of lactation for females. Females with no pregnancy were killed 26 days after the postcoitum date (1/12 in 200mg/kg bw group).

· ***Vehicle*:** 3 % gum arabic purified water.

· ***Satellite groups and reasons they were added*:** None.

· ***Mating procedures*:** Male/female per cage; 1/1, length of cohabitation; 7 days at the longest, until proof of pregnancy (formation of vaginal closing or sperm detection in vagina).

· ***Clinical observations performed and frequency*:**
Parent: General appearance once a day
Foetus: General appearance once a day after birth
Haematology and biochemistry for males conducted only at time of necropsy after 44 days of chemical exposure. Urinalysis was not done.

· ***Organs examined at necropsy*:**
Organ weight: for both sexes, brain, pituitary gland, thyroid gland, heart, liver, kidney, spleen, adrenal, thymus, and in addition for males, testes and epididymis.
Microscopic: all animals in control and 1,000 mg/kg bw group, and unfertilized animals in other groups: brain, spinal cord, pituitary gland, eyeball, thyroid gland (including parathyroid gland), thymus, heart, trachea, lung, liver, kidney, adrenal, spleen, stomach, small intestine, large intestine, pancreas, urinary bladder, bone marrow, sciatic nerve, lymph node, testes, epididymis, prostate, seminal vesicle, ovary, uterus, vagina, mammary gland and any organs, which might be expected to have histopathological changes and thymus and lung of dead animals.
Foetal: full macroscopic examinations on all live and dead pups.

· ***Parameters assessed during study*:**
Body wt. (for males, once a week, and the first, the last day of the administration, the day sacrificed, and for pregnant females, the day 0, 14 and 20 of gestation and on day 0 and 4 of lactation), food/water consumption (once a week, and on the same day when body wt. determined), No. of pairs with successful copulation, copulation index (No. of pairs with successful copulation/No. of pairs mated x 100), pairing days until copulation, No. of pregnant females, fertility index = (No. of pregnant animals/No. of pairs with successful copulation x 100), No. of corpora lutea, No. of implantation sites, implantation index (No. of implantation sites/No. of corpora lutea x 100), No. of living pregnant females, No. of pregnant females with parturition, gestation length, No. of pregnant females with live pups on day 0, gestation index (No. of females with live pups/No. of living pregnant females x 100), No. of pregnant females with live pups on day 4, delivery index (No. of pups born/No. of implantation sites x 100), No. of pups alive on day 0 of lactation, live birth index (No. of live pups on day 0/No. of pups born x 100), sex ratio (Total No. of male

pups/Total No. of female pups), No. of pups alive on day 4 of lactation, viability index (No. of live pups on day 4/No. of live pups on day 0 x 100), body wt. of live pups (on day 0 and 4)

RESULTS

- **NOAEL and LOAEL maternal toxicity:**

  NOAEL: 1,000 mg/kg bw/day

- **NOAEL and LOAEL foetal toxicity:**

  NOAEL: 1,000 mg/kg bw/day

- **Actual dose received by dose level by sex if available:**

  0, 100, 300, 1,000 mg/kg bw/day for 14 consecutive administrations for both sexes.

- **Maternal data with dose level :**

  No effects related to chemical exposure were observed at all doses, although there was a single unsuccessful copulation in control. At 200 mg/kg bw-group, one animal was not delivered of pups.

- **Foetal data with dose level :**

  No effects related to chemical exposure were observed at all doses.

REMARKS FIELD FOR RESULTS.

– ***Mortality and day of death:*** At 1,000 mg/kg bw, one male rat died 32 days after administration, but without apparent relation to the exposure.

– ***Body weight:*** No dose-related changes in body weight and body weight gains for both sexes.

– ***Food/water consumption:*** No dose-related changes in food consumption for both sexes.

– ***Reproductive data:*** No statistically significant difference from controls.

– ***Fetal data :*** No statistically significant difference from controls, although 3, 6, 5 and 1 dead pups at birth or soon after birth were observed at 0, 40, 200 and 1,000 mg/kg bw, respectively.

– ***Grossly visible abnormalities, external, soft tissue and skeletal abnormalities :***
No statistically significant effects were observed at all doses.

