FOREWORD INTRODUCTION

GLYCEROL

CAS N°: 56-81-5

SIDS Initial Assessment Report

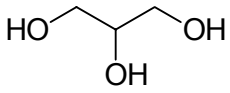
For

SIAM 14

Paris, France, 26-28 March 2002

1. Chemical Name:	Glycerol
2. CAS Number:	56-81-5
3. Sponsor Country:	United Kingdom SIDS Contact Point: Dr Steve Robertson Environment Agency National Centre for Ecotoxicology & Hazardous Substances Isis House, Howbery Park, Wallingford OX10 8BD, UK Fax: +44 1491 828 556 e-mail: steve.robertson@environment-agency.gov.uk
4. Shared Partnership with:	
5. Roles/Responsibilities of the Partners:	
• Name of industry sponsor /consortium	The industry contact point is Dr L. Hughes, ICI Uniqema, Wilton Centre, Wilton, Redcar, United Kingdom
• Process used	
6. Sponsorship History	
• How was the chemical or category brought into the OECD HPV Chemicals Programme ?	This substance is sponsored by the UK under the ICCA Initiative and is submitted for first discussion at SIAM 14.
7. Review Process Prior to the SIAM:	The industry consortium collected new data and prepared the updated IUCLID, and draft versions of the SIAR and SIAP. UK government peer-reviewed the documents, audited selected studies and conducted separate literature searches.
8. Quality check process:	
9. Date of Submission:	February 2002
10. Date of last Update:	
11. Comments:	No testing (X) Testing ( )

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	56-81-5
Chemical Name	1,2,3-Propanetriol (Glycerol)
Structural Formula	

RECOMMENDATIONS

The chemical is currently of low priority for further work.

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

All SIDS health endpoints are fulfilled. It should be noted that much of the data on glycerol is historic and of rather low quality compared to current guideline requirements. Nevertheless, there is an overall consistency within the available data that allows conclusions to be drawn. Glycerol is absorbed following ingestion and metabolised by glycerokinase in the liver to carbon dioxide and water or incorporated in the standard metabolic pathways to form glucose and glycogen. The weight of evidence indicates that glycerol is of low toxicity when ingested, inhaled or in contact with the skin.

Glycerol is of a low order of acute oral and dermal toxicity with LD_{50} values in excess of 4000 mg/kg bw. At very high dose levels, the signs of toxicity include tremor and hyperaemia of the gastro-intestinal -tract. Skin and eye irritation studies indicate that glycerol has low potential to irritate the skin and the eye. The available human and animal data, together with the very widespread potential for exposure and the absence of case reports of sensitisation, indicate that glycerol is not a skin sensitiser.

Repeated oral exposure to glycerol does not induce adverse effects other than local irritation of the gastro-intestinal tract. The 2-year study of Hine (1953) was chosen to establish the overall NOEL after prolonged treatment with glycerol of 10,000 mg/kg bw/day (20% in diet), which is in agreement with the findings in other studies. At this dose level no systemic or local effects were observed. For inhalation exposure to aerosols, the NOAEC for local irritant effects to the upper respiratory tract is 165 mg/m3 and 662 mg/m3 for systemic effects.

Glycerol is free from structural alerts, which raise concern for mutagenicity. Glycerol does not induce gene mutations in bacterial strains, chromosomal effects in mammalian cells or primary DNA damage *in vitro*. Results of a limited gene mutation test in mammalian cells were of uncertain biological relevance. *In vivo*, glycerol produced no statistically significant effect in a chromosome aberrations and dominant lethal study. However, the limited details provided and the absence of a positive control, prevent any reliable conclusions to be drawn from the *in vivo* data. Overall, glycerol is not considered to possess genotoxic potential.

The experimental data from a limited 2 year dietary study in the rat does not provide any basis for concerns in relation to carcinogenicity. Data from non-guideline studies designed to investigate tumour promotion activity in male mice suggest that oral administration of glycerol up to 20 weeks had a weak promotion effect on the incidence of tumour formation.

No effects on fertility and reproductive performance were observed in a two generation study with glycerol administered by gavage (NOAEL 2000 mg/kg bw/day). No maternal toxicity or teratogenic effects were seen in the rat, mouse or rabbit at the highest dose levels tested in a guideline comparable teratogenicity study (NOEL 1180 mg/kg bw/day).

Environment

All SIDS environmental endpoints are fulfilled. It should be noted that much of the data on glycerol is historic and of rather low quality compared to current guideline requirements. However, the weight of evidence indicates that glycerol is of low toxicity to aquatic organisms and this conclusion is supported by QSAR predictions. The lowest LC50 for fish is a 24-h LC_{50} of >5000 mg/l for *Carassius auratus (*Goldfish*)* and for aquatic invertebrates, a 24h EC50 of >10000 mg/l for *Daphnia magna* is the lowest EC50. Several tests on algae are available, which suggest very low toxicity to a range of species, however their validity is uncertain. A QSAR prediction for the 96h EC50 to algae was 78000 mg/l. No toxicity towards the microorganism *Pseudomonas putida* was observed at 10000 mg/l after exposure for 16 hours. No long-term aquatic toxicity data is available. Screening studies are available on frog and carp embryos which indicate some effects on growth and hatching rates respectively at very high concentrations of glycerol, >7000 mg/l. However, their ecological relevance is not clear.

In view of the limited robustness of the studies present, it was decided to derive a tentative PNEC for aquatic organisms using QSAR predictions of acute toxicity. The tentative PNEC for aquatic organisms is calculated to be 780 mg/L, based on the lowest QSAR value (calculated for algae EC_{50} 77,712 mg/L) and applying an assessment factor of 100 in accordance with the OECD guidance. An assessment factor of 1000 for the aquatic PNEC compartment could also be considered to reflect the uncertainty in the use of QSAR-predicted values. There are no sediment or terrestrial effect data, but partitioning to both soil and sediment is expected to be very low, based on the very low log K_{ow} of glycerol. The equilibrium partitioning method was used to calculated tentative PNECs for soil and sediment based on the $PNEC_{aquatic}$ of 777 mg/l, $PNEC_{sediment}$ = 479 mg/kg wwt and $PNEC_{soil}$ = 92.1 mg/kg wwt.

Exposure

The worldwide market for glycerol for the year 2000 was 500,000 tonnes. Glycerol has widespread use and can be found in industrial, professional and consumer products. Glycerol is used as a constituent in numerous products and as an intermediate in industrial applications for the manufacture of products such as soaps/detergents and glycerol esters. It is found in consumer products such as pharmaceuticals, cosmetics, tobacco, food and drinks and is present in numerous other products such as paints, resins and paper.

There is a potential for occupational exposure through inhalation and skin contact. Consumers may be exposed to glycerol by the oral and dermal routes of exposure. Smoking may lead to an additional glycerol uptake by inhalation.

There is potential exposure to the aquatic compartment arising from the production and processing of this substance. Glycerol will enter the aqueous and terrestrial environment from end uses such as in consumer products and down hole lubricants for oil and gas fields.

Glycerol is a liquid with a calculated vapour pressure of 0.000106 hPa (at 25ºC), is fully miscible with water and has a Log K_{ow} of –1.76 (measured). It has a calculated half-life for photo-oxidation of ~7 hours and is not susceptible to hydrolysis. The experimental data indicate that glycerol is readily biodegradable under aerobic conditions. Fugacity modelling (Mackay Level III) predicts that glycerol will partition to the aquatic compartment (100%). Based on the low Log Kow, it has a low potential for sorption to soil and is not expected to bioaccumulate.

NATURE OF FURTHER WORK RECOMMENDED

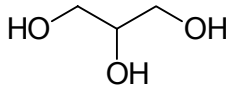
No further work is indicated, because of the low hazard potential of this substance.

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number: 56-81-5
Chemical Name: 1,2,3-Propanetriol
Molecular Formula: $C_3H_8O_3$
Structural Formula:



Molecular Weight: 92
Synonyms: Glycerol; glycerine; glycerin; glycyl alcohol; trihydroxypropane, 1,2,3-trihydroxypropane; Citifluor AF 2; Glycerin mist; Glyceritol; Clyzerin, wasserfrei (German); Grocolene; Moon; Osmoglyn; Star

1.2 Physico-Chemical properties

Glycerol (CAS no. 56-81-5) is a liquid at room temperature having the following physical–chemical properties and characteristics, which have been obtained from various reference sources (see the IUCLID dataset for further details).

Table 1 Summary of physico-chemical properties

PROPERTY	VALUE
Physical form	Liquid
Purity	95 – 99.5% (water as an impurity with trace levels of polyglycerol)
Melting point	18°C
Boiling point	290°C at 1013 hPa
Relative density	1.26 at 20°C
Vapour pressure	0.000106 hPa at 25 Deg C (calculated) and 0.0033 hPa at 50°C (measured)
n-octanol –water partition coefficient	log K_{ow} - 1.76
Water solubility	Miscible
Dissociation constant	0.07E-13
Flash point	160°C
Autoflammability	393°C
Viscosity	1410 mPa s at 20°C
Surface tension	63.4 mN/m at 20°C

For vapour pressure a measured value at 50°C is available. At this temperature vapour pressure is very low. It is expected that at room temperature this value will even be lower. This is confirmed by

model calculations with the Syracuse programme (EPIWIN vs 3.04) indicating a vapour pressure of 0.000106 hPa at 25°C. This value is used in model calculations.

Model calculations on the octanol-water partition coefficient differ by about one order of magnitude (see IUCLID dataset). Since a measured value of Log Kow = -1.76 is available, this has been selected as the key value. This measured value is supported by a QSAR prediction using KOWWIN version 1.66, predicted Log Kow = - 1.65.

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production Volumes and Use Pattern

Estimated Production or Import Volume

In 2000 the estimated world production of glycerol was 500,000 tonnes. The amount imported and/or produced in Europe was 227,000 tonnes for 1999 and for the UK, around 28,000 tonnes (data from APAG).

Uses

Glycerol has a ubiquitous use pattern and can be found in industrial, professional and consumer products. Glycerol is used as a constituent in numerous products and as an intermediate in industrial applications for the manufacture of products such as soaps/detergents and glycerol esters. It is found in consumer products such as pharmaceuticals, cosmetics, tobacco, food and drinks and is present in numerous other products such as paints, resins and paper. For example, it is used as a down hole lubricant in oil and gas fields and as a wetting agent in pesticide formulations. There is no single use which dominates the use pattern.

Table 2.1.1 gives an approximate breakdown of end uses and is derived from industry data in Europe (APAG, 1999) and from the Danish Products Register. More detailed information is available in the SIDS Dossier.

The NIOSH NOES Survey of 1981 – 1983 estimated that 137,302 workers were potentially exposed to glycerol in the United States.

The number of manufacturing and processing sites for glycerol will be significant based on the ubiquitous use of this substance and the source and quantity of releases will vary depending on the nature and pattern of use.

Table 2.1.1: Overview of Use

Type of end use	% of production volume (approx.)	Specific applications
Pharmaceuticals	<10	Excipient and formulation aid.
Chemical intermediate, nitration , and esters	15	Chemical synthesis
Cosmetic and Toiletries	20	Cosmetics including fragrances, bath and hair preparations, eye makeup, soaps and skin care preparations.
Resins, polyols and polyurethanes	20	Intermediate and monomer
Industrial Fluids	<10	Antifreezes, lubricants and hydraulic fluids
Tobacco	<10	Humectant
Cellulose films	<10	Intermediate.
Food	<10	Food additive
Other chemical uses	<10	

Table 2.1.2: Typical Routes of Exposure

Environmental exposure	Aquatic	Production
	Aquatic/terrestrial	Processing/ Industrial use
	Aquatic	Consumer use
Consumer exposure	Dermal	Cosmetics and pharmaceuticals
		Paints, printing inks and resins
		Paper and plastics
	Oral	Pharmaceuticals
		Cosmetics
		Cellulose films (meat casing, sausage skin)
		Food and drinks
	Inhalation	Smoking
Worker exposure	Inhalation	Production/Processing
	Dermal	Paints, printing inks, resins

2.2 Environmental Exposure and Fate

Glycerol is completely miscible with water, has a vapour pressure of 0.000106 hPa at 25°C and a calculated Henry's Law constant of 9.75E-6 Pa.m3/mol. The Henry's Law constant was calculated using the maximum solubility permitted in the EUSES model (100,000 mg/L). The following values were used in environmental fate and distribution modelling:

Parameter	Value	Discussion
Vapour pressure	0.000106 hPa	This value is obtained from Syracuse EPIWIN. Measured values were all obtained at higher temperatures. The differences have a negligible effect on modelling output.
Solubility	100,000 mg/L	Glycerol is completely miscible. For modelling the maximum solubility permitted in EUSES has been used.
Log K_{ow}	-1.76	Measured value
Biodegradability	readily	Based on a test according to OECD 301.

2.2.1 Sources of Environmental Exposure

During production, processing and use glycerol may be released to the environment.

There will be small amounts of glycerol released from the production and processing, which will typically be treated by the site wastewater treatment plant. Glycerol will enter the aqueous and terrestrial environment from end uses such as in cosmetics and pharmaceutical products and down hole lubricants for oil and gas fields.

There is little likelihood of emissions to the atmosphere from production, processing or downstream use.

2.2.2 Photodegradation

The calculated half-life for the photo-oxidation (reaction with hydroxyl radicals) of glycerol in air is 6.8 hours (EPIWIN vs 3.04).

2.2.3 Stability in Water

The stability of glycerol in water was not assessed. This is considered acceptable, because the molecule does not contain functional groups that are expected to react with water.

2.2.4 Transport between Environmental Compartments

From the EQC model (Mackay level III), it can be deduced that 100% of glycerol will end up in the water phase. Negligible amounts will be distributed towards soil, air and sediment.

Results of fugacity modelling	
Compartment	Distribution
Water	100 %
Air	0 %
Soil	0 %

From the measured log K_{ow} of −1.76 the log K_{oc} was determined to be 0.65 (EU Technical Guidance Document QSAR for alcohols, chapter 4 section 4.3, [1]) indicating a low potential for sorption to soil.

The distribution in a sewage treatment plant has been estimated using the SimpleTreat model to be 87% degraded, 13% to water, based on ready biodegradability, log Kow = -1.76, water solubility = $1x10^5$ mg/L and vapour pressure =0.000106 hPa.

Conclusion

Based on the relevant physical-chemical properties and the fact that glycerol is readily biodegradable, glycerol will partition primarily to water (Mackay level III modelling shows 100% in water). In the sewage treatment plant glycerol will undergo a substantial degree of degradation.

2.2.5 Biodegradation

A number of biodegradation assays have been carried out with glycerol. In a Closed Bottle test (performed according to OECD 301) 92% biodegradation was reported after 30 days. More than 60% biodegradation measured as ThOD was reached within the 10-day window (Henkel 2001). Glycerol is considered to be readily biodegradable.

In addition, the relationship between BOD_5, COD and ThOD was determined. The standard dilution method for a period of 5 days (BOD_5) and the standard potassium dichromate method (COD) were used for the determinations. Both tests were performed according to APHA and ASTM guidelines, respectively. BOD_5 was 82% of ThOD and 86% of COD. It can be concluded that glycerol has the potential to be rapidly biodegraded in a wastewater treatment plant (Bridie 1979). The BOD5/COD ratio is 0.86 and the fact that it is >0.5 further supports the ready biodegradability of glycerol.

[1] LogKoc = 0.39 logKow + 0.50 (alcohols)

Several other studies using adapted activated sludge or effluent from a sewage treatment plant demonstrates rapid biodegradation of glycerol (Matsui 1975, Matsui 1988, Pitter 1976, and Belly 1976).

Under anaerobic conditions, using microorganisms adapted to acetate, glycerol was biodegradable (Chou 1978).

Conclusion

Glycerol is considered to be readily biodegradable in the aquatic environment. Pre-adapted micro-organisms can degrade glycerol rapidly under both aerobic and anaerobic conditions.

2.2.6 Bioaccumulation

The calculated bioconcentration factor is 3.162 (EPIWIN vs 3.04).

Conclusions

Based on Log K_{ow} -1.76, glycerol will have a low bioaccumulation potential and is not expected to bioaccumulate.

2.3 Human Exposure

2.3.1 Occupational Exposure

There is potential for occupational exposure through inhalation and dermal exposure. Occupational exposure to glycerol can occur during production, during processing or during use of products containing glycerol. The dermal route is considered to be the most relevant exposure route although inhalation exposure may occur to aerosols released from the spray application of resins or paints

For occupational exposure to glycerol mist, typically an exposure limit is applied based on the low toxicity of the aerosol. This value is 10 mg/m^3 as an 8-hour time weighted average. (Belgium, Netherlands, Ireland, USA, UK).

2.3.2 Consumer Exposure

Glycerol is used extensively in cosmetics, toiletries and pharmaceutical products. It is used as a component in formulations mainly to provide emolliency and other performance benefits to the formulation. Consumer exposure to glycerol will occur principally through its use in food, cosmetics, toiletries and pharmaceuticals mainly through dermal exposure although oral exposure will occur as a consequence of use in foods as a direct food additive and indirectly from cellulose films used for food applications, orally administered drugs and oral hygiene products. There will be limited consumer dermal exposure through contact with paints, printing inks, resins and matrices containing glycerol.

- Glycerol has undergone review and approval for use as a direct food additive, indirect food additive and is recognised as generally safe for use in food. The use in food has been subject to review by expert assessment by organisations such as WHO, JECFA and the European SCF. (Joint FAO/WHO Expert Committee on Food Additives, 19th report. WHO Food Additive Series.8 1975.)
- SCF Reports of the Scientific Committee for Food, 33rd Series, European Commission, 1995.

The use of glycerol in tobacco products may lead to inhalation exposure as a constituent of tobacco smoke.

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

Data from studies in humans and animals indicate glycerol is rapidly absorbed in the intestine and the stomach, distributed over the extracellular space (Lin 1977, Tourtelotte 1970) and excreted. Glycerol is phosphorylated to alpha-glycerophosphate by glycerol kinase predominantly in the liver (80-90%) and kidneys (10-20%) and incorporated in the standard metabolic pathways to form glucose and glycogen (Tao 1983, Lin 1977). Glycerol kinase is also found in intestinal mucosa, brown adipose tissue, lymphatic tissue, lung and pancreas. Glycerol may also be combined with free fatty acids in the liver to form triglycerides (lipogenesis) which are distributed to the adipose tissues. The turnover rate is directly proportional to plasma glycerol levels (Bortz 1972).

3.1.2 Acute Toxicity

Studies in Animals

Inhalation

No data available

Dermal

No deaths were observed in a group of 6 rabbits after occlusive dermal application for 8 hours of synthetic or natural glycerol at 18,700 mg/kg bw. (Hine 1953).

Oral

In a study with limited reporting, twelve female rats received 27,260 mg natural or synthetic glycerol/kg bw by gavage (Jansson and de Rooy). Cageside observations included muscle spasms and convulsions and survivors appeared normal within 2.5 h of dosing. The number of deaths was not reported. Macroscopic examination of decedents and survivors showed hyperaemia of the pylorus, small intestine and cerebral meninges (3 animals), congestion of the lungs and pale spleen. For this study an LD_{50} value of 27,200 mg/kg bw was reported (Hine 1953). In other studies, with limited reporting, LD_{50}s of >25,300 and >24, 000 mg/kg were derived for Sprague-Dawley rats (Bartsch 1976) and female Fischer 344 rats (Clark 1979), respectively.

Hine (1953) also investigated the acute toxicity of synthetic or natural glycerol in mice and guinea pigs. Again the reporting was limited, however both species showed similar clinical signs (tremor and convulsions) and macroscopic findings (hyperaemia of pylores and small intestine, pale spleen, lung congestion). The LD_{50}s for mice and guinea pigs were reported to be 23, 000 and 10, 000 mg/kg, respectively.

A number of acute oral toxicity LD_{50} values for the rat (range from >5000 to 58400 mg/kg) and the mouse (4,250 to 38,000 mg/kg) are reported in the scientific literature (see table 3.1.2), although where values are very similar, it is not always clear whether or not these are from independent studies. Original reports for several secondary reported LD_{50} values were not available. The LD_{50} values reported are consistent with the range of values found in the available literature except in one case, where an oral LD_{50} value of 4250 mg/kg was reported for the mouse (Anon. 1977).

A number of studies conducted in several species on the acute oral and dermal toxicity of glycerol are included in table 3.1.2. Although the additional studies in table 3.1.2 are poorly reported, the LD_{50} values are generally similar to those obtained by Hine (1953)

Other Routes of Exposure

In rats and mice, LD_{50} values for glycerol were between 4,420 and 10,100 mg/kg bw after intraperitoneal administration and 4250-6700 (rabbit LD_{50} = 53000) mg/kg bw after intravenous administration. Glycerol is much more toxic after subcutaneous administration (LD_{50} 91-100 mg/kg bw). The key finding is that of haemolysis. Further details are available in the SIDS dossier.

Table 3.1.2 Summary of acute oral and dermal toxicity data (key studies emboldened)

Species	LD_{50} (mg/kg bw)	Reference
ORAL		
Rat	**27,200**	**Hine 1953**
Rat	**>25,300**	**Bartsch 1976**
Rat	>24,000	Clark 1979
Rat	26,000	Anderson 1950
Rat	27,500	Smyth 1941
Rat	>25,000	Tao 1983
Rat	58,400	Bornmann 1955, Loeser 1954,
Rat	>5000, 15750, 27500, 26250-28750,	Janssen and de Rooy
Rat	>10000, 12600	Anon, 1945
Mouse	**23,000**	**Hine 1953**
Mouse	**37,950**	**Bartsch 1976**
Mouse	4,250	Anon., 1977
Mouse	26,000	Anderson 1950
Mouse	38,000	From Bartsch 1976
Mouse	>38,000	Tao 1983
Mouse	37,763	Bornmann 1955, Loeser 1954
Mouse	25,888	Bornmann 1955, Loeser 1954
Mouse	12,500	Latven 1939
Mouse	22400, 38000, 31250, 28 000	Janssen and de Rooy
Rabbit	27000	Anon, 1959
Guinea pig	10,000	Hine 1953
Guinea pig	7,750	Smyth 1941, Sonntag
DERMAL		
Rabbit	**> 18,700 mg/kg bw**	**Hine 1953**

Studies in Humans

A single human 'lowest-lethal-dose' (LDLo) value is reported to be 1428 mg/kg (Anon., 1969). However, the reliability of this information is unknown, as the original literature reference was not available to the reviewer.

Anecdotal reports indicate that subcutaneous or intraperitoneal injection of glycerol in humans, results in albuminuria, haemoglobinuria, anaemia and renal damage.

Conclusion

Glycerol is of very low acute toxicity to mammals. The range of acute oral LD_{50} values derived from studies in experimental animals is between >4,000 and < 38,000 mg/kg, with the majority of values being between 23,000 and 38,000 mg/kg. For acute dermal toxicity a single LD_{50} of >18,700 mg/kg for rabbits is available. No information is available on the acute toxicity of inhaled glycerol. Glycerol is more toxic when administered intravenously, intraperitoneally or subcutaneously.

3.1.3 Irritation

Skin Irritation

There were no studies conducted to modern OECD guidelines. In a study conducted using contemporary protocols but prior to GLP standards it was demonstrated that dermal application of 0.5-mL glycerol to the rabbit's skin for 24 hours did not lead to signs of irritation 24 and 72 hours after application. Irritation scores according to Draize scale were 0-0.4, compared to a maximum score of 30 (Weil 1971).

Another test with similar methodology gave a similar outcome (Clark 1979) and there was no evidence of irritation in rabbits following repeated applications of 4 mL over 30% of the surface area 8 h/day for 90 days (Hine 1953).

Conclusion

No OECD guideline studies are available, however, **t**he data available indicate that glycerol is not irritating when in contact with the skin.

Eye Irritation

In a study conducted to a contemporary protocol and prior to GLP standards, 0.1 mL undiluted glycerol was instilled in the eyes of 6 rabbit) caused no evidence of irritation after 1, 24 and 72 hours and after 7 days. The overall irritation score using the Draize system was 0-2 on a scale up to a maximum of 110 (Weil 1971). In another study of similar design, using 4 rabbits, irritation of unspecified severity observed at 1 h after instillation of glycerol was absent after 24 h (Hine 1953). Another test with a similar design on a glycerol/water mixture (not further specified) gave a similar result and reactions, which were reversible within 24 h (Clark 1979). Due to the methodology and scoring systems used in these non-OECD guidelines it is not possible to directly compare the results to internationally agreed criteria for assessing eye irritation. However, it is apparent from these studies that glycerol has a very low potential to irritate the eyes.

In an OECD guideline study reported in a secondary source, slight to moderate corneal irritation was observed in all rabbits after 1h, however the effects were found to regress after 24h and were fully reversed by 48h (Janssen and de Rooy).

In a secondary source, there is an anecdotal report that in workers that glycerol caused a burning and stinging sensation with tear production but without injury (Grant 1974).

Conclusion

The data available indicate that glycerol is not irritating to the eyes.

3.1.4 Sensitisation

Studies in Animals

No studies conducted to current OECD guidelines are available. A group of male 24 Guinea pigs receiving 10 0.1 mL injections of 0.1 % synthetic or natural glycerol in isotonic saline every alternate day over 20 days showed no indication of sensitisation following challenge with further 0.05 mL injections of 0.1 % glycerol after a 2 week exposure-free period (Hine 1953). However, it is unclear from the protocol and reporting whether or not the study was capable of detecting sensitisation since it was not apparent whether maximal dose-levels were used, and the use of positive controls or a measure of strain sensitivity were not reported.

Human experience

Data is available from a briefly reported study, in which skin patch tests were conducted on workers in a foam rubber factory. No sensitising effects of a glycerol/water mixture became apparent (El-Nagdy 1973). Considering the extensive, widespread dermal exposure to glycerol in preparations repeatedly applied to the skin, the absence of case reports of humans showing skin reactions is consistent with glycerol having a very low skin sensitisation potential.

Conclusion

Based on the available information, there is no human or animal data that indicates glycerol to be a skin sensitiser. Considering the extensive, widespread dermal exposure to glycerol in preparations repeatedly applied to the skin, the absence of case reports of humans showing skin reactions is consistent with glycerol having a very low skin sensitisation potential.

3.1.5 Repeated Dose Toxicity

Studies in Animals

Inhalation

Two key studies were identified which had some limitations in the reporting and of the study protocols compared to current OECD guidelines (a reduced number of haematology and clinical chemistry investigations, and range of organs examined). However, these inhalation studies provide useful information as they used test and control groups of rats exposed to respirable aerosols of glycerol at measured concentrations and histopathological examination of a range of tissues including the respiratory tract was performed.

Sprague-Dawley rats (10/sex/treatment) were exposed nose-only to a respirable aerosol of glycerol during 14 days (5 days/week, 6 hours/day). The mean exposure concentrations achieved were 0, 1000, 1930 and 3910 mg/m^3. The mass median aerodynamic diameter (MMAD) was reported to be < 1.5 micrometres. Two males at 1000 mg/m^3 and 1 male and 1 female at 2000 mg/m^3 died (which were incidental to treatment). Body weight gain was decreased in all treated animals. This effect may be attributed to stress due to nose-only exposure. Serum glucose was decreased in treated females, but since it did not appear in males and no relationship with concentration was established, the biological relevance of this effect is not considered to be of toxicological significance. There was no effect on lung, liver, kidney, brain and heart weight nor any macroscopic findings reported. Histopathological examination of the respiratory tract, liver, kidneys and heart of controls and high dose animals revealed an increased incidence of minimal to mild squamous metaplasia of the epiglottis in all treated animals (1/10, 13/18, 16/19 and 13/14 at 0, 1000, 1930, and 3910 mg/m3, respectively). The frequency of animals with mild metaplasia was greatest at the highest exposure

concentration. No systemic effects were seen at the highest dose tested (Anderson 1950, Renne 1992).

In a further study by the same authors using a similar protocol, nose-only exposure of rats (SD 15/sex/treatment) 6h/day, 5d/w for 13 weeks to a respirable aerosol (MMAD <2 micrometres) of glycerol at measured concentrations of 0, 33, 165 and 662 mg/m^3 led to decreased triglyceride levels in males at 33 (34%) and 165 mg/m^3 (22%). This effect appears to be of little toxicological significance as there was no dose-response relationship and was seen in males only. There were no treatment related effects on cageside observations, haematology, organs weights or gross pathology. Microscopic evaluation of the tissues showed "minimal" (10 animals) or "mild" (one animal) squamous metaplasia of the epiglottis in 11 animals in total at the highest concentration. Since the effect on triglycerides did not show a relationship with concentration, was seen in males only and in the absence of any systemic target organ toxicity, the biological relevance of this effect is not considered to be of toxicological significance. Based on an increased incidence of "minimal" to "mild" squamous metaplasia of the epiglottis, the NOAEC for local irritant effects to the upper respiratory tract is 165 mg/m^3 and 662 mg/m^3 for systemic effects (Anderson 1950, Renne 1992).

Oral

No OECD guideline studies are available although there are a large number of older studies available. In the best available dietary study, groups of 22 rats (Long-Evans)/sex/treatment received 5, 10 and 20% glycerol (natural or synthetic) in their diet (males 2000, 4000 and 8000 mg/kg bw; females 2500, 5000 and 10000 mg/kg bw) for 2 years. Routine clinical observations were made, and bodyweight and food consumption was determined weekly. Deviations from the OECD guideline included the absence of clinical chemistry investigation and a limited range of haematological and urinary analyses were performed. A limited range of organs was investigated at necropsy and the liver, spleen, adrenals, small intestine, gonads and urinary bladder were examined microscopically. Glycogen and fat content of the liver was determined in surviving rats from the 0 and 20 % dose groups. No individual data were reported. For high dosed animals treatment was discontinued after 1 year (reason not stated in report, presumably as an 'interim' assessment for carcinogenicity; 3.1.7). No data on mortality and clinical observations were reported. Food consumption was slightly increased in males treated with 5 and 10% natural glycerol. Incidental observations considered by the report-authors to be without relationship to treatment included: bronchiectasis, pneumonia, pulmonary abcesses, hydronephrosis and pyelonephritis. Although the results were not described in detail, based on this limited dietary study it can be concluded that no adverse effects were observed at up to 10,000 mg/kg bw (Hine 1953).

A number of other studies have been incorporated in Table 3.1.5. These studies are considered less reliable indicators of the systemic effects of glycerol following repeated administration, mainly because of limited toxicity assessments and/or deficient experimental design. The effects they do report are consistent with those observed in the key studies and as such they may contribute to the overall assessment of toxicity of glycerol.

Table 3.1.5 Repeated dose oral studies (excluding key study)

Study type	Species	No. of animals	Doses(mg/kg)	Effects	NOAEL (mg/kg)	Reference
DIET						
28-day	Rat	n.i.	20% suppl. diet (= 8824 mg/kg bw)	No abnormal findings	-	Stoewsand 1966
50-wk	Dog	3	35% in diet (no reference value available to convert to mg/kg bw)	BWG↓	-	Johnson 1933
WATER						
3-mnth	Rat	n.i.	1-20% solution in drinking water (= 667-13340 mg/kg bw)	At 20%: Mortality 2/12 rats at top dose; initial growth and development ↓ (with recovery)	-	Loeser 1954, Bornmann 1955
6-mnth	Rat	5 females/ treatment	5% (natural or synthetic) in drinking water (= 3335 mg/kg bw)	Mortality 1/5 (synthetic) Small thymus and spleen, calcified kidney masses	-	Anderson 1950
GAVAGE						
6-mnth	Rat	n.i.	Oral 10 ml of 50% solution/ kg bw (= 6300 mg/kg bw)	No abnormal findings	-	Loeser 1954
50-day	Rat	n.i.	Oral 10 ml of 20% solution/kg bw (= 2520 mg/kg bw)	No abnormal findings	-	Loeser 1954
44-day	Rat	20 males/ treatment	1, 5, 10, 20% in water (gavage) (=115-2300 mg/kg bw)	Mortality 15% in all treatment groups and controls	-	Fisher 1949
44-day	Rat	20 males/ treatment	~1260 mg/kg bw (gavage)	No treatment related effects	-	Fisher 1949
21-day	Rat	8 males/ treatment	~1525 mg/kg bw (gavage)	Mortality at 1525 mg/kg 5/8, O2 consumption ↓	-	Fisher 1949
3-day	Rat	10 females/ treatment	950, 1900 and 3800 mg/kg bw (gavage)	GI-tract: hyperaemia, petechial haemorrhage or erosions (DR)	LOAEL (local) 950 mg/kg bw	Staples 1967

Study type	Species	No. of animals	Doses(mg/kg)	Effects	NOAEL (mg/kg)	Reference
3-day	Dog	1-2/ treatment	950, 1900 and 3800 mg/kg bw (gavage)	GI-tract: hyperaemia, petechial haemorrhage or erosions (DR)	NOAEL (local) 950 mg/kg bw	Staples 1967
30-40 day	Guinea pig	10	Oral 5 ml of 50% solution (= 6300 mg/kg bw)	All animals died RBC↓		Ostwald 1962

↑ = increase
BWG = body weight gain
CHO = cholesterol
CL = chloride
n.i.= not indicated
↓ = decrease
RBC=red blood cells
UV= urinary volume
WC = water consumption
DR = dose related

Human experience

In cases where glycerol was given intravenously to control cerebral oedema, there were no identified toxic signs attributed to glycerol (Meyer 1971). Chronic ingestion of glycerol gave increased levels of triglycerides (MacDonald 1970).

Conclusion

A considerable number of studies have been performed. However, many of these studies are considered to be of indeterminable reliability due to deficiencies in reporting or methodology, primarily because they were performed before internationalised guidelines were available.

Based on the studies of better quality, it can be concluded that repeated oral exposure by gavage to glycerol does not induce adverse effects other than local irritation of the gastro-intestinal tract. The lowest effect value was 950 mg/kg bw and found in a 3 day study with rats (Staples 1967). The design of this study was considered not to be representative for a repeated dose study, because the duration of exposure was only 3 days and only irritant properties were investigated. The 2-year study of Hine (1953) was chosen to establish the overall NOAEL after prolonged treatment of rats with glycerol. It was concluded that the NOEL is 10,000 mg/kg bw (20% in diet), which is in agreement with most of the findings reported in Table 3.1.3. At this dose level no systemic or local effects were observed in the parameters investigated. However, it is noted that gavage dosing with bolus administration of glycerol may enhance the local toxicity to the gastrointestinal tract compared with continuous administration via the diet, however, toxic effects are still only seen at relatively high dose levels and do not raise concern

For inhalation exposure, irritant effects were observed at 662 mg/m^3. No other target organ involvement was identified. The NOAEL for local effects on the respiratory tract following exposure by inhalation is 165 mg/m^3.

3.1.6 Mutagenicity

In vitro Studies

Glycerol did not induce mutations in bacteria in an Ames test, which used four *Salmonella* typhimurium strains both with and without metabolic activation (rat and hamster S-9). The test was performed in three different laboratories (Haworth 1983). No mutagenic effects were reported in an additional Ames test with 5 strains and rat S-9 as metabolic activation system (Doolittle 1988).

Glycerol was considered to be negative by the authors in a mammalian cell gene mutation test (HGPRT) since the increased number of mutations at the two highest dose levels was considered to be biologically irrelevant, because no concentration dependence was seen (Doolittle 1988). However, it is unknown why the concentrations tested were not maximised to those recommended in the OECD guideline and hence, the result is of uncertain biological relevance.

Chromosomal damage was investigated in the chromosomal aberration test using cultured mammalian cells (Chinese hamster ovary), which was reported as negative. In this test an isolated increase in number of aberrations was seen at 200 ug/mL (with metabolic activation). This finding was considered to be of no biological relevance, since there was no relationship with the concentration tested (Doolittle 1988). Glycerol did not induce sister chromatid exchanges in CHO cells (Doolittle 1988). In rat hepatocytes, the number of nuclear grains did not differ between glycerol treated and control cells (Doolittle 1988). Therefore, it can be concluded that no unscheduled DNA synthesis occurred.

The results of a bacterial recombination assay were positive, which may be attributed to the interference of glycerol with cellular surfaces or with osmotic effects (Nonakae 1989).

Other *in vitro* tests available are summarised in table 3.1.6.

Table 3.1.6 *In vitro* mutagenicity tests

Test type	Result	Reference
Ames	negative	Stolzenberg 1979, Ishidate 1984 , Clark 1979, Yamaguchi 1982,
Chromosome aberration	negative	Ishidate 1984

In vivo Studies

Two *in vivo* assays are available for glycerol (Varilyak and Kozachuk, 1985). In a rat bone marrow chromosome aberration test glycerol did not induce a statistically significant increase in chromosomal aberrations compared to controls. However, the lack of sufficient reported details on clinical toxicity and absence of a positive control limit the significance which can be attached to this result.

In the same study a rat dominant lethal assay was conducted. Although a dose related increase was seen in post implantation loss, this increase was not statistically significant compared to controls. However, the limited details on methodology, small number of animals per dose group and absence of a positive control, mean no reliable conclusions can be drawn from the data.

Conclusion

There are no structural alerts (expert judgement) which raise concern for the inherent mutagenic potential of glycerol. *In vitro*, glycerol was negative (with and without metabolic activation) in Ames tests and did not induce chromosomal effects in mammalian cells. The responses seen in a limited gene mutation study in mammalian cells are of uncertain biological relevance as the doses were not maximised. Only two *in vivo* studies are available. A negative result was observed in a chromosome aberration test, and an increase (not statistically significant) in post implantation loss was seen in a rat dominant lethal assay. However, for both assays, the limited details reported and absence of a positive control, mean no reliable conclusions can be drawn from the *in vivo* data. Thus, overall, there is no *in vitro* or *in vivo* data that indicates glycerol to have a genotoxic potential.

3.1.7 Carcinogenicity

In a limited and non OECD Guideline 12-24 month dietary study in rats, evidence of malignant neoplasms were reported in 5/26, 1/22, 5/22, 0/22, 0/21, 5/22 and 0/22 animals in controls and at 5%, 10% , 20% (natural glycerol) and at 5%, 10%, 20% (synthetic glycerol). At the top dose, the treatment period was one year. Benign neoplasms were encountered including pheochromacytomas and granulosa cell tumours in 0/26, 2/22, 1/22, 0/22, 4/21, 4/22 and 1/22 animals in controls and at 5%, 10%, 20% (natural glycerol) and at 5%, 10%, 20% (synthetic glycerol), respectively. The authors concluded that glycerol does not initiate tumour development in the rat (Hine 1953).

In male ddY mice administration of glycerol (5% in drinking water during 1-20 weeks) after a single s.c. injection with 4-nitroquinoline 1-oxide (4-NQO) was reported to enhance lung tumour development. Histopathologically most lung tumours were identified as adenomas (Nagahara 1987, Inayama 1986). The mechanism of tumour induction was independent from pulmonary cell kinetics (Nagahara 1987).

Conclusion

No studies conducted to modern regulatory guidelines are available. The studies that are available are therefore of lower quality. No increase in tumour formation was observed in a limited dietary carcinogenicity study in the rat. Data from non-guideline studies designed to investigate tumour promotion activity in male mice suggest that oral administration of glycerol up to 20 weeks had a weak promotion effect on the incidence of lung tumour formation. In the same studies, treatment with glycerol alone (administered in the drinking water) did not result in an increase in the number of tumour bearing mice relative to controls.. Overall, these data do not raise concern for carcinogenic potential.

3.1.8 Toxicity for Reproduction

Studies in Animals

Effects on Fertility

In a two generation study not fully matching current OECD Guidelines, male and female rats (10/treatment) were dosed daily with glycerol (20% solution in water) during 8 weeks before mating. Females received glycerol throughout pregnancy or until weaning of the F1 generation (5 each). When the F1 generation was ~100 days of age, pups were killed except for 10/sex. These animals were used to produce the F2-generation. No effects were found on the reproductive efficiency of the parents, nor on the growth, fertility, reproductive performance of the untreated F1 generation, and no histological changes occurred in the tissues of both the F1 and F2 generation. Although the data are limited, a NOAEL of 2000 mg/kg bw was identified from this study (Wegener 1953).

Intratesticular administration of glycerol decreased spermatogenesis, leading to complete loss of spermatogenic cells in rats, but did not affect sexual behaviour (Wiebe 1984). The intratesticular route of exposure is not considered appropriate to investigate effects on fertility. Furthermore, the author reports that no effects were observed following oral administration (data not shown).

Developmental Toxicity

Rats, mice and rabbits were treated daily with glycerol at dose levels up to 1310, 1280 and 1180 mg/kg bw (oral gavage), respectively, during part of the gestation period. The study protocol was in reasonable agreement with the requirements of the OECD 414 (1981). No maternal toxicity or

teratogenic effects were seen at the highest dose levels tested (NTIS 1974). From these studies a NOAEL of 1180 mg/kg bw can be derived.

The results from a Frog Embryo Teratogenesis Assay-Xenopus (FETAX, see also 4.1.4) were ambiguous. Since there is no other evidence of developmental effects especially on mammals, the results of this screening assay for developmental toxicity are not considered to be relevant to mammals. The authors considered the response to be a false positive (Bantle 1999).

Human experience

A fertility study involving 64 males workers involved in glycerol manufacture reported no significant differences in sperm quality parameters (sperm counts and percent "normal" forms) (Venable 1980).

Conclusion

Based on the available data, it can be concluded that glycerol does not have any adverse effects on reproductive parameters. There was no evidence of teratogenicity. The NOAEL for developmental toxicity is 1180 mg/kg bw. The evidence of effects on spermatogenesis following intratesticular administration are not considered relevant as an exposure route. These data do not cause concern in relation to reproductive effects from anticipated routes of exposure.

3.2 Initial Assessment for Human Health

The worldwide market for glycerol for the year 2000 was 500,000 tonnes. Glycerol has widespread use and can be found in industrial, professional and consumer products. There is a potential for occupational exposure through inhalation and skin contact. Consumers may be exposed to glycerol by the oral and dermal routes of exposure. Smoking may lead to an additional glycerol uptake by inhalation.

All SIDS health endpoints are fulfilled. It should be noted that much of the data on glycerol is historic and of rather low quality compared to current guideline requirements. Nevertheless, there is an overall consistency within the available data that allows conclusions to be drawn. Glycerol is absorbed following ingestion and incorporated in the standard metabolic pathways to form glucose and glycogen. The weight of evidence indicates that glycerol is of low toxicity when ingested, inhaled or in contact with the skin.

Glycerol is of a low order of acute oral and dermal toxicity with LD_{50} values in excess of 4000 mg/kg bw. At very high dose levels, the signs of toxicity include tremor and hyperaemia of the gastro-intestinal -tract.Skin and eye irritation studies indicate that glycerol has low potential to irritate the skin and the eye. The available human and animal data, together with the very widespread potential for exposure and the absence of case reports of sensitisation, indicate that glycerol is not a skin sensitiser.

Repeated oral exposure to glycerol does not induce adverse effects other than local irritation of the gastro-intestinal tract. The 2-year study of Hine (1953) was chosen to establish the overall NOEL after prolonged treatment with glycerol of 10,000 mg/kg bw (20% in diet), which is in agreement with the findings in other studies. At this dose level no systemic or local effects were observed. For inhalation exposure to aerosols, there is evidence of local irritant effects at and above 662 mg/m^3. The NOAEL is 167 mg/m^3.

Glycerol does not induce gene mutations in bacterial strains, chromosomal effects in mammalian cells or primary DNA damage in vitro. Results seen in a limited mammalian gene mutations test were of uncertain biological relevance. *In vivo*, glycerol produced no statistically significant effect

in a chromosome aberrations and dominant lethal study. However, the limited details provided and absence of a positive control prevent any reliable conclusions can be drawn from the *in vivo* data. Overall, glycerol is not considered to possess genotoxic potential.

The experimental data from a limited dietary study in the rat does not provide any basis for concerns in relation to carcinogenicity. Data from non-guideline studies designed to investigate tumour promotion activity in male mice suggest that oral administration of glycerol up to 20 weeks had a weak promotion effect on the incidence of tumour formation.

No effects on fertility and reproductive performance were observed in a two generation study with glycerol administered by oral gavage (NOAEL 2000 mg/kg bw). No maternal toxicity or teratogenic effects were seen in the rat, mouse of rabbit at the highest dose levels tested in a guideline comparable teratogenicity study (NOEL 1180 mg/kg bw).

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

Data are available on the acute toxicity of glycerol to fish, daphnia, algae and microorganisms.