Fertility and pregnancy data in rats treated orally with triacetin

Dose level (mg/kg bw/day)	0	40	200	1,000
No. of pairs mated	12	12	12	12
No. of pairs mated with successful copulation	11	12	12	12
Copulation index (%)	91.7	100	100	90
No. of pregnant females	10	12	12	12
Fertility index (%)	90.9	100	90	100

Pairing days until copulation (Mean ± S.D.)	2.6±1.4	2.3±1.4	3.4±1.4	3.0±1.7
No. of estrous stages without mating	0.0±0.0	0.0±0.0	0.1±0.3	0.1±0.3

Copulation index (%)= (No. of pairs with successful copulation / No. of pairs mated) x100
Fertility index (%) =(No. of pregnant females / No. Of pairs with successful copulation) x100

Delivery and litter data in rats treated orally with triacetin

Dose level (mg/kg bw/day)	**0**	**40**	**200**	**1,000**
No. of females examined	10	12	12	12
No. of females with live pups	10	12	11	12
Gestation index (%)	100	100	91.7	100
Gestation length (days, Mean ± SD)	22.6±0.5	22.4±0.5	22.4±0.5	22.6±0.4
No. of corpora lutea (Mean ± SD)	16.6±1.8	16.3±1.9	16.3±1.6	16.8±0.5
No. of implantation sites (Mean ± S.D.)	15.3±4.4	16.0±1.7	14.7±4.4	15.8±1.4
Implantation index (%, Mean ± S.D.)	90.2±23.2	98.2±4.8	89.5±26.4	93.8±4.8
Delivery index (%, Mean ± S.D.)	94.8±7.2	95.1±4.8	90.2±28.5	92.6±3.5
No. of pups born	14.4±4.1	15.3±2.1	15.6±0.8	14.6±1.4
No. of pups alive on day 0 of lactation	14.2±4.1	15.3±2.1	15.5±0.8	14.6±1.4
Live birth index (%)	98.7±2.7	100±0.0	98.9±2.5	100±0.0
Sex ratio (Male/Female)	1.25 (79/63)	0.89 (86/97)	1.18 (92/78)	0.88 (82/93)
No. of pups alive on day 4 of lactation	14.1±4.1	14.8±1.7	15.2±0.8	14.5±1.4
Viability index on day 4 of lactation (%)	14.1±4.1	14.8±1.7	15.2±0.8	14.5±1.4
Body weight of live pups (g)				
(On day 0)				
Male	7.1±0.6	6.8±0.6	6.5±0.6	7.1±0.6
Female	6.7±0.6	6.4±0.6	6.3±0.6	6.7±0.6
(On day 4)				
Male	11.1±1.7	10.8±1.3	10.2±0.5	11.3±1.0
Female	10.7±1.6	10.4±1.2	9.8±0.7	10.9±1.1
Body weight gain of pups (g)				
(On day 0-4)				
Male	4.0±1.1	4.0±0.9	3.7±0.5	4.5±0.7
Female	4.0±1.1	3.9±0.8	3.4±0.5	4.4±0.6

Gestation index (%)=(No. of females with live pups / No. of pregnant females) x100
Delivery index (%) = (No. of pups born/ No. of implantation sites) x100
Live birth index (%) =(No. of live pups on day 0 / No. of pups born) x100
Viability index (%) =(No. of live pups on day 4/ No. of live pups on day 0) x100
Sex ratio =Total No. of male pups/ Total No. of female pups
Values are expressed as Mean±S.D. Except sex ratio.

CONCLUSIONS

No effects related to chemical exposure were observed maternally at all dose levels, although there was a single undelivered animal at 200 mg/kg bw which was not statistically significantly different from the control ($p<0.05$). Similarly, no effects related to the chemical exposure were observed at all dose levels on reproductive parameters including the mating index, fertility index, gestation length, numbers of corpora lutea and implantations, implantation index, gestation index, delivery index, parturition and maternal behaviour at delivery and lactation. Therefore, a NOAEL was established at 1,000 mg/kg bw/day.

DATA QUALITY

- **Reliabilities:** Valid without restriction.