4.1.1 Fish and invertebrates

Species	Exposure (h)	LC/EC$_x$ (mg/L)	Reference
Leuciscus idus melanotus (Golden Orfe)	n.i.	LC_{50} >10,000	Juhnke 1978
Carassius auratus (Goldfish)	24	LC_{50} >5,000	Bridie 1979
Leuciscus idus (Golden Orfe)	48	LC_0 >250	Wierich 1968
Oncorhynchus mykiss (Rainbow trout)	96	LC_{100} = 51,000-57000	Johnson 1980 [n.r]
Not specified	96	LC_{50} = 184,000	ECOSAR - QSAR
Daphnia magna	24	EC_{50} >10,000	Bringmann 1977, 1982
Daphnia magna	24	EC_0 > 500	Henkel [n.r.]
Daphnia	48	EC_{50} = 153,000	ECOSAR - QSAR

n.i.= not indicated

n.r. = not retrievable

In a static test with the Golden orfe (*Leuciscus idus melanotus*), no mortality was reported up to a concentration of 10,000 mg/L. The test duration was not indicated and no other effects were mentioned (Juhnke, 1978). In a 24-hour test with the goldfish (*Carassius auratus*) a LC_{50} of >5000 mg/L was established (Bridie 1979). In a further test with Golden orfe (*Leuciscus idus melanotus*), fish were exposed to glycerol concentrations of up to 250 mg/l for 48 hours and no effects were observed at the highest test concentration (Wierich, 1968).

For *Daphnia magna* a 24-hour EC_{50} of >10,000 mg/L was found in several publications (Bringmann 1977, 1982). The studies are of rather low quality compared to current guideline requirements (non-GLP, no analytical measurement of test concentrations). However, the weight of evidence indicates that glycerol is of low acute toxicity to aquatic organisms with LC_{50}/EC_{50} values being in excess of 5000 mg/L.

A QSAR prediction for the 96-hour LC_{50} for fish of glycerol gave a value of 184,000 mg/L. For daphnia, a 48-hour LC50 of 153,000 mg/L was calculated (ECOSAR v0.99f). These QSAR predictions are based on a calculated Log Kow of -1.65 and a calculated water solubility of 2.16 x 10^4 mg/l using the neutral organics chemical class. They support the conclusion that glycerol is of low acute toxicity to fish and aquatic invertebrates. No information is available on toxicity to marine species.

Exposure of carp embryos in different developmental stages to a 1M glycerol solution after 5 minute or 1 hour exposure gave significantly decreased hatching rates (5 minutes 80-94%, 1 hour

14-78%, control values 91-95%) (Urbanyi, 1997). However, this study was designed to investigate the toxicity of glycerol when used as a cryoprotective substance. The result is not considered relevant to the hazard assessment since the test has a chronic endpoint but used only a short exposure duration and the exposure concentration was very high – 92 g/l. In addition, it is possible that the observed effects were due to physical effects due to high osmotic pressure.

Conclusions

Glycerol is of low acute toxicity to fish and aquatic invertebrates. LC/EC_{50} values are all in excess of 5000 mg/L.

4.1.2 Algae

For blue algae (*Microcystis aeruginosa*) no inhibition of growth was seen at 2900 mg/L after 8 days of exposure to a glycerol solution in water. The study was not fully in accordance with the current OECD guideline mainly due to no quantification of the relationship between the measured extinction and growth inhibition, and it was not possible to derive an EC_{50} value (Bringmann 1978, 1978, 1976, 1975). It is not possible to confirm the validity of the NOEC since it cannot be confirmed that algae were in the exponential growth phase for the test duration. An 8-day test with Scenedesmus *quadricauda* (green algae) showed a very low toxicity (EC_0 >10,000 mg/L). This study was not designed or conducted in line with current guidelines (Bringmann 1980, 1978, 1977, 1978).

An investigation of the effect of glycerol on the growth of 18 species of marine phytoplankton revealed that in the presence of light, glycerol generally enhanced growth at the lowest test concentration of 4600 mg/l. However, inhibition of growth was seen in *Agmenellum quadruplicatum* and *Anacystis marina* at a concentration of 4600 mg/l. The validity of this study could not be determined but it suggests that there is no significant difference in toxicity between the freshwater and marine species.

Based on the information available, it can be concluded from the weight of evidence that glycerol is of low toxicity towards algae. This conclusion is supported by a QSAR prediction for the 96-hour EC_{50} for algae of glycerol, which gave a value of 77712 mg/L (ECOSAR v0.99f), based on a calculated Log Kow of -1.65 and a calculated water solubility of 2.16×10^4 mg/l using the neutral organics chemical class.

Conclusions

Based on the information available glycerol is of low acute/chronic toxicity to algae.

4.1.3 Microorganisms

Glycerol is of low toxicity towards microorganisms. In a 16 hour test with *Pseudomonas putida* no inhibition of bacterial growth was found at concentrations between 100 and 10,000 mg/L (Henkel 1994). The information is considered sufficient to conclude that glycerol is of low toxicity to bacteria. Other studies on microorganisms are summarised in table 4.3.1. A NOEC is considered to be an effect level of 10% or less on cell growth. The validity of these studies could not be determined but the results support the conclusion that glycerol is of low toxicity to microorganisms.

Table 4.3.1. Toxicity towards microorganisms – additional studies

Species	**Exposure (h)**	**NOEC mg/L**	**Reference**
Chlimonas paramaecium	48	>10,000	Bringmann 1980, 1981
Clostridium sp.	n.i.	170,000	Dabrock 1992
Entosiphon sulcatum	72	3200	Bringmann 1978, 1980
Pseudomonas putida	16	>10,000	Bringmann 1976, 1977, 1980
Uronema parduzci	20	>10,000	Bringmann 1980, 1981

n.i.= not indicated

Conclusions

Glycerol is of low toxicity to bacteria with an EC_0 of 3200 - 10,000 mg/L.

4.1.4 Other

A whole-embryo developmental toxicity screening test with frog embryos showed effects on growth at concentrations of 7210 mg/L (with metabolic activation) or 9040 mg/L (without metabolic activation). The 96h EC_{50} value for malformations is 9290 mg/L (with metabolic activation) or 9680 mg/L (without metabolic activation) (Bantle 1999). The results are ambiguous since certain test criteria suggest that glycerol is non-teratogenic but severe malformations were observed at concentrations approaching the 96h LC50 with metabolic activation. The relevance of these results to the environment is not clear but effects were observed only at very high concentrations of glycerol. It is possible that the observed effects were physical effects due to high osmotic pressure. (It should be noted that no teratogenic effects were observed in a test with mammals, refer to section 3.1.6).

No conclusion can be drawn about the hazard posed by glycerol to amphibians.

4.1.5 Determination of PNEC aqua

Data are available from short term tests at 3 trophic levels. In view of the limited robustness of the studies present, the QSAR predictions are used to derive a tentative PNEC. Based on the lowest value (calculated for algae EC_{50} 77,712 mg/L) and applying an assessment factor of 100 in accordance with the OECD guidance the resultant $PNEC_{aqua}$ is 780 mg/L. However, an assessment factor of 1000 for the aquatic PNEC compartment could also be considered to reflect the uncertainty in the use of the QSAR predicted values.

Conclusions

Glycerol is of low hazard to the aquatic environment with a tentative $PNEC_{aqua}$ of 780 mg/L.

4.2 Terrestrial and Sediment Effects

There are no terrestrial and sediment effect data. Glycerol is not expected to partition to soil and sediment and exposure to these compartments is likely to be very low.

Calculations using the equilibrium partitioning method in the EUSES program and the tentative aquatic PNEC of 780 mg/l gave a tentative $PNEC_{sediment}$ of 479 mg/kg wwt and a tentative $PNEC_{soil}$ of 92.1 mg/kg wwt.

4.3 Other Environmental Effects

Based on the very low log K_{ow} of -1.76, glycerol is not expected to bioaccumulate significantly.

4.4 Initial Assessment for the Environment

There is potential exposure to the aquatic compartment arising from the production and processing of this substance. Glycerol will enter the aqueous and terrestrial environment from end uses such as in consumer products and down hole lubricants for oil and gas fields.

Glycerol is a liquid of calculated vapour pressure 0.000106 hPa (at 25ºC), is fully miscible with water and has a Log K_{ow} of -1.76 (measured). It has a calculated half-life for photo-oxidation of ~7 hours and is not susceptible to hydrolysis. The experimental data indicate that glycerol is readily biodegradable under aerobic conditions. Fugacity modelling (Mackay Level III) predicts that glycerol will partition to the aquatic compartment (100%). Based on the low Log Kow, it has a low potential for sorption to soil and is not expected to bioaccumulate.

All SIDS environmental endpoints are fulfilled. It should be noted that much of the data on glycerol is historic and of rather low quality compared to current guideline requirements. However, the weight of evidence indicates that glycerol is of low toxicity to aquatic organisms and this conclusion is supported by QSAR predictions. The lowest LC50 for fish is a 24-h LC_{50} of >5000 mg/l for *Carassius auratus (Goldfish)* and for aquatic invertebrates, a 24h EC50 of >10000 mg/l for *Daphnia magna* is the lowest EC50. Several tests on algae are available which suggest very low toxicity to a range of species, however their validity is uncertain. A QSAR prediction for the 96h EC50 to algae was 78000 mg/l. No long-term aquatic toxicity data is available.

Screening studies are available on frog and carp embryos which indicate some effects on growth and hatching rates respectively at very high concentrations of glycerol, >7000 mg/l. However, their ecological relevance is not clear.

In view of the limited robustness of the studies present, it was decided to derive a tentative PNEC for aquatic organisms using QSAR predictions of acute toxicity. The tentative PNEC for aquatic organisms is calculated to be 780 mg/L, based on the lowest QSAR value (algae EC_{50} 77,712 mg/L) and applying an assessment factor of 100 in accordance with the OECD guidance. In view of the limited robustness of the studies present, it was decided that this approach should be used. There are no sediment or terrestrial effects data, but partitioning to both soil and sediment is expected to be very low, based on the very low log K_{ow} of glycerol. The equilibrium partitioning method was used to calculated tentative PNECs for soil and sediment based on the $PNEC_{aquatic}$ of 780 mg/l, $PNEC_{sediment}$ = 479 mg/kg wwt and $PNEC_{soil}$ = 92.1 mg/kg wwt.

Glycerol is a naturally occurring substance of low hazard. The ecotoxicology data available is largely historical and reflects the quality standards of the time. The data could not be validated as thoroughly as current data however the aquatic toxicity data are considered valid using a weight of evidence approach supported by QSARs. An assessment factor of 1000 could be considered to reflect the uncertainty of using historical data underwritten by QSARs.

5 RECOMMENDATIONS

The chemical is currently of low priority for further work.

There are data on all SIDS endpoints and for many other toxicological and ecotoxicological endpoints. There is considerable data on glycerol and based on the overall weight of evidence, the substance is of low concern.

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ANNEX: SEARCH CRITERIA:

For transparency, some study summaries in the SIDS dossier were transferred from a previous version of IUCLID not intended for submission to OECD. In some cases, it was not possible to retrieve the original literature using the reported citation or as a result of literature searching, as detailed below. If references in the SIDS dossier on glycerol (IUCLID) were not retrievable, this was indicated in the SIDS dossier, or where relevant, in the SIAR also. Key studies are studies with the highest reliability/adequacy. If several studies showed comparable reliability/adequacy, the study with the lowest LC/LD/EC_{50} or NOEC/ NOAEL was indicated as the key study.

Physical-chemical properties are obtained from standard reference works such as Lide, Hawleys Condensed Chemical Dictionary, Beilstein, Sax and Merck Index, also some calculated values are given obtained mostly using Syracuse prediction software (EPIWIN).

Among others, the following databases were searched under the CAS number 56-81-5 and the name glycerol in March 2001: Medline, Toxline, Enviroline, Embase, BIOSIS (over the period 1992-2001). The search strategy was used with no cut off criteria applied to exclude historical investigations

The search profile used for environmental endpoints included the following keywords:

Environm? or ecotox? or fate; air or soil or water or aquatic? or sedim?; photo? or stab? or distribut? or degrad? or transp? or monitor? or BOD or COD or accumul?; solub? or partition? or Kow or Pow or Koc or hydrol?; fish? or invert? or daphn? or alg? or plant? or kinet? or acute or chronic?; vertebrat? or microorg? or micro-org? or bacter? or ?dwelling? or tranform? or terrestr?

The search profile used for human health endpoints included the following keywords:

toxic?; human and (epidem? or case-rep? or (field and stud?) or volunt?); mutag? or DNA or gentox? or Ames? or carcin?; placenta and transfer; reproduct? or terato? or prenatal? or fertil?; repeat? and expos?; animal; inhal? or ?acute? or ?chron? or derm?); (kinet? or metabol? or endocrin?); (PBPK or PB-PK); (irritat? or sensitis? or sensitiz? or sensibilis? or sensibiliz?;(vitro)

I U C L I D

Data Set

Existing Chemical	:	ID: 56-81-5
CAS No.	:	56-81-5
EINECS Name	:	glycerol
EC No.	:	200-289-5
TSCA Name	:	1,2,3-Propanetriol
Generic name	:	glycerine
Molecular Formula	:	C3H8O3
Structural Formula	:	CH2OH CH(OH) CH2OH
Substance Group	:	Not applicable
Molecular Weight	:	92

Producer related part

Company	:	Notox
Creation date	:	26.04.2001

Substance related part

Company	:	Notox
Creation date	:	26.04.2001
Status	:	
Memo	:	Revised including robust summaries
Printing date	:	29.01.2002
Revision date	:	
Date of last update	:	29.01.2002
Number of pages	:	1
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

Type	:	cooperating company
Name	:	other: ICI Uniqema
Contact person	:	L.Hughes
Date	:	
Street	:	
Town	:	
Country	:	
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

Flag : confidential
08.01.2002

Type	:	sponsor country
Name	:	UK
Contact person	:	Dr. S. Robertson
Date	:	
Street	:	
Town	:	
Country	:	
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

08.01.2002

08.01.2002

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name	:	Glycerine
Smiles Code	:	
Molecular formula	:	CH2OH CH(OH) CH2OH
Molecular weight	:	92
Petrol class	:	

08.01.2002

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type :
Substance type : Organic
Physical status : Liquid
Purity : > 95 % v/v
Colour :
Odour :

08.01.2002

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

glycerol; glycerine; glycerin; glycyl alcohol; trihydroxypropane; 1,2,3-trihydroxypropane; Citifluor AF 2; Glycerin mist; Glyceritol; Clyzerin, wasserfrei (German); Grocolene; Moon; Osmoglyn; Star

08.01.2002

1.3 IMPURITIES

Purity : typical for marketed substance
CAS-No :
EC-No :
EINECS-Name : Water
Molecular formula : H2O
Value : .5 - 5 % v/v

25.01.2002

1.4 ADDITIVES

1.5 TOTAL QUANTITY

Quantity : ca. 500000 - tonnes in 2000

08.01.2002

1.6.1 LABELLING

Labelling : as in Directive 67/548/EEC
Specific limits :

Remark : None

08.01.2002

1.6.2 CLASSIFICATION

Classified : no classification required (no dangerous properties)
Class of danger :
R-Phrases :
Specific limits :

08.01.2002

1.6.3 PACKAGING

1.7 USE PATTERN

Type of use : type
Category : Use in closed system

08.01.2002

Type of use : type
Category : Use resulting in inclusion into or onto matrix

08.01.2002

Type of use : type
Category : Wide dispersive use

08.01.2002

Type of use : industrial
Category : Chemical industry: used in synthesis

08.01.2002

Type of use : industrial
Category : Polymers industry

08.01.2002

Type of use : use
Category : Cleaning/washing agents and disinfectants

08.01.2002

Type of use : use
Category : Cosmetics

08.01.2002

Type of use : use
Category : Food/foodstuff additives

08.01.2002

Type of use : use
Category : Pharmaceuticals

08.01.2002

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

Type of limit : MAC (NL)
Limit value : 10 mg/m3

Remark : Glycerol mist
Aerosol form to be equivalent to a low toxicity particulate.
08.01.2002

Type of limit : OES (UK)
Limit value : 10 mg/m3

Remark : Glycerol mist
Aerosol form to be equivalent to a low toxicity particulate.
08.01.2002

Type of limit : TLV (US)
Limit value : 10 mg/m3

Remark : Glycerol mist
Aerosol form to be equivalent to a low toxicity particulate.
08.01.2002

Type of limit : other: Belgium
Limit value : 10 mg/m3

Remark : Glycerol mist
Aerosol form to be equivalent to a low toxicity particulate.
08.01.2002

Type of limit : other: Ireland
Limit value : 10 mg/m3

Remark : Glycerol mist
Aerosol form to be equivalent to a low toxicity particulate.
08.01.2002

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

Type : other
Additional information :

Remark : 10 most frequent industry groups:
Other printing works
Manufacture of fabricated metal products, except manchinery and equipment
Treatment and coating of metals on a fee or contract basis
Manufacture of machinery and equipment
Painting and glazing
Maintenance and repair of motor vehicles
Industrial cleaning
Social work activities
Private households with employed persons
All kinds of activities

Product types containing 0-100% of glycerol:
A02 Adhesives, binding agents: 30 products, 32 total tonnes /annum
A38 Pesticides, agricultural: 10 products, <1 total tonnes /annum
A43 Process regulators: 17 products, 23 total tonnes/annum
A54 Welding and soldering agents: 8 products, <1 total tonnes /annum
B10 Colouring agents: 33 products, 13 total tonnes /annum
B14 Corrotion inhibitors: 10 products, <1 total tonnes /annum
B15 Cosmetics: 75 products, 311 total tonnes /annum
B20 Fillers: 20 products, 30 total tonnes /annum
B31 Impregnation materials: 9 products, <1 total tonnes /annum
B32 Insulating materials: 13 products, 32 total tonnes /annum
B41 Pharmaceuticals: 10 products, 1 total tonne /annum
B45 Reprographic agents: 23 products, 2 total tonnes /annum
B50 Surface-active agents: 19 products, 80 total tonnes /annum
B55 Others: 9 products, 45 total tonnes /annum
C09 Cleaning/washing agents: 131 products, 23 total tonnes /annum
C13 Construction materials: 6 products, 11 total tonnes /annum
C39 Non-agricultural pesticides and preservatives: 12 products, 2 total tonnes /annum
D56 Cutting fluids: 9 products, 1 total tonne /annum
D59 Paints, laquers and varnishes: 126 products, 32 total tonnes /annum
D61 Surface treatment: 39 products, <1 total tonnes /annum

25.01.2002 (1)

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

2.1 MELTING POINT

Value : = 18.2 °C
Decomposition : no, at °C
Sublimation : no
Method : other
Year : 2000
GLP : no data
Test substance :

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
19.12.2001 (2)

Value : = 18 °C
Sublimation :
Method :
Year : 1981
GLP :
Test substance : other TS

Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Conclusion : Most reliable data available.
Reliability : (2) valid with restrictions
Handbook data are considered to be from a trusted source.
Flag : Critical study for SIDS endpoint
19.12.2001 (3)

Value : = 17.9 °C
Sublimation :
Method :
Year : 1996
GLP :
Test substance :

Conclusion : Most reliable data available.
Reliability : (2) valid with restrictions
Handbook data are considered to be from a trusted source.
Flag : Critical study for SIDS endpoint
19.12.2001 (4)

Value : = 18.2 °C
Sublimation :
Method :
Year : 1992
GLP :
Test substance :

Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Reliability : (4) not assignable
The information in the report was confined to the above.
19.12.2001 (5)

Value : ca. 18 °C
Decomposition : no, at °C
Sublimation : no
Method : other: Unknown (literature)

Year :
GLP : no data
Test substance :

Remark : Glycerol is seldom seen in its crystallized state, because of its tendency to supercool, and the pronounced effect of small amounts of water in depressing the melting (freezing) point.
Source : Unichema Chemie B.V. Gouda
EUROPEAN COMMISION - European Chemicals Bureau Ispra (VA)
11.06.2001 (6)

Value : ca. 18 °C
Decomposition : ambiguous, at °C
Sublimation : no
Method :
Year :
GLP :
Test substance :

Remark : Literature could not be retrieved.
Source : Pronova Oleochemicals a.s. Sandefjord
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
01.06.1995

2.2 BOILING POINT

Value : = 290 °C at 1013 hPa

Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Conclusion : Most reliable data available.
Reliability : (2) valid with restrictions
Handbook data are considered to be from a reliable source.
Flag : Critical study for SIDS endpoint
19.12.2001 (3)

Value : = 290 °C at 1013.25 hPa
Decomposition : yes
Method : other
Year : 2000
GLP : no data
Test substance :

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
19.12.2001 (2)

Value : = 290 °C at
Decomposition : yes
Method :
Year : 1996
GLP :
Test substance :

Remark : Partly decomposition
Reliability : (2) valid with restrictions
Handbook data are considered to be from a reliable source.
19.12.2001 (4)

Value : = 290 °C at 1013 hPa

Result : Boiling point = 222.4 °C at 133.3 hPa

Boiling point = 149 °C at 5.3 hPa

Boiling point = 166.1 °C at 13.3 hPa

Test substance : CAS 56-81-5 (glycerine), purity not indicated.

Reliability : (4) not assignable
The information in the report was confined to the above.

19.12.2001 (5)

Value : < 180 °C at

Decomposition : yes

Method :

Year : 1986

GLP : no data

Test substance :

Remark : In temperatures higher than 180 °C glycerol decomposes to Di/Polyglycolethers and acrolein.
Literature could not be retrieved.

Source : Unichema Chemie B.V. Gouda
EUROPEAN COMMISION - European Chemicals Bureau Ispra (VA)

19.12.2001 (7)

Value : ca. 290 °C at

Decomposition :

Method : other

Year :

GLP : yes

Test substance :

Remark : Literature could not be retrieved.

Source : UNION DERIVAN S.A. VILADECANS
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

21.05.1998

Value : = 290 °C at 1010 hPa

Decomposition :

Method :

Year : 1955

GLP :

Test substance : other TS

Test substance : CAS 56-81-5 (glycerine), purity 100%.

Reliability : (2) valid with restrictions
Also values at other pressures were reported. The most appropriate value is included in this summary and was based on several determinations by different investigators. These data are treated as handbook data.

19.12.2001 (8)

2.3 DENSITY

Type : density

Value : = 1.26 at 20 °C

Conclusion : Most reliable data available.
Reliability : (2) valid with restrictions
Handbook data at ambiguous temperature.
Flag : Critical study for SIDS endpoint
19.12.2001 (4) (8)

Type : relative density
Value : = 1.2613 g/cm³ at 20 °C
Method : other
Year : 2000
GLP : no data
Test substance :

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
19.12.2001 (2)

Type : density
Value : = 1.262 g/cm³ at 25 °C

Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Reliability : (4) not assignable
The information in the report was confined to the above.
19.12.2001 (5)

Type : density
Value : ca. 1.261 g/cm³ at 20 °C
Method : other
Year :
GLP : yes
Test substance :

Remark : Literature could not be retrieved.
Source : UNION DERIVAN S.A. VILADECANS
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
21.05.1998

Type : relative density
Value : ca. 1.2613 g/cm³ at 20 °C

Remark : Literature could not be retrieved.
Source : Wolff Walsrode AG Walsrode
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
14.05.1998

Type : density
Value : ca. 1.2 g/cm³ at 75 °C

Remark : Literature could not be retrieved.
Source : Pronova Oleochemicals a.s. Sandefjord
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
01.06.1995

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : = .0033 hPa at 50 °C
Decomposition :
Method :
Year : 1955
GLP :
Test substance : other TS

Test substance : CAS 56-81-5 (glycerine), purity 100%.
Conclusion Most reliable data available.
Reliability : (2) valid with restrictions
Handbook data at most appropriate temperature.
Flag : Critical study for SIDS endpoint
19.12.2001 (8a)

Value : = .00022 hPa at 25 °C
Decomposition :
Method : other (measured)
Year : 1989
GLP :
Test substance : other TS

Test substance : CAS 56-81-5 (glycerine), purity not indicated
Remark : The vapour pressure is cited as 0.000168 mmHg (=0.00022 hPa).
Reliability : (4) not assignable

19.12.2001 (8b)

Value : = .01 hPa at 96 °C

Remark : All values are extrapolated (beyond the region of experimental measurements).
Result : Vapour pressure = 0.1 hPa at 113 °C

Vapour pressure = 1 hPa at 136 °C

Vapour pressure = 10 hPa at 168 °C

Vapour pressure = 100 hPa at 213.4 °C

Vapour pressure = 1000 hPa at 287 °C
Reliability : (2) valid with restrictions
19.12.2001 (9)

Value : = .000106 hPa at 25 °C
Decomposition :
Method : other (calculated)
Year : 1999
GLP :
Test substance :

Reliability : (4) not assignable
19.12.2001 (10)

Value : = .0033 hPa at °C

Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Reliability : (2) valid with restrictions
Handbook data are considered to be from a trusted source.
19.12.2001 (4)

Value : = .0033 hPa at 50 °C

Result : Vapour pressure = 61 hPa at 200 °C

Vapour pressure = 5.73 hPa at 150 °C

Vapour pressure = .26 hPa at 100 °C
Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Reliability : (4) not assignable
The information in the report was confined to the above.
19.12.2001 (5)

2.5 PARTITION COEFFICIENT

Partition coefficient : octanol-water
Log pow : = -1.65 at °C
pH value :
Method : other (calculated)
Year : 1999
GLP :
Test substance :

Test substance : CAS 56-81-5 (Glycerine), purity not indicated.
Conclusion : Reliable calculation (method of calculation known).
Reliability : (4) not assignable
19.12.2001 (10)

Partition coefficient : octanol-water
Log pow : = -2.184 at °C
pH value :
Method : other (calculated)
Year :
GLP :
Test substance :

Method : log P = 3.028(+/-0.204)logMW-0.498(+/-0.0023)HB-3.649(+/-0.227)

MW= molecular weight
HB= maximum hydrogen-bond forming ability
Reliability : (4) not assignable
09.01.2002 (11)

Partition coefficient :
Log pow : -2.66 - -2.47 at °C
pH value : -
Method : other (calculated)
Year : 1992
GLP :
Test substance :

Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Reliability : (4) not assignable
The information in the report was confined to the above.

09.01.2002 (5)

Partition coefficient :
Log pow : = -3.07 at °C
pH value :
Method :
Year : 1998
GLP :
Test substance :

Remark : Literature could not be retrieved.
09.01.2002 (12)

Partition coefficient :
Log pow : = -1.76 at °C
pH value :
Method : other (measured)
Year : 1988
GLP :
Test substance :

Remark : Not all literature could not be retrieved.
Source : Unichema Chemie B.V. Gouda
EUROPEAN COMMISION - European Chemicals Bureau Ispra (VA)
Conclusion : Only measured value available and is supported by a valid QSAR prediction (reference 10).
Reliability : (4) not assignable
Flag : Critical study for SIDS endpoint
25.01.2002 (13) (14)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in : Water
Value : at °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :
Method :
Year : 1955
GLP :
Test substance :

Remark : Completely miscible with water.
Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Conclusion : Most reliable data available.
Reliability : (2) valid with restrictions
Handbook data for mixtures of water and glycerol (0-100%).
Flag : Critical study for SIDS endpoint
19.12.2001 (8)

Solubility in : Water
Value : at °C
pH value :

concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	
Year	:	1996
GLP	:	
Test substance	:	

Result	:	Miscible
Test substance	:	CAS 56-81-5 (glycerine), purity not indicated.
Conclusion	:	Most reliable data available.
Reliability	:	(2) valid with restrictions Handbook data are considered to be from a trusted source.

19.12.2001 (4)

Solubility in	:	Water
Value	:	at °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	14.4 at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	other: not mentioned
Year	:	1979
GLP	:	no data
Test substance	:	

Remark	:	Literature could not be retrieved.
Source	:	Unichema Chemie B.V. Gouda EUROPEAN COMMISION - European Chemicals Bureau Ispra (VA)

19.12.2001 (15)

Solubility in	:	
Value	:	= at °C
pH value	:	ca. 7
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	of very high solubility
Stable	:	
Deg. product	:	
Method	:	other
Year	:	1976
GLP	:	no data
Test substance	:	

Remark	:	Soluble in all proportions.
Reliability	:	(2) valid with restrictions

19.12.2001 (2) (16)

Solubility in	:	Water
Value	:	at °C

pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	soluble (1000-10000 mg/L)
Stable	:	
Remark	:	Literature could not be retrieved.
Source	:	Pronova Oleochemicals a.s. Sandefjord EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

05.12.2001

Solubility in	:	
Value	:	at °C
pH value	:	ca. 7 - 8.5
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	14.4 at 25 °C
Description	:	
Stable	:	
Remark	:	Literature could not be retrieved. Soluble in all proportions.
Source	:	Wolff Walsrode AG Walsrode EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

14.05.1998

2.6.2 SURFACE TENSION

Test type	:	
Value	:	= 63.4 mN/m at 20 °C
Concentration	:	100 vol%
Method	:	other: not indicated
Year	:	1955
GLP	:	no
Test substance	:	other TS
Test substance	:	CAS 56-81-5 (glycerine), purity 100%.
Reliability	:	(2) valid with restrictions Handbook data at ambiguous temperature.

19.12.2001 (8)

2.7 FLASH POINT

Value	:	= 160 °C
Type	:	closed cup
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS
Test substance	:	CAS 56-81-5 (Glycerine), purity not indicated.
Reliability	:	(2) valid with restrictions Handbook data are considered to be from a trusted source. The closed cup method is the preferred method for the determination of the

flash point.
03.01.2002 (17)

Value : = 160 °C
Type :
Method :
Year : 1981
GLP :
Test substance : other TS

Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Reliability : (2) valid with restrictions
Handbook data are considered to be from a trusted source.
03.01.2002 (3)

Value : = 170 °C
Type : open cup
Method : other: D 92-33 (Am. Soc. for Testing Materials)
Year : 1955
GLP : no
Test substance : other TS

Test substance : CAS 56-81-5 (glycerine), purity 99%.
Reliability : (2) valid with restrictions
Handbook data are considered to be from a trusted source.
03.01.2002 (8)

Value : = 177 °C
Type : open cup
Method :
Year : 1992
GLP :
Test substance :

Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Reliability : (4) not assignable
The information in the report was confined to the above.
03.01.2002 (5)

Value : ca. 160 °C
Type : open cup

Remark : Literature could not be retrieved.
Source : Pronova Oleochemicals a.s. Sandefjord
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
01.06.1995

Value : ca. 177 °C
Type : open cup
Method : other: Cleveland Open Cup (ASTM D92-85)
Year : 1991
GLP : no
Test substance :

Remark : When aqueous glycerol is tested it will not flash until enough water has evaporated to bring the glycerol concentration to about 97.5% by weight. It will then flash at 190 °C.
Literature could not be retrieved.
Source : Unichema Chemie B.V. Gouda

EUROPEAN COMMISION - European Chemicals Bureau Ispra (VA)
19.12.2001 (18)

Value : = 177 °C
Type : open cup
Method : other
Year : 1971
GLP : no data
Test substance :

Remark : Literature could not be retrieved.
Source : Croda Universal Ltd Goole, North Humberside
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
13.05.1994 (19)

Value : > 180 °C
Type : open cup
Method : other
Year :
GLP : yes
Test substance :

Remark : Literature could not be retrieved.
Source : UNION DERIVAN S.A. VILADECANS
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
21.05.1998

Value : ca. 180 °C
Type : open cup

Remark : Literature could not be retrieved.
Source : Wolff Walsrode AG Walsrode
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
14.05.1998

2.8 AUTO FLAMMABILITY

Value : = 393 °C at
Method :
Year : 1981
GLP :
Test substance : other TS

Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Reliability : (2) valid with restrictions
Handbook data are considered to be from a trusted source.
19.12.2001 (3)

Method :
Year : 1991
GLP :
Test substance : other TS

Remark : The auto ignition temperature of glycerol is 523 °C on platinum, 429 °C on glass, and 412 °C in oxygen at 1 atm.
Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Conclusion : Most reliable data available.
Reliability : (2) valid with restrictions

Handbook data are considered to be from a trusted source.
19.12.2001 (18) (8)

Value : = 388 °C at
Method :
Year :
GLP :
Test substance : other TS

Test substance : CAS 56-81-5 (Glycerine), purity not indicated.
Reliability : (2) valid with restrictions
Handbook data are considered to be from a trusted source.
03.01.2002 (17)

Value : > 350 °C at
Method : other
Year :
GLP : yes
Test substance :

Remark : Literature could not be retrieved.
Source : UNION DERIVAN S.A. VILADECANS
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
21.05.1998

Value : ca. 370 - 422 °C at 1013.25 hPa

Remark : Literature could not be retrieved.
Source : Wolff Walsrode AG Walsrode
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
14.05.1998

Value : 370 °C at
Method :
Year : 1996
GLP :
Test substance :

Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Reliability : (2) valid with restrictions
Handbook data are considered to be from a trusted source.
19.12.2001 (5) (4)

Value : = 422 °C at 1013.25 hPa
Method : other
Year : 1981
GLP :
Test substance :

Remark : Literature could not be retrieved.
Value given refers to autoignition temperature (739 Deg F)
Source : Croda Universal Ltd Goole, North Humberside
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
19.12.2001 (3)

2.9 FLAMMABILITY

Result : non flammable

Remark : It is not to be expected that glycerol:
- will produce flammable gasses if in contact with water;
- will show spontaneous ignition in contact with inert material and intense contact with air (i.e. pyrophoric properties).
Literature could not be retrieved.

Source : Unichema Chemie B.V. Gouda
EUROPEAN COMMISION - European Chemicals Bureau Ispra (VA)

12.06.2001

Result : non flammable
Method : other
Year :
GLP : no data
Test substance :

Remark : Literature could not be retrieved.
See flash point data.

Source : Croda Universal Ltd Goole, North Humberside
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

13.05.1994

2.10 EXPLOSIVE PROPERTIES

Result : not explosive

Remark : No explosive properties are to be expected.
Literature could not be retrieved.

Source : Unichema Chemie B.V. Gouda

03.02.1994

Result : not explosive

Remark : Literature could not be retrieved.
No explosive properties are to be expected.

Source : Simel S.p.A. Industria Chimica Cremona
Lever Brother Ltd. Kingston Upon Thames, Surrey
Unichema Chemie GmbH Emmerich
Lever GmbH Hamburg
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

03.02.1994

Result : not explosive

Remark : Literature could not be retrieved.

Source : Croda Universal Ltd Goole, North Humberside
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

13.05.1994

Result : not explosive

Remark : Literature could not be retrieved.

Source : Wolff Walsrode AG Walsrode
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

14.05.1998

Remark : Literature could not be retrieved.
No explosive properties are to be expected.
Source : UNION DERIVAN S.A. VILADECANS
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
21.05.1998

2.11 OXIDIZING PROPERTIES

Result : no oxidizing properties

Remark : No oxidizing properties are to be expected.
Literature could not be retrieved.
Source : Unichema Chemie B.V. Gouda
03.02.1994

Result : no oxidizing properties

Remark : Literature could not be retrieved.
No oxidizing properties are to be expected.
Source : Simel S.p.A. Industria Chimica Cremona
Lever Brother Ltd. Kingston Upon Thames, Surrey
Unichema Chemie GmbH Emmerich
Lever GmbH Hamburg
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
03.02.1994

Result : no oxidizing properties

Remark : Literature could not be retrieved.
Source : Croda Universal Ltd Goole, North Humberside
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
13.05.1994

Result : no oxidizing properties

Remark : Literature could not be retrieved.
Source : Wolff Walsrode AG Walsrode
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
14.05.1998

Remark : Literature could not be retrieved.
No oxidising properties are to be expected.
Source : UNION DERIVAN S.A. VILADECANS
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
21.05.1998

2.12 DISSOCIATION CONSTANT

Acid-base constant : .07e-13
Method : other: not indicated
Year : 1955
GLP : no
Test substance : other TS

Test substance : CAS 56-81-5 (glycerine), purity 100%.

Conclusion	:	Only data available.
Reliability	:	(2) valid with restrictions Handbook data are considered to be from a trusted source.
19.12.2001		(8)

2.13 VISCOSITY

Value	:	= 1410 - mPa s (dynamic) at 20 °C
Result	:	
Method	:	other: not indicated
Year	:	1955
GLP	:	no data
Test substance	:	other TS
Test substance	:	CAS 56-81-5 (glycerine), purity 100%.
Reliability	:	(2) valid with restrictions Handbook data at ambient temperature.
19.12.2001		(8)

2.14 ADDITIONAL REMARKS

Remark	:	Viscosity (20 °C) : 1410 mPa.s Surface Tension (20 °C) : 63.4 mN/m Solubility : Glycerol will dissolve a large number of organic and inorganic compounds and will be miscible with many other substances.. Thus, glycerol will be completely miscible with most of the lower aliphatic alcohols, phenol, ethylene, propylene, and trialkyl glycols, some glycol ethers, but only partially, or not at all, with others.
Source	:	Unichema Chemie B.V. Gouda
11.06.2001		(18)

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	1500000 molecule/cm³
Rate constant	:	= .000000001874 cm³/(molecule*sec)
Degradation	:	50 % after 6.8 hour(s)
Deg. product	:	
Method	:	
Year	:	1999
GLP	:	
Test substance	:	

Remark	:	Calculated with EPIWIN, part AOPWIN v.1.90.
Conclusion	:	Most reliable value available.
Reliability	:	(4) not assignable Calculated value.
Flag	:	Critical study for SIDS endpoint

19.12.2001 (10)

Type	:	water
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	
Rate constant	:	cm³/(molecule*sec)
Degradation	:	% after
Deg. product	:	
Method	:	other (measured)
Year	:	1973
GLP	:	no data
Test substance	:	

Remark	:	Literature could not be retrieved.
Result	:	Rate constant: 0.19 x 10exp10 l/mol.sec.
Source	:	Unichema Chemie B.V. Gouda
Test condition	:	- OH formed by pulsed radiolysis; - Neutral pH; - Oxidation by H-abstraction reaction.

19.12.2001 (20)

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	at °C
t1/2 pH7	:	at °C
t1/2 pH9	:	at °C

Remark	:	Expert Statement: Glycerol has no hydrolysable groups and is therefore not susceptible to

hydrolysis.

Reliability : (4) not assignable
11.12.2001

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

Type of measurement : background concentration
Media : biota
Concentration :
Method :

Remark : - Glycerol occurs naturally in all animals and vegetables, in combined form as glycerides in fats and oils, or, intracellulary as lipids.
- It is an important intermediate in the physiology of all forms of life.
- Glycerol is widely distributed in our food, both as natural constituent and as an additive; fat or oil molecules of either animal or vegetable origin contain about 10% glycerol by weight.
- Glycerol may be formed from sugars by microbial fermentation.

11.12.2001 (5)

Type of measurement :
Media : air
Concentration :
Method :

Remark : A validated method for the determination of glycerol in air is not available.

15.11.2001 (5)

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type : fugacity model level III
Media : other: air - water- soil -sediment
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: calculation
Year : 1997

Method : EQC (level III), release to surface water 1000 kg/y.
Input parameters:
Water solubility 100,000 mg/L
Vapour pressure 0.000106 hPa (at 25 degrees C)
Log Kow -1.76
Melting point 18 degC

Result : Distribution air/water/soil/sediment: 0%/100%/0%/0%
Reliability : (4) not assignable
Flag : Critical study for SIDS endpoint
24.01.2002 (21)

Type : adsorption
Media : water - soil
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method :
Year : 1981

Method : In this report a method was described handling about the permeability of clay-soils (indicative of the leaching of test substance from the soil into the ground water). The clay-soil used in the experiment with glycerol can be described as follows. Ranger shale soil: bulk density 1.73 kg/L, 0.48 %o.m., 4% montmorillonite, void ratio 0.4-0.53)

A moistured 1000-2000 g sample of sieved clay soil (dry weight) was placed in a permeability column, glycerol was added and the permeability was determined at 22+/-1 C, atmospheric pressure.

The coefficient of permeability (K) was calculated using the following formula: K=QL/AH with
Q=flow of the percolate in mL per second
L=height of the sample in the column in cm
A=cross-sectional area of the sample in square cm
H=the average head of the fluid medium on the sample in cm

Result : Coefficients of permeability (K) for water and glycerol were respectively 38 E-9 and 0.9 E-9 cm/sec.

The swell of the soil for water and glycerol were respectively 12 and 5%
Test substance : CAS 56-81-5 (glycerine), purity not indicated
Conclusion : Percolation through soil:
Water: 38 E-9 cm/sec
Glycerol: 0.9 E-9 cm/sec
Reliability : (4) not assignable
The study included here is not a standard OECD-test, but provides some information on the leaching behaviour/ adsorption to soil of glycerol.
19.12.2001 (22)

3.3.2 DISTRIBUTION

Media : other: Koc
Method : other (calculation)
Year : 1999

Result : Koc = 1
Test substance : CAS 56-81-5 (Glycerine), purity not indicated.
Reliability : (4) not assignable
19.12.2001 (10)

3.4 MODE OF DEGRADATION IN ACTUAL USE

Remark : Literature could not be retrieved.
When used in foods or injected as part of pharmaceutical preparations glycerol is metabolised by glycerokinase in the liver to carbon dioxide and water, or used in glucose or glycogen synthesis. Most of ingested material has been
metabolised within 2.5 hours.
Source : Croda Universal Ltd Goole, North Humberside
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
13.05.1994 (23)

Remark : Literature could not be retrieved.
When used in foods or injected as part of pharmaceutical preparations Glycerol is metabolised by glycerokinase in the liver to Carbon Dioxide and Water, or used in glucose or glycogen synthesis. Most of ingested material has been metabolised within 2.5 hours.
Source : Wolff Walsrode AG Walsrode
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
07.11.2001

3.5 BIODEGRADATION

Type : aerobic
Inoculum : other: garden mould suspension
Concentration : 2 mg/l related to Test substance
4 mg/l related to Test substance
Contact time :
Degradation : 92 (±) % after 30 day(s)
Result : readily biodegradable
Kinetic of testsubst. : 5 day(s) 57 %
15 day(s) 84 %
30 day(s) 92 %
%
%
Control substance : other: dodecylsulfate
Kinetic : 5 day(s) 66 %
15 day(s) 80 %
Deg. product :
Method : OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"
Year : 2001
GLP : no
Test substance : other TS

Method : A stock solution of 1000 mg test substance/l was prepared and aliquots were added to the test flasks to a final concentration of 2 and 4 mg/l. These were incubated with 1ml/l of garden-mould suspension (100 g garden-mould and 1 l water were shaken vigorously and filtered) resulting in a cell concentration of 10e3-10e5 cells/L . The flasks were incubated at 20 C for 30 days. A control containing only inoculum (blank) and a positive control (dodecylsulfate, ca. 2 mg/l) were included. The oxygen consumption in 2 bottles for each treatment and 4 for the blank was measured after 0, 5, 15 and 30 days with a iodometric titration. The percentage biodegradation was

based on ThOD(NH3).

Test substance : CAS 56-81-5 (Glycerine), purity not indicated.

Conclusion :

Readily biodegradable.
Only study available, which was conducted to an OECD guideline.

Reliability : (2) valid with restrictions
1. The reliability is lowered because it is not a GLP study.
2. The information in the report is confined to the above.
3. The report is a rewritten report; the original report dates from between 1984 and 1990.
4. The difference between replicates is < 20% as required by OECD 301.
5. The final inoculum concentration is not very clear reported in the test report. 1 mL of a garden mould suspension is added to 1 L test solution. We assume that the garden mould suspension contains 1E3 to 1E5 cells per mL. This corresponds to a total inoculum concentration in the test solution of 1E3-1E5 cells/L, which is comparable with the requirements of the OECD (1E4-1E6 cells/L).