Remarks field for Data Reliability

Well conducted study, carried out by Research Institute for Animal Science in Biochemistry and Toxicology (Japan).

REFERENCES

Ministry of Health & Welfare (MHW), Japan (1998), Toxicity Testing Reports of Environmental Chemicals vol.6 127-147.

Pharmacokinetics (Metabolism)

TEST SUBSTANCE

- **Identity:** Triacetin (CAS No. 102-76-1)
- **Remarks:** Source: British Drug Houses, purity: not available.

METHOD

- **Method/guideline:** Other.
- **Test type:** *In vitro*.
- **GLP:** No.
- **Year:** 1966.
- **Method:** The procedure used in most experiments followed closely that outlined by Parsons et al. (1958) (J. Physiol., 144 387-402). The sacs of the everted intestine, the middle fifth of the combined jejunum and ileum was used. The sacs contained initially 1 mL of bicarbonate saline and shaken for 1 hr at 37 °C. Acetins, glucose, acetate, or metabolic inhibitors were added to the saline. At the end of the incubation, fluid transfer was estimated by weighing the sac and its contents, and acetate determinations were made on samples of the mucosal and serosal fluids. Acetates were estimated by steam distillation from an all-glass Markham apparatus and titration of the distillate with 0.05 N-NaOH using phenol red as indicator.
- **Species:** White rat.
- **Strain:** Sheffield.
- **Sex:** Male.
- **Age:** Not stated.
- **Body weight:** 230 g.
- **Number of Animals/Donors:** Data not available.
- **Route of administration:** Not applicable.
- **Vehicle:** One mL of bicarbonate saline (Krebs, H. A. and Henseleit, K, 1932, Hoppe-Seyler's Z. Physiol. Chem., 210 33-66)/sac.
- **Doses/concentration levels:** 1, 2, 5, 10, 15, 20, 30, 40, 50 and 70 mM (glyceride)
- **Statistical methods:** Mean ± S.E.M.
- **Actual doses:** Not applicable.
- **Excretion routes:** Not applicable.

- **Body fluids sampled:** Not applicable.
- **Tissues sampled:** Not applicable.
- **Metabolites (CAS):** Acetic acid (64-19-7).
  Glycerol (56-81-5).

RESULTS

Effect of concentration of glyceride on hydrolysis by everted sacs.

	Acetate released (umoles)		
Concentration of glyceride (mM)	**Monoacetin**	**Diacetin**	**Triacetin**
1	-	-	31±1 (5)
2	-	-	61±2 (5)
5	40±3 (5)	84±4 (5)	139±4 (5)
10	71±4 (5)	144±9 (5)	211±12 (5)
15	92±4 (5)	206±12 (11)	307±11 (5)
20	-	231±10 (5)	-
30	195±6 (5)	310±16 (5)	-
40	274±12 (5)	-	
50	295±18 (5)	376±18 (5)	-
70	309±19 (5)	-	
5 mM monoacetin+5 mM diacetin	107±5 (5)	-	
5 mM monoacetin+5 mM triacetin	177±11 (5)	-	
5 mM diacetin+5 mM triacetin	198±11 (5)	-	

***The sacs contained initially I mL bicarbonate saline and were suspended in 15 mL of the same solution for I hr at 37 °C. Values are expressed as umoles/g initial wet wt. of tissue. All values are means S.E.M. with the number of experiments in brackets.**

Effect of concentration on entry into rat intestine from mucosal fluid.

	Glyceride entry rate (umoles)		
Concentration of glyceride (mM)	**Monoacetin**	**Diacetin**	**Triacetin**
1	-	-	10
2	-	-	20
5	40	42	46
10	71	72	70
15	92	103	102
20	-	115	-
30	195	155	-
40	274	-	-
50	295	188	-
70	309	-	-

Final concentration of acetate in mucosal and serosal fluid when glyceride is initially present in the mucosal fluid.