Flag : Critical study for SIDS endpoint
25.01.2002 (24)

Type : aerobic
Inoculum : activated sludge, industrial
Concentration : 238 mg/l related to COD (Chemical Oxygen Demand)
88 mg/l related to DOC (Dissolved Organic Carbon)
Contact time : 24 hour(s)
Degradation : 94 - 97 (±) % after 24 hour(s)
Result : inherently biodegradable
Kinetic of testsubst. : 2 hour(s) 50 - 60 %
4 hour(s) 86 - 92 %
24 hour(s) 94 - 97 %
%
%
Control substance : Ethylene glycol
Kinetic : 24 hour(s) 92 - 93 %
%
Deg. product : not measured
Method :
Year : 1975
GLP : no data
Test substance : other TS

Method : INOCULUM/TEST ORGANISM
- Inoculum (source/concentration): activated sludge (industrial)
- pretreatment: washed with tap water
METHOD OF PREPARATION OF TEST SOLUTION: not indicated
INITIAL TEST SUBSTANCE CONCENTRATION: 88 mg C/L (=226 mg TS/L)
TEST SYSTEM
- Test apparatus: fill and draw type unit; one with two aeration cylinders, each with a volume of 7 L, the other with two aeration cylinders, each with a volume of 30 L (no more information available in this report, Nanbu(1971) is given as a reference)
- Number of replicates: not indicated
- Aeration: yes (5 L/min)
- Measuring equipment:
TOC: TOC analyser
COD-Mn: water sample was oxidised with KMnO4-H2SO4 at 100 C for 30 minutes (catalyst: Ag2SO4)

DURATION OF THE TEST: 24 hours
SAMPLING: 0, 2, 4, 24 hours
ANALYTICAL PARAMETER: TOC and COD-Mn
ThOD: 1.21 mg/g = 275 mg/L (COD = 238 mg/L)
TEST CONDITIONS
- Test temperature: 25 C
CONTROLS: not included
REFERENCE SUBSTANCE: ethylene glycol was also included in this test and can be used as a positive control

Result : Probably no blank was included in the test, but it was stated, that the contribution of TOC and COD-Mn from the activated sludge was negligible.

Removal test substance as %COD, %TOC respectively:
0 hour: 0, 0
2 hour: 50, 60
4 hour: 92, 86
24 hour: 97, 94

REFERENCE SUBSTANCE
Removal test substance as %COD, %TOC respectively:
0 hour: 0, 0
2 hour: 14, 18
4 hour: 32, 38
24 hour: 92, 93

Test substance : CAS 56-81-5 (glycerine), purity not indicated
Conclusion : In this test glycerol is excellently biodegradable. However, the test used industrial activated sludge so the microorganisms may have been pre-adapted.
Most reliable data available.
Reliability : (2) valid with restrictions
This test was not a standard OECD 301 test, but gives information on the biodegradability of glycerol with pre-adapted microorganisms.

25.01.2002 (25)

Type : aerobic
Inoculum : activated sludge, industrial, adapted
Concentration : 220 mg/l related to Test substance
related to
Contact time :
Degradation : 97 (±) % after 14 day(s)
Result :
Deg. product :
Method : other: activated sludge degradability test
Year : 1988
GLP : no data
Test substance : other TS

Method : Aeration, neutral pH, 1 day adaptation, parameter: COD
Remark : 94% TOC removal.
Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Reliability : (4) not assignable
The information in the report was confined to the above.

19.12.2001 (26)

Type : aerobic
Inoculum : activated sludge, adapted
Concentration : 200 mg/l related to Test substance

related to

Contact time :
Degradation : = 98.7 (±) % after
Result : other: biodegradable under test conditions
Deg. product :
Method : other: not mentioned
Year : 1976
GLP : no data
Test substance :

Remark : Rate of degradation: 85 mg COD/g.hour.
Test condition : - Medium stirred, containing mineral salts;
- 20 °C, pH 7.2;
- % removal expressed as COD.
Reliability : (4) not assignable
The information in the report was confined to the above.

19.12.2001 (27)

Type : aerobic
Inoculum : activated sludge, industrial
Contact time :
Degradation : 75.2 (±) % after 5 day(s)
Result :
Deg. product :
Method : other: radiorespirometric test
Year : 1976
GLP : no data
Test substance : other TS

Method : INOCULUM/TEST ORGANISM
- Inoculum: Fresh sludge was obtained daily from a 7.5E4 L/day capacity activated sludge unit continuously fed with photographic processing effluent (1969-1976)
- Preparation of inoculum: Sludge was centrifuged and subsequently one part of sludge pellet was mixed with 2 parts of water in a homogeniser.
METHOD OF PREPARATION OF TEST SOLUTION: 1-2 mL sludge, 3 mL salt solution, 0.2 mL 1 M potassium phosphate buffer (pH 7.3). After sealing 0.1-0.2 mL 14C-glycerol was added.
INITIAL TEST SUBSTANCE CONCENTRATION (ug C/L): 7.7-139
TEST SYSTEM
- Culturing apparatus: 30 mL serum bottle sealed with rubber stoppers
- Measuring equipment: 14CO2 trapped with phenethylamine in scintillation fluid.
DURATION OF THE TEST: 5 days
SAMPLING: day 5
TEST CONDITIONS
- Test temperature: room temperature
- Other relevant factors: test was performed in the dark (pH 7.3) and stopped by the addition of 2 mL 1 M perchloric acid.
Result : TEST SUBSTANCE
14CO2 recovery after 5 days: 75.2%
Degradation based on BOD5 values: 43.5-52.9%

CONTROL
At 0 hours recovery 14CO2 <1.5%
Test substance : CAS 56-81-5 (U-14C-glycerol (0.111 mC/mg)), purity not indicated.
Reliability : (4) not assignable
1. The information was confined to what is included in the current summary, therefore the reliability of this study cannot be assessed.
2. Inoculum was activated sludge from laboratory unit fed

continously with photographic processing effluent.

19.12.2001 (28)

Type : anaerobic
Inoculum : anaerobic microorganisms
Concentration : 500 mg/l related to Test substance
related to
Contact time :
Degradation : 90 (±) % after 8 day(s)
Result : other: anaerobic degradation
Deg. product :
Method :
Year : 1978
GLP : no data
Test substance : other TS:

Method : INOCULUM
Source: well-digested domestic sludge
Acclimation: fed with acetate for several years
Concentration suspended solids: 1000 mg/L

INITIAL TEST SUBSTANCE CONCENTRATION (mg C/L): 500-1000 mg/L; the test substance was injected in intervals. the first 6 injections yielded an initial test substance concentration of 500 mg/L, thereafter the test substance concentration was increased to 1000 mg/L
TEST SYSTEM
- Culturing apparatus: Serum bottles, oxygen free (purged with CO2 & N2
- Number of culture flasks per concentration: duplicate
- Aeration: no, anaerobic system
- Measuring equipment: manometrically
DURATION OF THE TEST: not clearly indicated
ANALYTICAL PARAMETER: gas production in mL
TEST CONDITIONS
- Composition of mineral solution: 400 mg/L NH4Cl, 400 mg/L KCl, 400 mg/L MgSO4.6H2O, 40 mg/L FeCl2.6H2O, 4 mg/L CoCl3, 80 mg/L (NH4)2HPO4, 10 mg/L cysteine, 10 mg/L KI, 10 mg/L Na hexameta phosphate, 0.5 mg/L MnCl2, 0.5 mg/L NH4V2O3, 0.5 mg/L ZnCl2, 0.5 mg/L Na2MoO4.2H2O, 0.5 mg/L H3BO3, NaHCO3 (to maintain an alkalinity of 3000 mg CaCO3/L)
- Test vessels contained initially 50 mL inoculum, 100 mg acetate and 25 mg test substance
Result : After 8 days a lag time was reached at which 90% of glycerol was degraded. The removal rate is 200 mg/L/d.
Test substance : CAS 56-81-5 (glycerine), purity not indicated
Conclusion : Glycerol is biodegradable under circumstances described in this test.
Reliability : (4) not assignable
1. This test was set up to determine whether bacteria developed on acetate substrate can metabolise other compounds (e.g. glycerol).
2. Secondary literature with information essentially confined to what is included in the current summary.
3. Since adapted inoculum (adapted to acetate) is used, nothing can be said about the potency of glycerol to be readily biodegradable.

19.12.2001 (29)

Type : anaerobic
Inoculum : anaerobic microorganisms
Concentration : 47 mmol/l related to Test substance
related to
Contact time :
Degradation : 100 (±) % after 2 day(s)

Result	:	other: anaerobic biodegradation test. Degradation rate based on disappearance of test substance form the test solution.
Deg. product	:	yes
Method	:	
Year	:	1991
GLP	:	no data
Test substance	:	other TS:
Deg. products	:	1,3-propanediol acetate propionate
Method	:	INOCULUM/TEST ORGANISM - Inoculum (source): mixed microbial culture from a fermenter fed with waste water from an industrial distillery containing glycerol (INRA-Narbonne, France) METHOD OF PREPARATION OF TEST SOLUTION: 50/50 v/v inoculum/test medium (sulphate free or sulphate containing) INITIAL TEST SUBSTANCE CONCENTRATION (mg/L): ~47 mM = 4371 mg/L = 1692 mg C/L TEST SYSTEM - Anaerobic system with 20 mM or without sulphate DURATION OF THE TEST: 4 weeks SAMPLING: ~0, 1, 2, 3, 4, 5, 7, 12, 15, 20 days; TOC: 0, 1, 2, 3, 4, 5, 7, 12, 15 days ANALYTICAL PARAMETER: Glycerol (enzymatically), 1.3-propanediol (GC-FID), propionate and acetate; TOC; OD at 580 nm TEST CONDITIONS - Composition of mineral solution: sulphate free basal medium with anorganic salts, vitamins and trace elements - Test temperature: 37 C INTERMEDIATES / DEGRADATION PRODUCTS: see analytical parameter
Result	:	Without sulphate (pH 7..2) glycerol disappeared within 2 days from the test solution. Analyses were performed on glycerol, propanediol, propionate and acetate. -1,3-propanediol was found in the reaction mixture between day 1 and day 20 with a maximum of 17-21 mM at day 2-5. -Acetate was formed between day 5 and 20 reaching a maximum concentration of 27 mM at day 12-15. -The formation of propionate was analytically confirmed between day 5 and day 20 with a maximum concentration of 16 mM at day 7. -TOC (measured): 142 mM (d 0) decreased to 118 mM (d 5-15) -TOC (calculated): 142 mM (d 0); decreased to 45 mM (d 3); increase to 118 mM (d 7), decreaese to 100 mM (d 15) With sulphate (pH 7.2) glycerol disappeared within 2 days from the test solution. Analyses were performed on glycerol, propanediol, propionate and acetate. -1,3-propanediol was found in the reaction mixture up to day 7 (maximum concentration 4 mM at day 2). -Acetate was formed from day 5; maximum concentrations of 40-43 mM from day 12. -The formation of propionate was analytically confirmed between day 2 and day 20 with a maximum concentration of 20 mM at day 5. -Sulphate was maximum at day 0 (23 mM) and was around 0 mM from day 12 on. -TOC (measured): 142 mM (d 0), decreased to 12 mM (d 3), increased to 112 mM (d 12), lag phase at d 15-20 of 105 mM -TOC (calculated): 142 mM (d 0); decreased to 95 mM (d 3-15)
Test substance	:	CAS 56-81-5 (glycerine), purity not indicated

Conclusion	:	Glycerol is degraded very easily to other reaction products, but ultimate biodegradation (formation CO2) is limited in this experiment.
Reliability	:	(4) not assignable 1. Secondary literature with information essentially confined to what is included in the current summary. 2. TOC analyses show that for the glycerol degradation without sulphate between day 1-7 probably another important degradation product is formed. This product is not identified. From day 7 onwards the measured TOC is also higher than the calculated one, assuming an additional degradation product (may be accumulated CO2). For the glycerol degradation with sulphate the measured TOC is lower than the calculated one. This cannot be explained.

19.12.2001 (30)

Type	:	aerobic
Inoculum	:	other
Concentration	:	.5 mg/l related to Test substance related to
Contact time	:	8 day(s)
Degradation	:	100 (±) % after 8 day(s)
Result	:	
Deg. product	:	yes
Method	:	other: not indicated
Year	:	1988
GLP	:	no data
Test substance	:	other TS

Method	:	Microbial transformation rate of glycerol was measured in surface water from two sites at the Great Salt Lake. Properties surface water: Site I: 22.0% salt, pH 7.8, T = 22 C. Site II: 8.5% salt, pH 8.3, T = 22 C. In surface water from both sites glycerol concentration was below the detection limit (10.0 micromol/L) as determined enzymatically. For each site 10 mL of surface water was transferred into an aerobic, sterile, 58-ml rubber-stoppered vial containing 17.5 KBq [U-14C] glycerol (321.9 MBq/mmol; 0.50 mg/L). These mixtures were incubated at 25 C and two replicates were stopped after 0, 3, 6, 12, 24, 96 and 192 h by quenching with 10 M sodium hydroxide. 0.4 mL gas from the headspace of acidified samples was analyzed by a combined gas chromatograph-gas proportional counting technique and corrected for dissolved 14CO2 by the Bunsen solubility coefficient. The remaining labelled carbon in the liquid phase was determined by scintillation counting after neutralization with 6 M sodium hydroxide and centrifugation.
Result	:	After 8 days, <= 10% of glycerol was present in the liquid phase and about 70% of the labelled substrate was recovered as 14CO2. It is assumed that 30% of labelled substrate was incorporated into cell mass, which had been separated from the liquid by centrifugation.
Test substance	:	CAS 56-81-5 (glycerine), reagent grade purity.
Conclusion	:	From this study it can be deduced that glycerol can be degraded.
Reliability	:	(4) not assignable 1. Secondary literature. The information was essentially confined to the above summary. No information on bacteria, negative control. The study was no guideline study and no data on GLP were available. 2. The high salinity may result in poor degradation.

25.01.2002 (31)

Type	:	aerobic
Inoculum	:	activated sludge

Concentration	:	100 mg/l related to Test substance related to
Contact time	:	
Degradation	:	= 63 (±) % after 14 day(s)
Result	:	readily biodegradable
Deg. product	:	
Method	:	OECD Guide-line 301 C "Ready Biodegradability: Modified MITI Test (I)"
Year	:	1992
GLP	:	no data
Test substance	:	
Remark	:	Degree of biodegradation is expressed as BOD. Literature could not be retrieved.
Source	:	Unichema Chemie B.V. Gouda EUROPEAN COMMISION - European Chemicals Bureau Ispra (VA)
Test condition	:	Concentration of activated sludge: 30 mg/l.

19.12.2001 (32)

Type	:	aerobic
Inoculum	:	
Contact time	:	
Degradation	:	= 87 (±) % after
Result	:	
Method	:	SIMPLETREAT prediction of fate in wastewater treatment plant: Input parameters for model calculations: Molecular weight 92 Melting point 18 degC Boiling point 290 degC Vapour pressure 0.0106 Pa Log Kow -1.76 Water solubility 100,000 mg/L
Result	:	In a Sewage Treatment Plant 87% will be degraded.
Test substance	:	CAS 56-81-5 (Glycerine)

25.01.2002 (33)

3.6 BOD5, COD OR BOD5/COD RATIO

BOD5		
Method	:	other: standard dilution method (APHA No. 219)
Year	:	1971
Concentration	:	related to
BOD5	:	mg/l
GLP	:	no data
COD		
Method	:	other: standard potassium dichromate method (ASTM D 1252-67)
Year	:	1979
COD	:	1160 mg/g substance
GLP	:	no data
RATIO BOD5 / COD		
BOD5/COD	:	= .86
Method	:	In this test the relation between BOD, COD and ThOD is determined. The ThOD is the Theoretical Oxygen Demand. BIOLOGICAL OXYGEN DEMAND (BOD): BOD is determined using the standard dilution method at 20+/-1 C for a

period of 5 days and is reported to be conducted in accordance with the guideline (APHA), with the exception that 0.5 mg/L allylthiourea is added. 500 mL test solutions were seeded with a filtered 10 mL volume of the effluent from a biological sanitary waste treatment plant.
Control: mixture of glucose and glutamic acid to check the activity of the inoculum.

CHEMICAL OXYGEN DEMAND (COD):
COD is obtained using the standard potassium dichromate method. The test was reported to be conducted in accordance with the guideline (ASTM).

Result : ThOD: 1.22 g/g
BOD5: 1.00 g/g (=82% ThOD)
COD: 1.16 g/g (=95% ThOD)

Conclusion : Glycerol has the potency to be degraded in a wastewater treatment plant. The BOD5/COD ratio is >0.5 which suggests that glycerol is readily biodegradable.

Reliability : (2) valid with restrictions
1. Although the information available in the report (secondary) is confined to what is included in the current summary, the study is still thought to be reliable (Klimisch 2). A reliability of 2 is given, because it is stated that the test is performed in accordance with (acceptable) guidelines and the deviations are clearly reported.
2. The addition of 0.5 mg/L allylthiourea is believed to have no influence on the study results. Allylthiourea is added to prevent nitrification. This is not applicable for glycerine, but it is applicable to other substances tested in this report.

25.01.2002 (34)

BOD5
Method : other: respirometric method according to Wagner R. Vom wasser 42: 271-305 (1974)
Year :
Concentration : related to
BOD5 : mg/l
GLP : no data
COD
Method : other: The ThOD was used
Year : 1977
COD : 1216.1 mg/g substance
GLP : no data
RATIO BOD5 / COD
BOD5/COD : .753

Method : Degradation of glycerol was tested in a matrix containing municipal wastewater. The concentration of test substance was probably 6 g/L.
Result : BOD5: 898 mg/g
ThOD: 1216.1 mg/g
BOD5/ThOD [%]: 75.3
Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Reliability : (4) not assignable
The information in the report was confined to the above.

19.12.2001 (35)

BOD5
Method : other
Year :
Concentration : 100 g/l related to Test substance
BOD5 : ca. 700 mg/l

GLP :
COD
Method : other
Year :
COD : ca. 1160 mg/g substance
GLP :

Remark : Literature could not be retrieved.
Source : Wolff Walsrode AG Walsrode
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
15.11.2001

BOD5
Method : other: see remark
Year :
Concentration : related to
BOD5 : mg/l
GLP : no data

Remark : RS: BOD5: 0.65 g/g
TC: Standard dilution method using sewage as seed.
RE: Gellmann, I. Masters Thesis, Rutgers University (1950).

RS: BOD5: 0.80 g/g
TC: Standard dilution method using sewage as seed.
RE: Gellmann, I. PhD Thesis, Rutgers University (1952).

RS: BOD5: 0.617 g/g
TC: Standard dilution method using sewage as seed.
RE: Meissner, B. Wasserwirtsch.-Wassertechn. 4 (1954), 166.

RS: BOD5: 0.78 g/g
TC: Sier method using sewage (10%) as seed.
RE: Gellmann, I. Masters Thesis, Rutgers University (1950).

RS: BOD5: 0.83 g/g
TC: Warburg method using sewage (10%) as seed.
RE: Gellmann, I. Masters Thesis, Rutgers University (1950).

RS: BOD5: 0.81 g/g
TC: Standard dilution method using sp. cult as seed.
RE: Zobell, C.E., Biol. Bull., vol. 78 (1940), 388.

RS: BOD5: 0.64 g/g
TC: Standard dilution method using sewage as seed.
RE: Burford, M.G. et al. Rpt New Engl Intern. Water Poll.
Con. Comm. (1953).
Literature could not be retrieved.
Source : Unichema Chemie B.V. Gouda
15.11.2001

3.7 BIOACCUMULATION

BCF : = 3.16
Elimination :
Method : OECD Guide-line 305 C "Bioaccumulation: Test for the Degree of Bioconcentration in Fish"
Year : 1999
GLP :

Test substance :

Method : Calculation with Epiwin model.
Input logKow -1.65

Result : log BCF = 0.5
19.12.2001 (10)

3.8 ADDITIONAL REMARKS

Memo : An overview of rate constants concerning reactions of glycerol with hydrogen atoms and hydroxyl radicals

Method : In this report an overview is given of rate constants concerning reactions of glycerol with hydrogen atoms and hydroxyl radicals in aqueous solutions. The available information on the method is limited to the following
Hydrogen atoms reaction:
A. pH 1, method: Fe(CN)6 3-, 20-25 C
B. method: pulse radiolysis technique/Ag+, 20-25 C
Hydroxyl radicals reaction:
C. pH 7, method: pulse radiolysis technique/CNS-, 20-25 C
D. pH 10.7, method: pulse radiolysis technique/CO3 2-, 20-25 C
E. pH 9, method: PNDA, 20-25 C

Result : SPECIFIC RATE CONSTANTS:
Hydrogen atoms reaction:
A. 2E7
B. 1.45E7
Hydroxyl radicals reaction:
C. 9.5E8
D. 1.0E9
E. 1.1E9

Test substance : CAS 56-81-5 (glycerine), purity not indicated.
15.11.2001 (36)

Memo : Microbial degradation

Remark : This study was performed to test the growth of Aspergillus versicolor and Pseudomonas aeruginosa on esters and alcohols. In this test glycerol was used as the control substrate. It can be concluded that both micro-organisms (A. versicolor and P. aeruginosa) are capable of growth using glycerol as the carbon source.

Test substance : CAS 56-81-5 (glycerine), chemically pure (probably >99%)
15.11.2001 (37)

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	Static
Species	:	Leuciscus idus melanotus (Fish, fresh water)
Exposure period	:	
Unit	:	mg/l
LC0	:	> 10000
LC50	:	> 10000
LC100	:	> 10000
Limit test	:	
Analytical monitoring	:	no data
Method	:	
Year	:	1978
GLP	:	no data
Test substance	:	other TS

Method :

TEST ORGANISMS
- Species: Leuciscus idus melanotus
- Supplier: not specified
- Age/size/weight/loading: not specified
- Feeding (pretreatment): not specified
- Feeding during test: not specified

STOCK AND TEST SOLUTION AND THEIR PREPARATION
- no information included in the report

DILUTION WATER
- no information included in the report

TEST SYSTEM
- only information available about the test system was that this test was based on the static fish toxicity test with the Goldorfe after Mann (1975/1976)

DURATION OF THE TEST: not specified

TEST PARAMETER: mortality
OBSERVATION TIMES: not specified

STATISTICAL METHOD: not specified

Result : RESULTS:
- Nominal concentrations (mg/L): 10000
- Mortality: none
- Other effects: no data
- Dose related effects: no data

Test substance : CAS 56-81-5 (glycerine), purity not indicated

Conclusion : Most appropriate study available.

Reliability : (4) not assignable
The report was essentially confined to what is included in the current summary. There was no information on control mortality, physical-chemical parameters, actual tested concentrations, feeding rate, number and size of fish tested and photoperiod during the test and the duration of the test.

Flag : Critical study for SIDS endpoint

19.12.2001 (38)

Type	:	Static

Species	:	Carassius auratus (Fish, fresh water)
Exposure period	:	24 hour(s)
Unit	:	mg/l
LC50	:	> 5000
Limit test	:	
Analytical monitoring	:	Yes
Method	:	other: Standard Methods for Examination of Water and Wastewater. Am. Publ. Health Assoc. Inc., New York, Method No. 231
Year	:	1979
GLP	:	no data
Test substance	:	other TS
Method	:	TEST ORGANISMS - Species: Carassius auratus - Size;weight;loading: 62+/-7 mm; 3.3+/-1.0 g; 1.3 g/L DILUTION WATER - Source: local tap-water - Chemistry: Alkalinity 30 mg Na+/L; 65 mg/L (Cl)-, 4 mg/L (NO3)-, 35 mg/L (SO4)2-, 0.15 mg/L (PO4)3-, 25 mg/L (HCO3)-, 25 mg/L SiO2, 0.05 mg/L Fe, 100 mg/L (Ca)2+, 8 mg/L (Mg)2+; pH 7.8 TEST SYSTEM - Test type: static - Concentrations: 5000 mg/L - Exposure vessel type: 33 Lglass vessels containing 25 L of test solution. - Number of fish: 10 per replicate, 1 replicate/treatment - Test temperature: 20+/-1 C - Dissolved oxygen: >4 mg/L DURATION OF THE TEST: 24 hours TEST PARAMETER: mortality OBSERVATION TIMES: 24 hours ANALYSES: - Method: TOC analysis or extraction followed by GC analysis - Sampling times: 0 and 24 hours
Result	:	RESULTS: - Nominal concentrations (mg/L): 5000 - Measured concentrations (mg/L): not reported - Mortality: <50%
Test substance	:	CAS 56-81-5 (glycerine), purity not indicated.
Conclusion	:	Although the study has an exposure time of 24-hours, it is marked as the critical study, because the underlying publication provides relative much information on the test design.
Reliability	:	(4) not assignable 1. The information in the report (Secondary literature) was essentially confined to what is included in the current summary. Actually the report consists of an overview of the fish toxicity for a number of petrochemicals. No actual mortality rates at the tested concentration was reported. 2. The loading is with 1.3 g/L slightly higher than recommended by OECD 203 (1 g/L).
Flag	:	Critical study for SIDS endpoint

23.01.2002 (39)

Type	:	other: embryogenesis
Species	:	Cyprinus carpio (Fish, fresh water)
Exposure period	:	
Unit	:	

Limit test	:	
Analytical monitoring	:	no data
Method	:	other
Year	:	1997
GLP	:	no data
Test substance	:	other TS

Method : This test was set up to study the toxicity of different cryoprotective agents on carp embryos at different developmental stages. This is important for the design of cryopreservation protocols for carp embryos.

Embryos were selected at three developmental stages (morula, half-epiboly and heartbeat) and subsequently equilibrated for 5 minutes and 1 hour at 24 C in 1 M solution of glycerol in water (=92 g/L). A control group was included in which embryos were equilibrated to water of 24 C. At the end of the equilibration period, embryos were transferred into water and incubated at 24 C. Survival was defined as percentage of treated embryos that hatched.

Statistical method: Chi-square method.

Result : Hatching rates of carp embryos (%) for embryos exposed respectively at morula stage, half-epiboly stage and heartbeat stage:
- Control: 95, 94, 91
- Glycerol (5 min): 80*, 94, 86*
- Glycerol (1 h): 14*, 14*, 78*

*Statistically different from control treatment

Test substance : CAS 56-81-5 (glycerine), purity not indicated.

Reliability : (4) not assignable
1. The information in the report was confined to the above mentioned.
2. The study was designed to test the toxicity of glycerol, when used as a cryoprotective substance. The results of this test are not relevant for ecotoxicological purposes, because the tested concentration is extremely high.

08.01.2002 (40)

Type	:	static
Species	:	Leuciscus idus (Fish, fresh water)
Exposure period	:	48 hour(s)
Unit	:	Mg/l
LC0	:	> 250
Limit test	:	
Analytical monitoring	:	No
Method	:	other: Bestimmung der Wirkung von Wasserinhaltsstoffen auf Fische, DIN 38412 Teil 15
Year	:	1968
GLP	:	No
Test substance	:	other TS

Remark : 250 mg/l was highest concentration tested.
Test method conforms with OECD Guideline 203. 10 fish per tested concentration were used.

Test substance : CAS 56-81-5 (Glycerine), purity 99.5%.

02.01.2002 (41)

Type	:	static
Species	:	Oncorhynchus mykiss (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	Mg/l

LC100	:	= 51000 - 57000
Limit test	:	
Analytical monitoring	:	no data
Method	:	other: not mentioned
Year	:	1980
GLP	:	no data
Test substance	:	
Remark	:	Literature could not be retrieved.
Source	:	Unichema Chemie B.V. Gouda
Test condition	:	- Rainbow trout of 0.9 g; - 12 °C, hardness 40-50 mg/l CaCO3, alkalinity 30-35 mg/l CaCO3, pH 7.2-7.5; - Reconstituted dilution water; - Unmeasured concentration.

25.01.2002 (42)

Type	:	
Species	:	
Exposure period	:	96 hour(s)
Unit	:	Mg/l
LC50	:	= 184000
Method	:	other: calculated
Year	:	1999
GLP	:	
Test substance	:	
Remark	:	Calculated with EPIWIN, part ECOSAR v0.99f.
Reliability	:	(4) not assignable

19.12.2001 (10)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	static
Species	:	Daphnia magna (Crustacea)
Exposure period	:	24 hour(s)
Unit	:	Mg/l
EC50	:	> 10000
EC100	:	> 10000
Analytical monitoring	:	no data
Method	:	
Year	:	1982
GLP	:	no data
Test substance	:	other TS
Method	:	TEST ORGANISMS - Species: Daphnia magna STRAUS IRCHA - Source/supplier: not indicated - Breeding method: 20-30 Daphnia in 2L beaker glasses with at least 1.6 L water (286 mg CaCO3/L, pH 7.6-7.7), fed daily, 9 h light, 20 C; young daphnids were removed daily - Age: <=24 h - Feeding (pretreatment): daily - Feeding during test: not specified STOCK AND TEST SOLUTION AND THEIR PREPARATION - Vehicle, solvent: none

DILUTION WATER
- Source: synthetic test medium in accordance with ISO 6341 (medium recommended by OECD 202)
- Chemistry (sum of Ca and Mg: 2.5 mmol/L; Na/K ratio: 10/1; pH: 8.0+/- 0.2)

TEST SYSTEM
- Test type: static
- Concentrations: not specified
- Exposure vessel type: 50 mL glass beakers containing 20 mL test medium
- Number of individuals: 10 per replicate, 2 replicates/treatment
- Photoperiod (intensity of irradiation): not specified
PHYSICAL MEASUREMENTS
- Measuring times: 0 and 24 hours
- Test temperature: 20 C
- Dissolved oxygen: measured but not reported
- pH: 8.0+/-0.2 (0 hour), measured but not reported (24 hours)
- Adjustment of pH: no

DURATION OF THE TEST: 24 hours

TEST PARAMETER: immobility
OBSERVATION TIMES: 24 hours

REFERENCE SUBSTANCE: Potassium dichromate

STATISTICAL METHOD: Chi-Square test

Result : RESULTS:
- Nominal concentrations (mg/L): 10 000
- Immobility: <50%
- Other effects: no data
- Dose related effects: no data

RESULTS: TEST WITH REFERENCE SUBSTANCE
- Results: EC50 1.3 mg/L

Test substance : CAS 56-81-5 (glycerine), purity not indicated
Conclusion : Most elaborate study available.
Reliability : (4) not assignable
The report was essentially confined to what is included in the current summary. There was no information or limited information on control mortality, physico-chemical parameters, actual tested concentrations and feeding rate.
Flag : Critical study for SIDS endpoint
19.12.2001 (43)

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 24 hour(s)
Unit : Mg/l
EC50 : > 10000
Analytical monitoring : No data
Method : other: not indicated
Year : 1977
GLP : No data
Test substance : other TS

Remark : Daphnia magna collected from small pond, were exposed to several test substance concentrations for 24 h at

20 - 22 degr. C (pH before addition of test substance: 7.6 - 7.7, no adjustment of pH after addition of test substance). For the experiment 10 animals per replicate and 3 replicates were used.

Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Reliability : (4) not assignable
The information in the report was confined to the above.

19.12.2001 (44)

Type :
Species : Daphnia magna (Crustacea)
Exposure period : 24 hour(s)
Unit : mg/l
EC0 : > 500
Analytical monitoring : No
Method : other: Daphnien-Kurzzeittest, DIN 38412 Teil 11, Bestimmung der Wirkung von Wasserinhaltsstoffen auf Kleinkrebse
Year :
GLP : No
Test substance : other TS: as prescribed by 1.1-1.4 (Henkel KGaA).

Remark : 500 mg/l was highest concentration tested.
Test method conforms with OECD Guideline 202 A.
Literature could not be retrieved.
Source : Unichema Chemie B.V. Gouda

15.11.2001 (45)

Type :
Species : other: Daphnia
Exposure period : 48 hour(s)
Unit : mg/l
LC50 : = 153000
Method : other: calculated
Year : 1999
GLP :
Test substance :

Remark : Calculated with EPIWIN, part ECOSAR v0.99f.
Reliability : (4) not assignable

19.12.2001 (10)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species : Microcystis aeruginosa (Algae, blue, cyanobacteria)
Endpoint : other: inhibition of cell growth after 8 days
Exposure period : 8 day(s)
Unit : mg/l
EC3 : 2900
Limit test : No
Analytical monitoring : No data
Method :
Year : 1978
GLP : No data
Test substance : other TS

Method : TEST ORGANISMS
- Species: Microcystis aeruginosa
- Source/supplier: not specified
- Method of cultivation: stemculture and preculture were

maintained for 10 days in closed 100 mL erlenmeyer
containing 20 mL medium at 27 C and relative humidity of 50% before a new culture was set up
- Initial cell concentration: equivalent to a turbidity value corresponding to TE/F/578 nm = 20

DILUTION WATER
- Source: dist. water

GROWTH/TEST MEDIUM CHEMISTRY
- Test medium contains 24.8 mg/L NaNO3, 2.0 mg/L K2HPO4, 75 mg/L MgSO4.7H2O, 36 mg/L CaCl2.2H2O, 40 mg/L Na2SiO3, 58 mg/L Na2CO3, 3 mg/L C6H8O7.H2O, 3 mg/L C6H5FeO7.5H2O, 10 mg/L C10H14N2Na2O8.2H2O, 114 ug/L H3BO3, 72 ug/L MnCl2.4H2O, 8.8 ug/L ZnSO4.7H2O, 3.2 ug/L CuSO4.5H2O, 0.96 ug/L Na2MoO4.2H2O, 1.6 ug/L CoCl2.6H2O
- Chemistry (Hardness: 0.55 mmol/L Ca+Mg; P: 0.34 mg/L; N: 4.1 mg/L; chelators 0.03 mmol/L)
- pH 7.0

TEST SYSTEM
- Test type: static, daily shaken
- Concentrations: 10 solutions with unspecified concentrations (stock solution is 2, 4, 8, 16, 32, 64, 128, 256, 512 and 1024 times diluted)
- Exposure vessel type: culture tubes containing 10 mL test solution
- Number of replicates: 3 (test substance), 1 (control)
- Photoperiod (intensity of irradiation): continuous
PHYSICAL MEASUREMENTS
- no data

DURATION OF TEST: 8 days

TEST PARAMETER: inhibition of turbity after 8 days (extinction at 578 nm); more than 3% difference in extinction is considered as an effect
OBSERVATION TIMES: after 8 days

STATISTICAL METHOD: not specified

Result : RESULTS:
EC3 2900 mg/L

Test substance : CAS 56-81-5 (glycerine), purity not indicated

Conclusion : Most sensitive toxicity treshold value available.

Reliability : (4) not assignable
1. The test was not in accordance with OECD 201: test medium was different and extinction was only measured after 8 days.
No quantitative relationship changes between extinction and growth inhibition was provided. Therefore it was not possible to deduce a 72-hours EC50 value for the test substance. It is clear from this report, that glycerine is not very toxic for algae in the aquatic environment. It is not possible to confirm, however, whether algae were in the exponential growth phase for the duration of the test.
2. The turbidity of the test solution is expressed in "TE/F/578 nm". This refers to a measurement of the extinction of the test solution at 578 nm. The extinction is based on a calibration with test solutions containing different concentrations of formazine and therefore a relative turbidity value is given (see also DIN 38412 part 8, ISO 10712 and ISO 7027).
3. All publications refer to the same study.
4. Review articles containing multiple substances. Bringmann & Kuehn (GWF Wasser/abwasser, 117, 410-413, 1976) contained a comparison of

the toxicity of Pseudomonas putida with Microcystis aeruginosa and in Bringmann & Kuehn (Mitt. Internat. Verein. Limnol. 21: 275-284, 1978) the toxicity of Microcystis aeruginosa was compared to the toxicity of Scenedesmus quadricauda.

Flag :
25.01.2002 (46) (47) (48) (49)

Species	:	Scenedesmus quadricauda (Algae)
Endpoint	:	other: inhibition in cell growth after 8 days
Exposure period	:	8 day(s)
Unit	:	mg/l
EC3	:	> 10000
Limit test	:	
Analytical monitoring	:	no data
Method	:	
Year	:	1978
GLP	:	no data
Test substance	:	other TS

Method :

TEST ORGANISMS
- Species: Scenedesmus quadricauda
- Source/supplier: not specified
- Method of cultivation: stemculture and preculture were maintained for 10 days in closed 100 mL erlenmeyer containing 20 mL medium at 27 C and relative humidity of 50% before a new culture was set up
- Initial cell concentration: corresponding to an extinction value corresponding to a turbidity value of TE/F/578 nm = 20

DILUTION WATER
- Source: dist. water

GROWTH/TEST MEDIUM CHEMISTRY
- Chemistry (Hardness: 0.55 mmol/L Ca+Mg; P: 0.34 mg/L; N: 4.1 mg/L; chelators 0-0.03 mmol/L)
- pH 7.0

TEST SYSTEM
- Test type: static, daily shaken
- Concentrations: not specified
- Exposure vessel type: culture tubes containing 10 mL of test solution
- Number of replicates: 3
- Photoperiod (intensity of irradiation): continuous

PHYSICAL MEASUREMENTS
- no data

DURATION OF TEST: 7-8 days

TEST PARAMETER: inhibition of turbity after 8 days (extinction at 578 nm); 3% reduction of extinction is considered as an inhibitory effect
OBSERVATION TIMES: after 8 days

STATISTICAL METHOD: not specified

Result : RESULTS:
EC3 >10000 mg/L

All publications refer to the same study.

Test substance	:	CAS 56-81-5 (glycerine), purity not indicated
Reliability	:	(4) not assignable

1. The test was not in accordance with OECD 201: the test medium was different and extinction was only measured after 8 days. No quantitative relationship changes between extinction and growth inhibition were provided. Therefore it was not possible to deduce a 72-hours EC50 value for the test substance. It is clear from this report, that glycerine is not very toxic for algae in the aquatic environment.
2. The turbidity of the test solution is expressed in "TE/F/578 nm". This refers to a measurement of the extinction of the test solution at 578 nm. The extinction is based on a calibration with test solutions containing different concentrations of formazine and therefore a relative turbity value is given (see also DIN 38412 part 8, ISO 10712 and ISO 7027).
3. All publications probably refer to the same study.
4. In Bringmann & Kuehn (Mitt. Internat. Verein. Limnol. 21: 275-284, 1978) a comparison was made for the toxicity of several substances for Microcystis aeruginosa and Scenedesmus quadricauda.

19.12.2001 (46) (50) (51) (48)

Species : other algae: Green Algae
Endpoint :
Exposure period : 96 hour(s)
Unit : mg/l
EC50 : = 77712
Method : other: calculated
Year : 1999
GLP :
Test substance :

Remark : Calculated with EPIWIN, part ECOSAR v0.99f.
Reliability : (4) not assignable

19.12.2001 (10)

Species : other aquatic plant
Endpoint : growth rate
Exposure period : 28 day(s)
Unit :
Limit test :
Analytical monitoring : no data
Method : other: not mentioned
Year : 1970
GLP : no data
Test substance :

Method : TEST ORGANISMS
- Species: several species with their suppliers are included below.
CHLOROPHYCEAE:
1. Dunaliella tertiolecta Butcher (Wood Hole clone "Dun", Dr J. Strickland)
2. Tetraselmis maculata Butcher (Nanaimo strain "TMD", Dr T. Parsons)
3. Nannochloris oculata Droop (Millport strain no. 66, Dr M. Droop)
4. Brachiomonas submarina (Bohlin) Droop var. pulsifera 7/2a (Millport strain no. 44, Dr M. Droop)
CHRYSOPHYCEAE
5. Monochrysis lutheri Droop (Millport strain no. 60, Dr J. Strickland)
6. Isochrysis galbana Parke (Woods Hole clone "Iso", Dr J. Strickland)
7. Coccolithus huxleyi (Lohm) Kamptner (Woods Hole clone "BT-6", Dr T. Parsons
8. Prymnesium parvum Carter (Reich's Israeli strain, Dr M. Rahat)
BACILLARIOPHYCEAE
9. Phaedactylum tricornutum Bohlin (Lewin strain 74-M, Dr J. Lewin)

10. Skeletonema costatum (Grev.) Cleve (Woods Hole clone "Skel", Dr R. Guillard
11. Cyclotella nana Hustedt (Woods Hole clone "3H", Dr. R. Guillard)
CRYPTOPHYCEAE
12. Chroomonas salina (Wislouch) Butcher (Woods Hole undetermined cryptomonad clone "3C", Dr F Haxo)
13. Rhodomonas lens Pascher and Ruttner (Lasker's Gulf-stream strain, Dr L. Provasoli)
14. Hemiselmis virescens Droop (Millport strain no. 64, Dr L. Provasoli)
DINOPHYCEAE
15. Amphidinium carteri Hulburt (Woods Hole clone "Amphi 1" Dr L. Provasoli)
RHODOPHYCEAE
16. Porphyridium cruentum naegeli (Vischer's strain no. 107, Dr F. Haxo)
CYANOPHYCEAE
17. Agmenellum quadruplicatum (Menegh.) Brebisson (Van Baalen's strain "PR-6", Dr C. Van Baalen)
18. Anacystis marina (Hansg.) Drouet and Daily (Van Baalen's strain "6", Dr C. Van Baalen)

- Initial cell concentration: 2.5E4 cells/mL (test 1); 2.5E4-2.5E5 cells/mL (test 2)

DILUTION WATER
- Source: sea water, open ocean (salinity 33 ppt)

GROWTH/TEST MEDIUM CHEMISTRY
- Chemistry: Salinity 18 g Cl/L; pH 7.6-7.8; EDTA 21.8 uM. Further the medium contained anorganic salts (KNO3, NaH2PO4 and Na2SiO2), vitamins, trace metals (chelated) and buffer (=tris HCl)

TEST SYSTEM-TEST 1
- Test type: static
- Concentrations: 0, 4.6 and 46 g/L
- Exposure vessel type: 125 mL screw capped erlenmeyer flasks containing 40 mL of test solution
- Number of replicates: not indicated
- Photoperiod (intensity of irradiation): continuously (2690-3228 lux) or dark
- Test temperature: 20+/-2 C
- Shaken: mechanical agitation for a few minutes once every 24 hours
TEST SYSTEM-TEST 2
- Test type: static
- Concentrations: 0, 4.6, 46 and 92 g/L
- Exposure vessel type: 8 mL screw capped culture tubes containing 4 mL of test solution
- Number of replicates: not indicated
- Photoperiod (intensity of irradiation): continuously (2690-3228 lux) or dark

DURATION OF TEST: 28 days

TEST PARAMETER: growth (OD 600 mu (test 1 and 2) & haemacytometrically (test 1))
OBSERVATION TIMES: weekly (test 1); daily (test 2)

Result : RESULTS:

Apart from P. parvum and C. salina, none of the species showed any significant growth on glycerol in the absence of light. However in the presence of light, glycerol enhanced the growth of 16 species, in particular members of the Chrysophyceae and Cryptophyceae, one diatom (P. tricornutum), one rhodophyte (P. cruentum), and one chlorophyte (N.

oculata). A high concentration of glycerol was required for inducing or asserting growth enhancement of certain species, but was equally effective as the low concentrations or was inhibitory to other species.

Some species showed obvious cytological and metabolic changes from growth on glycerol.

The lowest effect concentration was a 28 day effect on growth at a concentration of 4600 mg/l for Agmenellum quadruplicatum and Anacystis marina.

Test substance : CAS 56-81-5 (glycerine), purity not indicated
Attached document : attached document ref 100.xls
Reliability : (4) not assignable
Secondary literature, non-GLP and not a standard OECD-test.

25.01.2002 (52)

Species : other aquatic plant: duckweed
Endpoint :
Exposure period :
Unit :
Method :
Year : 1997
GLP :
Test substance :

Remark : Literature could not be retrieved.
Result : Glycerol produces the same effects as ethylene glycol on Lemna gibba. The effects described for ethylene glycol are a relatively high EC50 with regard to frond reproduction, no metabolisation by duckweed, the fronds of duckweed are dark green, translucent and the growth medium contains gas bubbles which result from an enhanced uptake and subsequent respiration of sucrose. It is hypothesized that these effects are due to a disruption, of the pectin layer between cells as evidenced by the appearance of intercellular holes in the aerenchymatous tissues and a lifting of the cutin layer on the upper surface of the fronds. This disruption causes the plants to take up more water, lose their hydrophobicity and sink.
Conclusion : The result of the creation of intercellular holes by these compounds is to increase the uptake of soluble materials from the plant's aqueous growth medium. In case of a nutrient this can lead to stimulated growth; in case of a heavy metal ion or an organic toxicant, it can lead to enhanced toxicity.

19.12.2001 (53)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type : aquatic
Species : Pseudomonas putida (Bacteria)
Exposure period : 16 hour(s)
Unit : mg/l
EC0 : 10000
Analytical monitoring : no
Method : DIN 38412, part8
Year : 1994
GLP : yes
Test substance : other TS

Method : TEST ORGANISMS
- Species: Pseudomonas putida MIGULA Stamm Berlin 33/2 (DSM 50026
- Source/supplier: TTB-Mikrobiologie, Henkel KGaA

TEST DESCRIPTION
A stock solution of glycerine of 99.6 g/L (pH 5.3) was prepared. Test solutions (100 mL) were prepared by adding together the required volume of stock solution, nutrient medium (according to DIN 38412), water and inoculum of Pseudomonas putida. Test concentrations were 100, 300, 1000, 3000 and 10000 mg/l. One replicate from each treatment was shaken (100 rpm) for 16 h at 21-22°C. For the highest test concentration 3 replicates were included and also 3 replicates of a control treatment were included. At the end of the test, the extinction (436 nm) was measured.