Glyceride (mM)	**Monoacetin**			**Diacetin**			**Triacetin**		
	No. of expts.	**Final mucosal acetate (mM)**	**Final serosal acetate (mM)**	**No. of expts.**	**Final mucosal acetate (mM)**	**Final serosal acetate (mM)**	**No. of expts.**	**Final mucosal acetate (mM)**	**Final serosal acetate (mM)**
1	-	-	-	-	-	-	5	1.39±0.07	5.06±0.06
2	-	-	-	-	-	-	5	2.70±0.17	11.31±0.83
5	5	1.78±0.07	8.50±0.34	10	3.12±0.10	14.67±0.54	5	5.39±0.14	27.75±0.52
10	5	2.78±0.05	16.35±0.51	9	4.98±0.13	27.56±1.24	10	10.56±0.18	40.02±1.45
15	9	4.76±0.09	25.25±0.22	9	6.25±0.22	42.00±1.23	5	17.94±0.18	26.60±1.42
20	-	-	-	9	7.98±0.15	47.78±0.73	-	-	-
30	5	6.19±0.25	43.56±1.72	5	11.31±0.31	54.87±1.41	-	-	-
40	5	8.41±0.25	50.37±0.74	-	-	-	-	-	-
50	6	9.37±0.49	45.62±0.92	5	18.21±0.14	39.75±2.70	-	-	-
70	5	14.31±0.75	46.56±2.12	-	-	-	-	-	-

***The sacs contained initially I mL bicarbonate saline and were suspended in 15 mL of the same solution for I hr at 37 °C. Values are expressed as umoles/g initial wet wt. of tissue. All values are means S.E.M. with the number of experiments in brackets.**

Summary

(1) When triacetin, mono- and diacetins were incubated with the sacs of rats everted intestine, the glycerides entered the epithelial cells and were completely hydrolyzed to free glycerol and acetic acid. The activity of the preparation, as measured by acetate release, increased with the number of acetic acid residues in the glyceride (15 mM). Monoacetin, diacetin and triacetin released 92 ± 4, 206 ± 12 and 307 ± 11 umoles of acetate, respectively. With increasing concentrations of glyceride (5, 10 and 15 mM), the amount of acetate released increased linealy up to about a total amount of 300 umoles of acetates released. There is no absolute positional specificity, and all three ester linkages can be split.

(2) The rate limiting step in the process was the entry of glyceride into the epithelial cell.
(3) The three acetins entered the epithelial cells at the same rate.
(4) The acetate released appeared in higher concentrations on the serosal sides.
(5) Volatile fatty acids, which released from acetins could be transferred into the cells by the rat ..... intestine against a concentration gradient.

CONCLUSIONS

When triacetin, mono- and diacetins were incubated with the sacs of rats everted intestine, every glyceride was hydrolyzed completely to free glycerol and acetic acid. There was no absolute positional specificity for three ester linkages.

DATA QUALITY

- **Reliabilities:** Valid with restriction.

Remarks field for Data Reliability

Data is historic. This study, however, clearly demonstrated that triacetin is hydrolysed to free glycerol and acetic acid by rat intestine without positional specificity for ester linkages.

REFERENCES

Barry, R.J.C. et al. (1966), J. Physiol. 185 667-683.

GENERAL REMARKS

Pharmacokinetics

TEST SUBSTANCE

- **Identity:** Triacetin (CAS No. 102-76-1)
- **Remarks:** Source: data not available.

METHOD

- **Method/guideline:** Other.
- **Test type:** *In vivo*
- **GLP:** No.
- **Year:** 1993.
- **Method:**

Triacetin was administered intravenously to mongrel dogs (n=10) 2 weeks after surgical placement of blood-sampling catheters in the aorta and in the portal, hepatic, renal, and femoral veins.
[1-^{14}C] Acetate was infused to allow quantification of organ uptake of acetate as well as systemic turnover and oxidation.
After 3 hr of tracer infusion, a 5 % (v/v) aqueous solution of triacetin was administered intravenously to mongrel dogs at a rate of 47 umol/kg bw/min (estimated resting energy expenditure: REE) for an additional 4 hours, after [1-^{14}C] acetate was infused at a rate of ca. 30 kBq/min for 3 hours (continued to the end of study) to allow quantification of organ uptake of acetate as well as systemic turnover and oxidation.

- **Species:** Dog.
- **Strain:** Mongrel.
- **Sex:** Data not available.
- **Age:** Data not available.
- **Body weight:** 23.4±0.3 kg.
- **Number of Animals/Donors:** Ten animals.
- **Route of administration:** Infusion via postcava.
- **Vehicle:** 150 mmol NaCl/L containing 2mmole $NaHCO_3$/L.
- **Doses/concentration levels:** 47 umol/kg bw/min (triacetin).
- **Statistical methods:** Average values for plasma acetate concentration and specific activity, mean values for $^{14}CO_2$ excretion rate for breath samples. Systemic acetate turnover and oxidation were determined by using steady-state formulas.

- **Actual doses:** Not applicable.
- **Excretion routes:** Breath.
- **Body fluids sampled:** 15-min Intervals over the last 30 min of the triacetin infusion.
- **Tissues sampled:** Blood.
- **Metabolites:** Not stated.
- **Metabolites CAS:** Not stated.

RESULTS

Plasma acetate concentration after steady-state conditions were achieved.(umol/L)

Aorta	Renal vein	Portal vein	Femoral vein	Hepatic vein
1180	935	817	752	473

Acetate turnover rate during triacetin infusion.
2214±95 umol/min, 68±3 % of the known rate of triacetin-derived acetate infusion, on the assumption that there was complete hydrolysis of the triglyceride.

Acetate oxidation during triacetin infusion.
1876±132 umol/min, 85±5 % of the acetate turnover.

Acetate clearance during triacetin infusion.
2.0±0.1 L/min.

Organ acetate uptake in dogs, postabsorptively.

Tissue	No. of animals	Uptake (umol/min)
Hindlimb	9	89±7
Total skeletal muscle*		445±35
Intestine	10	342±23
Liver	6	559±68
Kidney	4	330±37

*It was assumed that 20 % of whole-body skeletal muscle is represented in the hindlimb.

Systemic acetate kinetics was obtained in all animals tested. Systemic acetate turnover accounted for approximately 70 % of triacetin-derived acetate, assuming complete hydrolysis of the triglyceride. Approximately 80 % of systemic acetate uptake was rapidly oxidized. Significant acetate uptake was demonstrated in all tissues (liver, 559 ± 68; intestine, 342 ± 23; hindlimb, 89 ± 7; and kidney, 330 ± 37 umol/min).

CONCLUSIONS

During intravenous administration in dogs, the majority of infused triacetin undergoes intravascular hydrolysis, and the majority of the resulting acetate is oxidized. Thus, energy in the form of short-chain fatty acids can be delivered to a resting gut via intravenous infusion of a short-chain triglyceride.

DATA QUALITY

- **Reliabilities:** Valid with restriction.

Remarks field for Data Reliability

REFERENCES

Bleiberg, Batia et al., (1993), Am. J. Clin. Nutr. 58 908-911.

GENERAL REMARKS

Triacetin is a water-soluble short-chain triglyceride that may have a role as a parenteral nutrient.

Appendix : Parameters used in calculation of distribution by Mackay level III fugacity model.
(Part 1)

Physico-Chemical Properties
(water solubility : 70g/L)

Chemical		Triacetin	Method
Molecular weight		218.21	calculated
Melting point [℃]		3	unkown
Vapour pressure [Pa]		0.331	unkown
Water solubility [g/m^3]		70000	measured
log Kow		0.21	measured
Half life [h]	In air	48	estimated
	In water	168	measured
	In soil	504	estimated
	In sediment	504	estimated

Temp. [℃]	25

Emission Scenario

Scenario	emission rate [kg/h]		
case	b.air E_1	b.w. E_2	b.soil E_3
1	1000	0	0
2	0	1000	0
3	0	0	1000
4	600	300	100
5	333	333	333

Theoretical Distribution of Triacetin

Compartment	Scenario 1	Scenario 2	Scenario 3	Scenario 4	Scenario 5
	100% to air	100% to water	100% to soil	60% to air, 30% to water, 10% to soi	Equal emission air:water:soil=1: 1: 1
Air	0.9%	0.0%	0.0%	0.6%	0.3%
Water	20.0%	99.7%	12.9%	31.6%	30.1%
Soil	79.1%	0.0%	87.1%	67.8%	69.5%
Sediment	0.1%	0.3%	0.0%	0.1%	0.1%