Result : Based on the turbidity of the solution the growth of the bacteria can be estimated. For all test concentrations (100-10000 mg/L) no effects on the growth of bacteria were found. Compared to the control a positive effect of 0.5-3.4% was seen on the growth.

Test substance : CAS 56-81-5 (glycerine), purity 99.5%.

Reliability : (2) valid with restrictions
1. The EC0 is set on the highest tested concentration of 10000 mg/L.
2. The guideline DIN 38412, part 8 contains the following validity criterium: the turbidity in the control treatment should be increased with a factor of 100 during the test. Because there is no information on the initial turbidity, it is not clear whether this validity criterium was met. If however the test was performed in accordance with the guideline mentioned in the report, the initial turbidity was "TE/F=5". From the report it was clear that at the end of the test the turbidity in the control was "TE/F=592", which suggests that the validity criterium was met.
3. The turbidity of the test solution is expressed in "TE/F/436 nm". This refers to a measurement of the extinction of the test solution at 436 nm. The extinction is based on a calibration with test solutions containing different concentrations of formazine and therefore a relative turbity value is given (see also DIN 38412 part 8, ISO 10712 and ISO 7027).
4. The report was essentially confined to what is included in the current summary. According to the reviewer there is enough information to give this study a reliability of 2.

19.12.2001 (54)

Type : aquatic
Species : Chilomonas paramaecium (Protozoa)
Exposure period : 48 hour(s)
Unit : mg/l
EC5 : > 10000
Method :
Year : 1980
GLP : no data
Test substance : other TS

Method : TEST ORGANISMS
- Species: Chilomonas paramaecium Ehrenberg
- Laboratory culture: yes
- Initial cell concentration: 3.0E3 cells/ml

STOCK AND TEST SOLUTION AND THEIR PREPARATION
- Test substance is dissolved in sterile bidistilled water (pH 6.9). A series of dilutions is made using 1 part of test substance solution and 1, 2, 4, 8, 16, 32, 64, 128, 256, 512, 1024, 2048, 4096, 8192 and 16384 parts of water. Dilutions are prepared starting with a total test substance solution of 16 mL and subsequently preparing the following solution by 50% dilution with bidistilled water.

DILUTION WATER
- bidistilled water

GROWTH/TEST MEDIUM CHEMISTRY
- Medium (pre- and stem culture): 3190 mg/L glycine, 115 mg/L Ca(NO3)2.4H2O, 28 mg/L Mg(NO3)2.7H2O, 16 mg/L KNO3, 10 mg/L K2HPO4, 0.8 mg/L biotin (as D-Biotin), 8.0 mg/L nicotinic acid, 4.0 mg/L thiamin.HCl, 4.0 mg/L p-aminobenzoic acid, 2.0 mg/L panthotenic acid (as D-Panthotenic acid, Na-salt), 20 mg/L pyridoxamine (as pyridoxaminedihydrochlorid), 8.0 mg/L cyanocobalamin (vitamine B12); sterilised and pasteurised.
- Test medium: mixture of solution 1 (sterilised) an solution 2 (pasteurised) containing 7940 mg/L glycine, 288 mg/L Ca(NO3)2.4H2O, 69 mg/L Mg(NO3)2.7H2O, 40 mg/L KNO3, 26 mg/L K2HPO4, 15 ug/L biotin (as D-Biotin), 149 ug/L nicotinic acid, 74 ug/L thiamin.HCl, 74 ug/L p-aminobenzoic acid, 37 ug/L panthotenic acid (as D-Panthotenic acid, Na-salt), 372 ug/L pyridoxamine (as pyridoxaminedihydrochlorid), 149 ug/L cyanocobalamin (vitamine B12)

TEST SYSTEM
- Test cultures are prepared from pre-cultures (7 d, 20 C). Pre-cultures are prepared from stem cultures (3-4 d, 20 C).
- Test solution: 8 mL of test substance solution, 8 mL of test medium and 4 mL of pre-culture (15,000 cells/mL).
- Temperature: 20 C

DURATION OF TEST: 48 hours

TEST PARAMETER: cell growth using a Coulter counter
OBSERVATION TIMES: 48 hours

Result : At 10,000 mg/L the effect of glycerine was less than 5%.
Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Conclusion : >10,000 mg/L
Reliability : (4) not assignable
The test design was clearly described, but there was no information on the (actual) tested concentrations. Individual data are also not included in this review article (171 substances included).

19.12.2001 (55) (56)

Type : aquatic
Species : Clostridium sp. (Bacteria)
Exposure period :
Unit :
Analytical monitoring : no
Method :
Year : 1992
GLP : no data
Test substance : other TS

Method : Clostridium pasteurianum is known as a classical acid producer and usually ferments carbohydrates to butyrate, acetate, carbon dioxide and molecular hydrogen. Recent reports indicate the ability of Clostridium pasteurianum to produce acetone, butanol and ethanol in media with high glucose concentrations.

Therefore this test was set up to study the ability of Clostridium pasteurianum to produce solvents from renewable biomass. In the test glucose and glycerol were included, but in this summary only the part related to glycerol is included.

GROWTH MEDIUM
- Components: 1.74 g/L K2HPO4, 0.66 g/L NH4Cl, 0.251 g/L MgSO4.7H2O, 0.596 g/L KCl, 69 mg/L Fe-Na-EDTA, 6 g/L NaHCO3, 4 mg p-aminobenzoic acid, 0.24 mg/L biotin, 0.5 g/L yeast extract, 1 mg/L resazurin, 0.5 g/L cysteine-HCl and 20-200 g/L glycerol
- pH 7.0
- gas phase: 80% v/v N2 and 20% v/v CO2

TEST DESIGN
- EXPERIMENT 1: The effect on different concentrations of glycerol in the growth medium is determined using concentrations of 20, 40, 60, 80, 100, 120, 170 and 200 g glycerol/L.
- EXPERIMENT 2: The effect of iron limitation on glycerol fermentation is tested using an adapted growth medium (no yeast extract or Fe-Na-EDTA, supplemental FeSO4.H2O added (0, 3 or 20 uM) containing 40 g/L glycerol.

ENDPOINT
- Growth: measured spectrophotometrically by determination of the optical density at 578 nm.
- Products (ethanol, acetate, butanol, butyrate and propanediol) are measured by a gas chromatographic method

Result : EXPERIMENT 1:
- Fermentation resulted in the production of mainly ethanol, propanediol and butanol. Acetate and butyrate were only produced in trace amounts.
- The tolerance of C. pasteurianum to glycerol was rather high. Good growth was obtained at glycerol concentrations of up to 170 g/L. The optimum growth was found at glycerol concentrations of 100 g/L.
EXPERIMENT 2:
- Less iron in the medium resulted in lower amounts of reaction products with a changed pattern (ethanol/butanol decreased, lactate increased)

Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Conclusion : Good growth at glycerol concentrations up to 170 g/L.
Reliability : (4) not assignable
1. Secondary literature.
2. The test was not set up to determine the toxicity of glycerol, but can be used for this purpose. The sensitivity of the tested organism in comparison with other micro-organisms is not known.

19.12.2001 (57)

Type : aquatic
Species : Entosiphon sulcatum (Protozoa)
Exposure period : 72 hour(s)
Unit : mg/l
EC5 : 3200
Analytical monitoring : no
Method :
Year : 1980
GLP : no data
Test substance : other TS

Method : TEST ORGANISMS
- Species: Entosiphon sulcatum
- Laboratory culture: yes
- Initial cell concentration: 1.5E3 cells/ml

STOCK AND TEST SOLUTION AND THEIR PREPARATION
- Test substance is dissolved in sterile bidistilled water (pH 6.9). A series of dilutions is made using 1 part of test substance solution and 1, 2, 4, 8, 16,

32, 64, 128, 256, 512, 1024, 2048, 4096, 8192 and 16384 parts of water. Dilutions are prepared starting with a total test substance solution of 16 mL and subsequently preparing the following solution by 50% dilution with bidistilled water.

DILUTION WATER
- bidistilled water

GROWTH/TEST MEDIUM CHEMISTRY
- Medium (stem-, pre- and test culture): 290 mg/L Ca(NO3)2.4H2O, 70 mg/L Mg(NO3)2.6H2O, 40 mg/L KNO3; pH 6.9.

TEST SYSTEM
- Test cultures are prepared from precultures (72 h, 25 C). Pre-cultures are prepared from stem cultures (72-96 h, 25 C).
- Test solution: 8 mL of test substance solution, 8 mL of test medium, 2 mL bacteria suspension and 2 mL of preculture (15,000 cells/mL).
- Temperature: 25 C

DURATION OF TEST: 72 hours

TEST PARAMETER: cell growth using a Coulter counter
OBSERVATION TIME: 72 hours

Result : EC5 = 3200 mg/L
Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Reliability : (4) not assignable
The test design was clearly described, but there was no information on the (actual) tested concentrations. Individual data are also not included in this review article (171 substances included).

19.12.2001 (50) (55) (58)

Type : aquatic
Species : Pseudomonas putida (Bacteria)
Exposure period : 16 hour(s)
Unit : mg/l
EC3 : > 10000
Analytical monitoring : no data
Method : other: cell multiplication inhibition test
Year : 1980
GLP : no data
Test substance : other TS: glycerol. No indication about purity.

Method : TEST ORGANISMS
- Species: Pseudomonas putida
- Source/supplier: not specified
- Method of cultivation: stemculture and preculture were renewed weekly (incubation at 25 C for 24 h)
- Initial cell concentration: equivalent to an extinction value corresponding to a turbidity value of TE/F/436 nm = 10

DILUTION WATER
- Source: bidistilled water

GROWTH/TEST MEDIUM CHEMISTRY
- Chemistry: 1 g/L glucose, 0.21 g/L NaNO3, 0.12 g/L K2HPO4, 60 mg/L KH2PO4, 10 mg/L FeSO4.7H2O, 0.2 g/L MgSO4.7H2O, 0.083 mg/L Al2(SO4)3.18H2O, 0.042 mg/L KI, 0.042 mg/L KBr, 0.083 mg/L TiO2, 0.042 mg/L SnCl2.2H2O, 0.042 mg/L LiCl, 0.58 mg/L MnCl2.4H2O, 0.92 mg/L H3BO3, 0.083 mg/L ZnSO4.7H2O, 0.083 mg/L CuSO4.5H2O, 0.089 mg/L NiSO4.6H2O, 0.083 mg/L Co(NO3)2.6H2O

TEST SYSTEM
- Test type: static
- Concentrations: not specified, dilutions of stock in 1 to 16384 (2EXP0-2EXP14) parts of stock; controls containing saline instead of bacteria-suspension
- Temperature: 25 C

DURATION OF TEST: 16 h

TEST PARAMETER: inhibition of turbity after 16 hours (extinction at 436 nm); 3% reduction of extinction is considered as an inhibitory effect
OBSERVATION TIMES: after 16 hours

STATISTICAL METHOD: not specified

Result : EC3 >10000 mg/L
Test substance : CAS 56-81-5 (glycerine), purity not indicated
Reliability : (4) not assignable
1. The test is not in accordance with the current accepted guidelines, but gives an indication of the toxicity of glycerine to Pseudomonas putida.
2. The turbidity of the test solution is expressed in "TE/F/436 nm". This refers to a measurement of the extinction of the test solution at 436 nm. The extinction is based on a calibration with test solutions containing different concentrations of formazine and therefore a relative turbidity value is given (see also DIN 38412 part 8, ISO 10712 and ISO 7027).
3. Secondary literature with information essentially confined to what is included in the current summary.

25.01.2002 (59) (50) (51)

Type : aquatic
Species : Pseudomonas putida (Bacteria)
Exposure period : 75 minute(s)
Unit : mg/l
Method :
Year : 1998
GLP : no data
Test substance : other TS

Method : Test solutions (6 mL) were prepared by adding together
A. 5 mL distilled water, 0.5 mL imidazol buffer, 1 mL resazurin solution and 0.5 mL test culture (=reagent control)
B. 5.5 mL borate buffer, 1 mL resazurin solution (=blank sample)
C. solution of glycerol, 0.5 mL imidazol buffer, 1 mL resazurin solution and 0.5 mL test culture (= test sample)

Test concentrations were not specified. Two replicates from each treatment were incubated for 75 minutes at 37 C. At the end of the test, the extinction (615 nm) was measured.

Remark : Literature could not be retrieved.
Result : Mean of 5 experiments:
IC50 760000 mg/L
Test substance : CAS 56-81-5 (glycerine), purity not indicated.

19.12.2001 (12)

Type : aquatic
Species : Uronema parduzci (Protozoa)
Exposure period : 20 hour(s)

Unit	:	mg/l
EC5	:	> 10000
Analytical monitoring	:	no
Method	:	
Year	:	1981
GLP	:	no data
Test substance	:	other TS

Method :

TEST ORGANISMS
- Species: Uronema parduczi Chatton-Lwoff
- Laboratory culture: yes
- Initial cell concentration: 1.5E3 cells/ml
- Feeding before test: Escherichia coli (alive)
- Feeding during test: Escherichia coli (inactivated)

STOCK AND TEST SOLUTION AND THEIR PREPARATION
- Test substance is dissolved in sterile bidistilled water (pH 6.9). A series of dilutions is made using 1 part of test substance solution and 1, 2, 4, 8, 16, 32, 64, 128, 256, 512, 1024, 2048, 4096, 8192 and 16384 parts of water. Dilutions are prepared starting with a test substance solution of 16 mL and subsequently preparing the following solution by 50% dilution with bidistilled water.

DILUTION WATER
- bidistilled water

GROWTH/TEST MEDIUM CHEMISTRY
- medium used for stem-culture: 228 mg/L CaCl2.2H2O, 86 mg/L MgSO4.7H2O, 29 mg/L KH2PO4, 57 mg/L K2HPO4
- medium used for pre-and test culture: 290 Ca(NO3)2.4H2O, 70 mg/L Mg(NO3)2.6H2O, 40 mg/L KNO3

TEST SYSTEM
- Test cultures are prepared from pre-cultures (22 h, 25 C). Precultures are prepared from stem-cultures (max 72 h, 25 C).
- Test solution: 8 mL of test substance solution, 8 mL of test medium, 2 mL bacteria suspension and 2 mL of micro-organisms (15,000 cells/mL).
- Temperature: 25 C

DURATION OF TEST: 20 hours

TEST PARAMETER: cell growth using a Coulter counter
OBSERVATION TIMES: 20 hours

Result	:	At 10,000 mg/L the effect of glycerine was less than 5%.
Test substance	:	CAS 56-81-5 (glycerine), purity not indicated.
Reliability	:	(4) not assignable The test design was clearly described, but there was no information on the (actual) tested concentrations. Individual data are also not included in this review article (169 substances included).

19.12.2001 (60) (55)

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

Remark : A validated method for biological monitoring of glycerol is not available.
Source : Unichema Chemie B.V. Gouda
EUROPEAN COMMISION - European Chemicals Bureau Ispra (VA)
24.09.2001 (5)

4.8 BIOTRANSFORMATION AND KINETICS

Remark : Glycerol is readily absorbed into the gastrointestinal tract, metabolised by standard pathways in mammals and its products used to produce glucose, glycogen and fats. Literature could not be retrieved.
Source : Croda Universal Ltd Goole, North Humberside
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
15.11.2001 (61) (62)

4.9 ADDITIONAL REMARKS

Memo : Frog Embryo Teratogenesis Assay - Xenopus (FETAX)

Method : FETAX is a 96-h whole-embryo developmental toxicity screening assay according to test guideline ASTM E1439-91 (1991). The test was performed in triplo at three different laboratories.

Groups of 20 embryos were exposed to 10 concentrations of glycerol in presence and absence of metabolic activation (microsomes from Aroclor 1254 induced rats and an NADPH- generating system) during 96 hours. Exposure medium was FETAX-AB (reconstituted water which includes 100 U/mL penicillin and streptomycin).
Controls included were treated with FETAX-AB (4 dishes), FETAX (4 dishes), metabolic activation system (2 dishes) and activated cyclophosphamide (2 dishes with microsomes, 2 with NADPH-generating system and 2 without any activation).

Statistical method: Probit analysis (Litchfield-Wilcoxon), trimmed Spearman Karber, Steel and Torrie

Criteria for evaluating results: TI (teratogenic index i.e. 96-h LC50/96-h EC50(malformations)) > 1.5 and inhibition of growth > 30% compared to tests with microsomal fraction only.

Result : Laboratory 1 without rat liver microsomes (Aroclor treated)
96-h LC50 14.84 mg/ml (95% CI 10.41-19.26 mg/ml)
96-h EC50 (malformations) 10.89 mg/ml (95% CI 10.21-11.56 mg/ml)
LOEC (growth) 12.67 mg/ml (95% CI 8.09-17.24 mg/ml)
TI 1.35 (95% CI 1.02-1.68); TI = teratogenic index (LC50/EC50 malformations)

Laboratory 1 with rat liver microsomes (Aroclor treated)
96-h LC50 10.33 mg/ml (95% CI 6.18-14.48 mg/ml)
96-h EC50 (malformations) 10.76 mg/ml (95% CI 10.26-11.25 mg/ml)
LOEC (growth) 8.67 mg/ml (95% CI 6.05-11.28 mg/ml)
TI 0.97 (95% CI 0.54-1.40); TI = teratogenic index (LC50/EC50 malformations)

Laboratory 2 without rat liver microsomes (Aroclor treated)
96-h LC50 19.10 mg/ml (95% CI 17.52-20.69 mg/ml)
96-h EC50 (malformations) 11.48 mg/ml (95% CI 10.81-12.15 mg/ml)
LOEC (growth) 10.83 mg/ml (95% CI 10.02-11.65 mg/ml)
TI 1.67 (95% CI 1.44-1.90); TI = teratogenic index (LC50/EC50 malformations)

Laboratory 2 with rat liver microsomes (Aroclor treated)
96-h LC50 18.85 mg/ml (95% CI 16.72-20.98 mg/ml)
96-h EC50 (malformations) 11.26 mg/ml (95% CI 10.92-11.60 mg/ml)
LOEC (growth) 10.83 mg/ml (95% CI 9.20-12.47 mg/ml)
TI 1.67 (95% CI 1.52-1.83); TI = teratogenic index (LC50/EC50 malformations)

Laboratory 3 without rat liver microsomes (Aroclor treated)
96-h LC50 9.42 mg/ml (95% CI 8.27-10.56 mg/ml)
96-h EC50 (malformations) 6.67 mg/ml (95% CI 5.67-7.66 mg/ml)
LOEC (growth) 3.63 mg/ml
TI 1.41 (95% CI 1.33-1.50); TI = teratogenic index (LC50/EC50 malformations)

Laboratory 3 with rat liver microsomes (Aroclor treated)
96-h LC50 13.46 mg/ml (95% CI 11.05-15.87 mg/ml)
96-h EC50 (malformations) 5.84 mg/ml (95% CI 4.79-6.88 mg/ml)
LOEC (growth) 2.13 mg/ml (95% CI 0.66-3.60 mg/ml)
TI 2.33 (95% CI 1.82-2.85); TI = teratogenic index (LC50/EC50 malformations)

Conclusion : With metabolic activation:
96-h LC50 14.2 mg/ml (RSD 31%)
96-h EC50 (malformations) 9.29 mg/ml (RSD 29%)
LOEC (growth) 7.21 mg/ml (RSD 58%)
TI 1.66 (RSD 40%); TI = teratogenic index (LC50/EC50 malformations)

Without metabolic activation:
96-h LC50 14.5 mg/ml (RSD 33%)
96-h EC50 (malformations) 9.68 mg/ml (RSD 24%)
LOEC (growth) 9.04 mg/ml (RSD 51%)

TI 1.48 (RSD 16%); TI = teratogenic index (LC50/EC50 malformations)

According to the criteria set, glycerol gave an ambiguous result. Certain criteria suggested that glycerol is non-teratogenic, but others suggested it is. Severe malformations were observed at concentrations approaching the 96h LC50 with metabolic activation.

25.01.2002 (63)

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	= 27200 mg/kg bw
Species	:	rat
Strain	:	Long-Evans
Sex	:	female
Number of animals	:	12
Vehicle	:	
Doses	:	
Method	:	other: not indicated
Year	:	1953
GLP	:	
Test substance	:	

Method :
TEST ORGANISMS:
- Number: 12
- Mean weight at study initiation: 114 g

ADMINISTRATION:
- Dose: 27.26 mg/kg bw
- Route: oral (gavage)
- Vehicle: none (undiluted)
- Post dose observation period: 10 days

EXAMINATIONS: mortality, clinical signs, body weight (frequency not indicated), macroscopy in animals that died and selected survivors, histopathology of brain, heart, liver, spleen, stomach, intestine and kidney.

STATISTICAL METHOD: LD50 was calculated using logarithmic-probit graph paper

Result : MORTALITY: not indicated

CLINICAL SIGNS: muscle spasms and clonic convulsions prior to death. Survivors appeared normal within 2.5 hours after administration.

NECROPSY FINDINGS: hyperaemia of pylores and small intestine; congestion of the lungs; pale spleen; 3 animals showed hyperaemia of the cerebral meninges

Test substance : CAS 56-81-5 (glycerine)
Natural glyerine, achieved from market stock, purity not indicated (impurities were fatty acids and esters)
Synthetic glycerin, purity 99.5% (rest mainly water with very small amounts of glycerin polymers and glyceraldehyde)

Conclusion : Results for natural and synthetic glycerine were comparable
Most reliable and elaborate study available.

Reliability : (2) valid with restrictions
The report was limited to the above mentioned.

Flag : Critical study for SIDS endpoint
17.12.2001 (64) (65)

Type : LD50

Value	:	= 23000 mg/kg bw
Species	:	mouse
Strain	:	Swiss
Sex	:	male
Number of animals	:	
Vehicle	:	
Doses	:	
Method	:	other: not indicated
Year	:	1953
GLP	:	
Test substance	:	

Method :

TEST ORGANISMS:
- Number: 91 in total (not further specified)
- Mean weight at study initiation: 20 g

ADMINISTRATION:
- Doses: 15000 - 31500 mg/kg bw
- Route: oral (gavage)
- Vehicle: none (undiluted)
- Post dose observation period: 10 days

EXAMINATIONS: mortality, clinical signs, body weight (frequency not indicated), macroscopy in animals that died and selected survivors, histopathology of brain, heart, liver, spleen, stomach, intestine and kidney.