Environmental Parameter

		volume [m3]	depth [m]	area [m2]	organic carbon	lipid content [-]	density [kg/m3]	residense time [h]
Bulk Air	air	1E+13					1.2	100
	water	2E+03						
	total	1E+13	1000	1E+10				
Bulk Water	water	2E+10					1000	1000
	susp. particles	1E+06			0.0		1500	
	fish	2E+05				0.05	1000	
	total	2E+10	10	2E+09				
Bulk Soil	air	3.2E+08					1.2	
	water	4.8E+08					1000	
	solid	8E+08			0.04		2400	
	total	1.6E+09	0.2	8E+09				
Bulk Sediment	water	8E+07					1000	
	solid	2E+07			0.06		2400	50000
	total	1E+08	0.05	2E+09				

Scenario	emission rate [kg/h]			fugacity [Pa]				concentration [g/m^3]			
case	b.air E_1	b.wat. E_2	b.soil E_3	b.air f_1	b.w. f_2	b.soil f_3	b.sed. f_4	b.air C_1	b.wat. C_2	b.soilC_3	b.sed.C_4
1	1000	0	0	4.3E-06	2.0E-08	3.0E-06	1.3E-08	3.8E-07	4.3E-03	2.1E-01	2.2E-03
2	0	1000	0	1.7E-10	4.6E-08	1.2E-10	2.9E-08	1.5E-11	9.7E-03	8.6E-06	5.1E-03
3	0	0	1000	5.1E-08	1.6E-08	4.2E-06	1.0E-08	4.5E-09	3.5E-03	2.9E-01	1.8E-03
4	600	300	100	2.6E-06	2.8E-08	2.2E-06	1.8E-08	2.3E-07	5.8E-03	1.6E-01	3.0E-03
5	333	333	333	1.4E-06	2.8E-08	2.4E-06	1.8E-08	1.3E-07	5.8E-03	1.7E-01	3.0E-03

Scenario	amount [kg]				total	transformation rate by reaction [kg/h]				transformation rate by advection [kg/h]		
case	b.air m_1	b.wat. m_2	b.soil m_3	b.sed. m_4	[kg]	b.air	b.wat. R_2	b.soil R_3	b.sed. R_4	b.air A_1	b.wat. A_2	b.sed. A_4
1	3.8E+03	8.6E+04	3.4E+05	2.2E+02	4.3E+05	5.4E+01	3.5E+02	4.7E+02	3.1E-01	3.8E+01	8.6E+01	4.5E-03
2	1.5E-01	1.9E+05	1.4E+01	5.1E+02	2.0E+05	2.2E-03	8.0E+02	1.9E-02	7.0E-01	1.5E-03	1.9E+02	1.0E-02
3	4.5E+01	6.9E+04	4.7E+05	1.8E+02	5.4E+05	6.6E-01	2.9E+02	6.4E+02	2.5E-01	4.5E-01	6.9E+01	3.6E-03
4	2.3E+03	1.2E+05	2.5E+05	3.0E+02	3.7E+05	3.3E+01	4.8E+02	3.5E+02	4.2E-01	2.3E+01	1.2E+02	6.1E-03
5	1.3E+03	1.2E+05	2.7E+05	3.0E+02	3.9E+05	1.8E+01	4.8E+02	3.7E+02	4.2E-01	1.3E+01	1.2E+02	6.1E-03

Scenario	transport rate between spheres [kg/h]						
case	air→ water	water→ air	air→ soil	soil→ air	soil→ water	water→ sed.	sed.→ water
1	1.8E+02	1.8E-02	7.3E+02	8.8E+00	2.6E+02	8.6E-01	5.5E-01
2	7.5E-03	4.1E-02	3.0E-02	3.6E-04	1.0E-02	1.9E+00	1.2E+00
3	2.2E+00	1.4E-02	8.8E+00	1.2E+01	3.5E+02	6.9E-01	4.4E-01
4	1.1E+02	2.4E-02	4.4E+02	6.5E+00	1.9E+02	1.2E+00	7.4E-01
5	6.2E+01	2.4E-02	2.5E+02	7.0E+00	2.0E+02	1.2E+00	7.4E-01

Z and D values

	Z_B [mol/m^3·Pa]	D_R [mol/Pa·h]	D_A [mol/Pa·h]
Bulk Air (1)	4.0E-04	5.8E+07	4.0E+07
Bulk Water (2)	8.0E+02	6.6E+10	1.6E+10
Bulk Soil (3)	2.7E+02	5.9E+08	0.0E+00
Bulk Sediment (4	6.6E+02	9.0E+07	1.3E+06

D_{12} [mol/Pa·h]	D_{21} [mol/Pa·h]	D_{13} [mol/Pa·h]	D_{31} [mol/Pa·h]
1.6E+08	4.0E+06	6.6E+08	1.3E+07

D_{32} [mol/Pa·h]	D_{24} [mol/Pa·h]	D_{42} [mol/Pa·h]
3.2E+08	1.6E+08	1.6E+08

Appendix : Parameters used in calculation of distribution by Mackay level III fugacity model.
(Part 2)

Physico-Chemical Properties

(water solubility : 58g/L)

Chemical		Triacetin	Method
Molecular weight		218.21	calculated
Melting point [℃]		3	unkown
Vapour pressure [Pa]		0.331	unkown
Water solubility [g/m^3]		58000	measured
log Kow		0.21	measured
Half life [h]	In air	48	estimated
	In water	168	measured
	In soil	504	estimated
	In sediment	504	estimated

Temp. [℃]	25

Emission Scenario

Scenario	emission	rate [kg/h]	
case	b.air E_1	b.w. E_2	b.soil E_3
1	1000	0	0
2	0	1000	0
3	0	0	1000
4	600	300	100
5	333	333	333

Theoretical Distribution of Triacetin

Compartment	Scenario 1	Scenario 2	Scenario 3	Scenario 4	Scenario 5
	100% to air	100% to water	100% to soil	60% to air, 30% to water, 10% to soi	Equal emission air:water:soil=1: 1: 1
Air	1.1%	0.0%	0.0%	0.7%	0.4%
Water	19.9%	99.7%	12.9%	31.7%	30.2%
Soil	79.0%	0.0%	87.1%	67.5%	69.4%
Sediment	0.1%	0.3%	0.0%	0.1%	0.1%

Environmental Parameter

		volume [m^3]	depth [m]	area [m^2]	organic carbon content [-]	lipid content [-]	density [kg/m^3]	residense time [h]
Bulk Air	air	1E+13					1.2	100
	water	2E+03						
	total	1E+13	1000	1E+10				
Bulk Water	water	2E+10					1000	1000
	susp. particles	1E+06			0.0		1500	
	fish	2E+05				0.05	1000	
	total	2E+10	10	2E+09				
Bulk Soil	air	3.2E+08					1.2	
	water	4.8E+08					1000	
	solid	8E+08			0.04		2400	
	total	1.6E+09	0.2	8E+09				
Bulk Sediment	water	8E+07					1000	
	solid	2E+07			0.06		2400	50000
	total	1E+08	0.05	2E+09				

Scenario	emission rate [kg/h]			fugacity [Pa]				concentration [g/m^3]			
case	b.air E_1	b.wat. E_2	b.soil E_3	b.air f_1	b.w. f_2	b.soil f_3	b.sed. f_4	b.air C_1	b.wat. C_2	b.soilC_3	b.sed.C_4
1	1000	0	0	5.0E-06	2.4E-08	3.6E-06	1.5E-08	4.5E-07	4.2E-03	2.1E-01	2.2E-03
2	0	1000	0	2.5E-10	5.6E-08	1.8E-10	3.5E-08	2.2E-11	9.7E-03	1.0E-05	5.1E-03
3	0	0	1000	7.1E-08	2.0E-08	5.0E-06	1.3E-08	6.2E-09	3.5E-03	2.9E-01	1.8E-03
4	600	300	100	3.0E-06	3.3E-08	2.7E-06	2.1E-08	2.7E-07	5.8E-03	1.5E-01	3.0E-03
5	333	333	333	1.7E-06	3.3E-08	2.9E-06	2.1E-08	1.5E-07	5.8E-03	1.7E-01	3.0E-03

Scenario	amount [kg]				total	transformation rate by reaction [kg/h]				transformation rate by advection [kg/h]		
case	b.air m_1	b.wat. m_2	b.soil m_3	b.sed. m_4	[kg]	b.air	b.wat. R_2	b.soil R_3	b.sed. R_4	b.air A_1	b.wat. A_2	b.sed. A_4
1	4.5E+03	8.4E+04	3.3E+05	2.2E+02	4.2E+05	6.4E+01	3.5E+02	4.6E+02	3.0E-01	4.5E+01	8.4E+01	4.4E-03
2	2.2E-01	1.9E+05	1.6E+01	5.1E+02	2.0E+05	3.1E-03	8.0E+02	2.2E-02	7.0E-01	2.2E-03	1.9E+02	1.0E-02
3	6.2E+01	6.9E+04	4.7E+05	1.8E+02	5.4E+05	9.0E-01	2.9E+02	6.4E+02	2.5E-01	6.2E-01	6.9E+01	3.6E-03
4	2.7E+03	1.2E+05	2.5E+05	3.0E+02	3.7E+05	3.9E+01	4.8E+02	3.4E+02	4.2E-01	2.7E+01	1.2E+02	6.0E-03
5	1.5E+03	1.2E+05	2.7E+05	3.0E+02	3.8E+05	2.2E+01	4.8E+02	3.7E+02	4.2E-01	1.5E+01	1.2E+02	6.0E-03

Scenario	transport rate between spheres [kg/h]						
case	air→ water	water→ air	air→ soil	soil→ air	soil→ water	water→ sed.	sed.→ water
1	1.8E+02	2.1E-02	7.2E+02	1.0E+01	2.5E+02	8.4E-01	5.4E-01
2	8.9E-03	4.9E-02	3.5E-02	4.9E-04	1.2E-02	1.9E+00	1.2E+00
3	2.5E+00	1.7E-02	1.0E+01	1.4E+01	3.5E+02	6.9E-01	4.4E-01
4	1.1E+02	2.9E-02	4.3E+02	7.5E+00	1.9E+02	1.2E+00	7.4E-01
5	6.1E+01	2.9E-02	2.4E+02	8.1E+00	2.0E+02	1.2E+00	7.4E-01

Z and D Values

	Z_B [$mol/m^3 \cdot Pa$]	D_R [$mol/Pa \cdot h$]	D_A [$mol/Pa \cdot h$]
Bulk Air (1)	4.0E-04	5.8E+07	4.0E+07
Bulk Water (2)	8.0E+02	6.6E+10	1.6E+10
Bulk Soil (3)	2.7E+02	5.9E+08	0.0E+00
Bulk Sediment (4	6.6E+02	9.0E+07	1.3E+06

D_{12} [$mol/Pa \cdot h$]	D_{21} [$mol/Pa \cdot h$]	D_{13} [$mol/Pa \cdot h$]	D_{31} [$mol/Pa \cdot h$]
1.6E+08	4.0E+06	6.6E+08	1.3E+07

D_{32} [$mol/Pa \cdot h$]	D_{24} [$mol/Pa \cdot h$]	D_{42} [$mol/Pa \cdot h$]
3.2E+08	1.6E+08	1.6E+08

Environmental parameter

		volume [m^3]	depth [m]	area [m^2]	organic carbon content [-]	lipid content [-]	density [kg/m^3]	residence time [h]
bulk air	air	1E+13					1.2	100
	particles	2E+03						
	total	1E+13	1000	1E+10				
bulk water	water	2E+10					1000	1000
	particles	1E+06			0.04		1500	
	fish	2E+05				0.05	1000	
	total	2E+10	10	2E+09				
bulk soil	air	3.2E+08					1.2	
	water	4.8E+08					1000	
	solid	8E+08			0.04		2400	
	total	1.6E+09	0.2	8E+09				
bulk sediment	water	8E+07					1000	
	solid	2E+07			0.06		2400	50000
	total	1E+08	0.05	2E+09				