STATISTICAL METHOD: LD50 was calculated using logarithmic-probit graph paper

Result :

MORTALITY: not indicated

CLINICAL SIGNS: body tremor, Straub tail and clonic convulsions prior to death

NECROPSY FINDINGS: hyperaemia of small intestine and lungs at the two highest dose levels; hyperaemia of the kidneys and mucosa of the small intestine (not further specified)

Test substance :

CAS 56-81-5 (glycerine)
Natural glycerine, achieved from market stock, purity not indicated (impurities were fatty acids and esters)
Synthetic glycerin, purity 99.5% (rest mainly water with very small amounts of glycerin polymers and glyceraldehyde)

Conclusion : Results for natural and synthetic glycerine were comparable
Most reliable and elaborate study available.

Reliability : (2) valid with restrictions
The report was limited to the above mentioned

Flag : Critical study for SIDS endpoint

17.12.2001 (64)

Type	:	LD50
Value	:	= 10000 mg/kg bw
Species	:	guinea pig
Strain	:	
Sex	:	male
Number of animals	:	
Vehicle	:	
Doses	:	
Method	:	other: not indicated
Year	:	1953
GLP	:	

Test substance :

Method : TEST ORGANISMS:
- Number: 29 in total (probably 9-10/treatment)
- Mean weight at study initiation: 325 g

ADMINISTRATION:
- Dose: 7250 mg/kg bw (middle dose)
- Route: oral (gavage)
- Vehicle: none (undiluted)
- Post dose observation period: 10 days

EXAMINATIONS: mortality, clinical signs, body weight (frequency not indicated), macroscopy in animals that died and selected survivors, histopathology of brain, heart, liver, spleen, stomach, intestine and kidney.

STATISTICAL METHOD: LD50 was calculated using logarithmic-probit graph paper

Result : MORTALITY: not indicated

CLINICAL SIGNS: tremor of head and body after auditory stimuli immediately after administration, tremor prior to death

NECROPSY FINDINGS: hyperaemia of pylores and small intestine; congestion of the lungs; pale spleen

Test substance : CAS 56-81-5 (glycerine)
Natural glycerine, achieved from market stock, purity not indicated (impurities were fatty acids and esters)
Synthetic glycerin, purity 99.5% (rest mainly water with very small amounts of glycerin polymers and glyceraldehyde)

Conclusion : LD50 10000 mg/kg bw for natural glycerin
LD50 11500 mg/kg bw for synthetic glycerin

Reliability : (2) valid with restrictions
The report was limited to the above mentioned.

Flag : Critical study for SIDS endpoint

17.12.2001 (64)

Type : LD50
Value : > 25300 mg/kg bw
Species : rat
Strain : Sprague-Dawley
Sex : male/female
Number of animals : 10
Vehicle :
Doses :
Method : other: not indicated
Year : 1976
GLP :
Test substance :

Method : TEST ORGANISMS:
- Source: Gassner of Sulzfeld
- Age: not indicated
- Number: 5/sex/treatment
- Weight at study initiation: 170-230 g

ADMINISTRATION:
- Doses: not indicated

- Post dose observation period: 7 days

EXAMINATIONS: LD50 calculation

STATISTICAL METHOD: Probit analysis (Finney)

Test substance : CAS 56-81-5 (glycerine), purity not indicated (DAB 7 purity).
Reliability : (4) not assignable
1 The report is limited to the above mentioned
2 Only an LD50 value was mentioned
17.12.2001 (66)

Type : LD50
Value : = 27500 mg/kg bw
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Doses :

Reliability : (4) not assignable
The information was confined to the above.
16.11.2001 (65)

Type : LD50
Value : > 25000 mg/kg bw
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method :
Year : 1983
GLP :
Test substance : other TS

Test substance : CAS 56-81-5 (Glycerine), purity not indicated.
Reliability : (4) not assignable
The information was confined to the above.
17.12.2001 (67)

Type : LD50
Value : = 26250 - 28750 mg/kg bw
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Doses :

Reliability : (4) not assignable
The information was confined to the above.
16.11.2001 (65)

Type : LD50
Value : > 5000 mg/kg bw
Species : rat
Strain :
Sex :

Number of animals :
Vehicle :
Doses :

Reliability : (4) not assignable
The information was confined to the above.
16.11.2001 (65)

Type : LD50
Value : = 15750 mg/kg bw
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method : other
Year :
GLP : no data
Test substance : other TS

Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Reliability : (4) not assignable
The information in the report was confined to the above.
17.12.2001 (65)

Type : LD50
Value : = 58400 mg/kg bw
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method :
Year : 1954
GLP :
Test substance :

Test substance : CAS 56-81-5 (glycerine), purity 83-87%.
Reliability : (4) not assignable
The information was confined to the above.
17.12.2001 (68) (65) (69)

Type : LD50
Value : = 27500 mg/kg bw
Species : rat
Strain : Wistar
Sex : male
Number of animals : 10
Vehicle : water
Doses :
Method :
Year : 1941
GLP :
Test substance :

Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Reliability : (4) not assignable
The information was confined to the above.

17.12.2001 (70)

Type : LD50
Value : > 10000 mg/kg bw
Species : Rat
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method : other
Year :
GLP :
Test substance :

Remark : Literature could not be retrieved.
Source : UNION DERIVAN S.A. VILADECANS
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
25.01.2002

Type : LD50
Value : = 12600 mg/kg bw
Species : Rat
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method : other
Year : 1987
GLP : no data
Test substance : no data

Remark : Literature could not be retrieved.
Source : Croda Universal Ltd Goole, North Humberside
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
25.01.2002 (71)

Type : LD50
Value : > 24000 mg/kg bw
Species : Rat
Strain : Fischer 344
Sex : Female
Number of animals : 5
Vehicle :
Doses : several doses up to 24 g/kg
Method : other: not indicated
Year : 1979
GLP : no data
Test substance : other TS

Method : TEST ORGANISMS:
- Age: 12-14 weeks
- Number: 5/treatment
- Weight at study initiation: 150-200 g

ADMINISTRATION:
- Doses: several doses up to 24 g/kg

- Doses per time period: single dose
- Volume administered: undiluted test substance
- Post dose observation period: 14 days

EXAMINATIONS: mortality and clinical signs daily; necropsy on half of animals that died and selection of surviving animals in highest dose group at day 14

Result : MORTALITY:
- Number of deaths at each dose: none after 48 h

CLINICAL SIGNS: not reported

NECROPSY FINDINGS: not reported

Test substance : CAS 56-81-5 (glycerine), purity not indicated (glycerine/water mixture of unknown composition).

Reliability : (4) not assignable
1. Secondary literature; the information in the report is confined to the above.
2. The LD50 is based on mortality at 24 h post treatment. No information after a 48 h observation period is given.

17.12.2001 (72)

Type : LD50
Value : ca. 26000 mg/kg bw
Species : Mouse
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method : other
Year : 1950
GLP : no data
Test substance :

Remark : Comparative acute toxicity of synthetic and natural glycerin.
LD50 (natural glycerin) : 20.65 cc/kg
LD50 (synthetic glycerin): 20.81 cc/kg

Test substance : CAS 56-81-5 (glycerine), purity 99.8% for synthetic glycerine and for natural not indicated.

Reliability : (4) not assignable
The information was confined to the above.

17.12.2001 (73) (65)

Type : LD50
Value : = 38000 mg/kg bw
Species : Mouse
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method :
Year : 1976
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : Literature could not be retrieved.
Source : Unichema Chemie B.V. Gouda

EUROPEAN COMMISION - European Chemicals Bureau Ispra (VA)
Test substance : CAS 56-81-5 (glycerine), DAB 7 purity.
Reliability : (4) not assignable
25.01.2002 (74)

Type : LD50
Value : = 22400 ml/kg bw
Species : Mouse
Strain :
Sex :
Number of animals :
Vehicle :
Doses :

Reliability : (4) not assignable
The information was confined to the above.
16.11.2001 (65)

Type : LD50
Value : = 37736 mg/kg bw
Species : Mouse
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method :
Year :
GLP :
Test substance : other TS

Test substance : CAS 56-81-5 (glycerine), purity 83-87%.
Reliability : (4) not assignable
The information was confined to the above.
16.11.2001 (65)

Type : LD50
Value : = 31250 mg/kg bw
Species : Mouse
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method :
Year :
GLP :
Test substance : other TS

Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Reliability : (4) not assignable
The information was confined to the above.
16.11.2001 (65)

Type : LD50
Value : = 28000 mg/kg bw
Species : Mouse
Strain :
Sex :
Number of animals :

Vehicle	:	
Doses	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS
Test substance	:	CAS 56-81-5 (glycerine), purity not indicated.
Reliability	:	(4) not assignable The information was confined to the above.
16.11.2001		(65)
Type	:	LD50
Value	:	= 25888 mg/kg bw
Species	:	mouse
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS
Test substance	:	CAS 56-81-5 (glycerine), purity not indicated.
Reliability	:	(4) not assignable The information was confined to the above.
16.11.2001		(65)
Type	:	LD50
Value	:	= 37950 mg/kg bw
Species	:	mouse
Strain	:	NMRI
Sex	:	male/female
Number of animals	:	10
Vehicle	:	
Doses	:	
Method	:	other: not indicated
Year	:	
GLP	:	
Test substance	:	
Method	:	TEST ORGANISMS: - Source: Gassner of Sulzfeld - Age: not indicated - Number: 5/sex/treatment - Weight at study initiation: 15-25 g ADMINISTRATION: - Doses: not indicated - Post dose observation period: 7 days EXAMINATIONS: LD50 calculation STATISTICAL METHOD: Probit analysis (Finney)
Test substance	:	CAS 56-81-5 (glycerine), DAB 7, purity not specified
Reliability	:	(4) not assignable 1 The report is limited to the above mentioned 2 Only an LD50 value was mentioned

20.11.2001 (66)

Type : LD50
Value : > 38000 mg/kg bw
Species : mouse
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method :
Year :
GLP :
Test substance : other TS

Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Reliability : (4) not assignable
The information was confined to the above.

20.11.2001 (67)

Type : LD50
Value : = 37763 mg/kg bw
Species : mouse
Strain :
Sex :
Number of animals :
Vehicle :
Doses :

Test substance : CAS 56-81-5 (glycerine), purity 83-87%.
Reliability : (4) not assignable
The information was confined to the above.

15.11.2001 (68) (69)

Type : LD50
Value : = 25888 mg/kg bw
Species : mouse
Strain :
Sex :
Number of animals :
Vehicle :
Doses :

Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Reliability : (4) not assignable
The information was confined to the above.

15.11.2001 (68) (69)

Type : LD50
Value : = 12500 mg/kg bw
Species : mouse
Strain :
Sex :
Number of animals :
Vehicle :
Doses :

Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Reliability : (4) not assignable
The information was confined to the above.

15.11.2001 (75)

Type	:	LD50
Value	:	ca. 26000 mg/kg bw
Species	:	mouse
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	

Remark : Comparative acute toxicity of synthetic and natural glycerin.
LD50 (natural glycerin) : 20.65 cc/kg
LD50 (synthetic glycerin): 20.81 cc/kg

Test substance : CAS 56-81-5 (glycerine), purity 99.8% for synthetic glycerine and not indicated for natural glycerine.

Reliability : (4) not assignable
The information was confined to the above.

16.11.2001 (73)

Type	:	LD50
Value	:	= 4250 mg/kg bw
Species	:	mouse
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Method	:	
Year	:	1977
GLP	:	no data
Test substance	:	no data

Remark : Literature could not be retrieved.

Source : Croda Universal Ltd Goole, North Humberside
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (4) not assignable

25.01.2002 (76)

Type	:	LD50
Value	:	= 27000 mg/kg bw
Species	:	rabbit
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	no data

Remark : Literature could not be retrieved.

Source : Unichema Chemie B.V. Gouda
EUROPEAN COMMISION - European Chemicals Bureau Ispra (VA)

Reliability : (4) not assignable
25.01.2002 (77)

Type : LD50
Value : = 7750 mg/kg bw
Species : guinea pig
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method : other
Year :
GLP : no data
Test substance : other TS

Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Reliability : (4) not assignable
The information was confined to the above.
15.11.2001 (70) (78)

Type : LDLo
Value : = 1428 mg/kg bw
Species : human
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method : other
Year :
GLP : no data
Test substance : no data

Remark : Literature could not be retrieved.
Source : Unichema Chemie B.V. Gouda
EUROPEAN COMMISION - European Chemicals Bureau Ispra (VA)
16.11.2001 (79)

5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

Type : LD0
Value : > 18700 mg/kg bw
Species : rabbit
Strain :
Sex :
Number of animals : 6
Vehicle :
Doses : 6200-18700 mg/kg bw
Method : other
Year : 1953
GLP : no data
Test substance : other TS

Remark : No. of animals: 6.

Initial body weight of the tested animals: 3 kg.
Treatment: 8 hours under occlusion.

Comparative acute toxicity of synthetic and natural glycerin.

Result : No signs of clinical toxicity were observed for either synthetic or natural glycerol.
Test substance : CAS 56-81-5 (glycerine), purity 99.5%
Conclusion : Most reliable study available.
Reliability : (4) not assignable
The information in the report was confined to the above.
Flag : Critical study for SIDS endpoint
17.12.2001 (64) (65)

Type : other
Value :
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method :
Year : 1960
GLP : no data
Test substance : other TS

Method : TESTORGANISMS
- Weight at study initiation: 105-125 g
- Number of animals: 5 males/treatment

ADMINISTRATION:
- Type of exposure: dermal (animals dipped in test substance)
- Exposure duration: 20 and 40 min (after 24 hours animals were dipped in chloroform for 2 min)
- Size of application area: 4.5 X 5.5 cm
- Concentrations: 2 mL test substance

EXAMINATIONS:
Amount of urine excreted and colour of urine (excreted spontaneously or after squeezing) 60, 120 and 180 min after application; kidney histopathology

Result : Total urine excreted after 20 minutes exposure ~12.5 mL, after 40 minutes exposure ~ 9 mL. Heamoglobinuria was observed in 1/5 rats after 20 min and in 3/5 rats after 40 min exposure.
Subsequent exposure to chloroform gave haemoglobinuria in all animals.
Test substance : CAS 56-81-5 (glycerine), DAB 6, purity not specified
Conclusion : Treatment with glycerine induced haemoglobinuria in rats. From the effect of chloroform, it was concluded that the capillaries of the skin area were not distroyed.
Reliability : (4) not assignable
1. The experimental design was poorly described. The report was limited to the above. The study was not conducted to current regulatory test guidelines.
2. It cannot be excluded that the result is influenced by the way of application (dipping into the test substance), the size of the application area and the squeezing of the animals to obtain urine.
21.01.2002 (80)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

Type	:	LD50
Value	:	7500 - 10100 mg/kg bw
Species	:	Rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Route of admin.	:	i.p.
Exposure time	:	
Method	:	
Year	:	1976
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Test substance	:	CAS 56-81-5 (glycerine), purity not retrievable (DAB 7 purity).
Reliability	:	(4) not assignable The information in the report is confined to the above.

14.11.2001 (66) (67)

Type	:	LD50
Value	:	= 4420 mg/kg bw
Species	:	Rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Route of admin.	:	i.p.
Exposure time	:	
Method	:	
Year	:	
GLP	:	no data
Test substance	:	no data
Remark	:	Literature could not be retrieved.
Source	:	Unichema Chemie B.V. Gouda EUROPEAN COMMISION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable

25.01.2002 (81)

Type	:	LD50
Value	:	8600 - 9500 mg/kg bw
Species	:	Mouse
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Route of admin.	:	i.p.
Exposure time	:	
Method	:	
Year	:	1976
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Test substance	:	CAS 56-81-5 (glycerine), purity not retrievable (DAB 7 purity).
Reliability	:	(4) not assignable The information in the report is confined to the above.

14.11.2001 (66) (67)

Type	:	LD50
Value	:	= 8700 mg/kg bw
Species	:	Mouse
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Route of admin.	:	i.p.
Exposure time	:	
Method	:	
Year	:	1978
GLP	:	no data
Test substance	:	no data
Remark	:	Literature could not be retrieved.
Source	:	Croda Universal Ltd Goole, North Humberside EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable

25.01.2002 (82)

Type	:	LD50
Value	:	= 100 mg/kg bw
Species	:	Rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Route of admin.	:	s.c.
Exposure time	:	
Method	:	
Year	:	
GLP	:	no data
Test substance	:	no data
Remark	:	Literature could not be retrieved.
Source	:	Unichema Chemie B.V. Gouda EUROPEAN COMMISION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable

25.01.2002 (83)

Type	:	LD50
Value	:	= 91 mg/kg bw
Species	:	Mouse
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Route of admin.	:	s.c.
Exposure time	:	
Method	:	
Year	:	
GLP	:	no data
Test substance	:	no data
Remark	:	Literature could not be retrieved.
Source	:	Unichema Chemie B.V. Gouda EUROPEAN COMMISION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable

25.01.2002 (83)

Type	:	LD50

Value	:	5200 - 6600 mg/kg bw
Species	:	Rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Route of admin.	:	i.v.
Exposure time	:	
Method	:	
Year	:	1976
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Test substance	:	CAS 56-81-5 (glycerine), purity not retrievable (DAB 7 purity).
Reliability	:	(4) not assignable The information in the report is confined to the above.

14.11.2001 (66) (67)

Type	:	LD50
Value	:	5700 - 6700 mg/kg bw
Species	:	mouse
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Route of admin.	:	i.v.
Exposure time	:	
Method	:	
Year	:	1976
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Test substance	:	CAS 56-81-5 (glycerine), purity not retrievable (DAB 7 purity).
Reliability	:	(4) not assignable The information in the report is confined to the above.

14.11.2001 (66) (67)

Type	:	LD50
Value	:	4250 - 4370 mg/kg bw
Species	:	mouse
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Route of admin.	:	i.v.
Exposure time	:	
Method	:	
Year	:	
GLP	:	no data
Test substance	:	other TS
Remark	:	Comparative acute toxicity of synthetic and natural glycerin. LD50 (natural glycerin) : 4.37 g/kg LD50 (synthetic glycerin): 4.25 g/kg
Test substance	:	CAS 56-81-5 (glycerine), purity 99.8% for synthetic and no data for natural glycerine.
Reliability	:	(4) not assignable The information in the report is confined to the above.

16.11.2001 (73)

Type	:	LD50
Value	:	= 4250 mg/kg bw
Species	:	mouse
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Route of admin.	:	i.v.
Exposure time	:	
Method	:	
Year	:	1950
GLP	:	no data
Test substance	:	no data
Remark	:	Literature could not be retrieved.
Source	:	Croda Universal Ltd Goole, North Humberside EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable

25.01.2002 (84)

Type	:	LD50
Value	:	= 53000 mg/kg bw
Species	:	rabbit
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Route of admin.	:	i.v.
Exposure time	:	
Method	:	
Year	:	
GLP	:	no data
Test substance	:	no data
Remark	:	Literature could not be retrieved.
Source	:	Unichema Chemie B.V. Gouda EUROPEAN COMMISION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable

25.01.2002 (83)

Type	:	LD50
Value	:	> 25000 mg/kg bw
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Route of admin.	:	
Exposure time	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS
Test substance	:	CAS 56-81-5 (glycerine), purity not indicated.
Reliability	:	(4) not assignable The information was confined to the above.

20.11.2001 (67)

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	no data
Exposure time	:	24 hour(s)
Number of animals	:	8
Vehicle	:	
PDII	:	
Result	:	not irritating
Classification	:	
Method	:	other: not indicated
Year	:	1971
GLP	:	no
Test substance	:	other TS

Method :
TEST ANIMALS:
- Sex: male
- Weight at study initiation: >= 2 kg
- Number of animals: 8

ADMINISTRATION/EXPOSURE
- Area of exposure: 6.25 cm2
- Total volume applied: 0.5 ml
- Exposure period: 24 h

EXAMINATIONS
- Scoring system: Draize
- Examination time points: 24 and 72 h after application

This method was used by 19 different laboratories.

Result :
AVERAGE SCORE
- Overall irritation score per laboratory (24 and 72 h reading were added): 0.0-0.4 (max. 30 for each time point)

Test substance : CAS 56-81-5 (glycerine), purity not indicated.

Reliability :
(2) valid with restrictions
The information in the report is confined to the above.

17.12.2001 (85)

Species	:	rabbit
Concentration	:	
Exposure	:	no data
Exposure time	:	no data
Number of animals	:	6
Vehicle	:	
PDII	:	
Result	:	not irritating
Classification	:	
Method	:	other: Draize
Year	:	1979
GLP	:	no data
Test substance	:	other TS

Method :
TEST ANIMALS:
- Strain: New Zealand White
- Sex: female
- Source: Keene Ridge Farms, Moriarty, NM
- Weight at study initiation: 2-6 kg
- Number of animals: 6

ADMINISTRATION/EXPOSURE
- Preparation of test substance: undiluted

- Total volume applied: 0.5 ml
EXAMINATIONS
- Scoring system: Draize
- Examination time points: 24 and 72 h after application

Result : AVERAGE SCORE (score represents the mean of application to intact and abraded skin): 0.1
Test substance : CAS 56-81-5 (glycerine), purity not indicated (Glycerol/Water mixture of unknown composition).
Conclusion : Not irritating.
Reliability : (4) not assignable
1. Secondary literature; the information in the report is confined to the above.
2. The exposure time is not indicated.

25.01.2002 (86)

Species : rabbit
Concentration :
Exposure :
Exposure time :
Number of animals :
Vehicle :
PDII :
Result : not irritating
Classification :
Method : Draize Test
Year : 1953
GLP : no data
Test substance : other TS

Method : TEST ANIMALS:
- Weight at study initiation: 2.0-3.8 kg
- Number of animals: 6/treatment
ADMINISTRATION/EXPOSURE
- Doses: 0.5-4.0 mL/kg bw
- Area of exposure: 30% of body surface
- Occlusion: none at the two lower dose levels, occlusion at the two higher dose levels
- Exposure period: 8 hours/day, 5 days/week, 45 weeks
- Vehicle: none
- Total volume applied: 0.5-4.0 mL
EXAMINATIONS
- Scoring system: Draize (1944)
- Examination time points: not indicated
- Other: body weight and urinalysis, macroscopy and microscopy of thyroid, heart, lung, stomach, liver, spleen, adrenal gland, kidney, small intestine, bladder and treated skin.

Remark : Comparative acute toxicity of synthetic and natural glycerin.
No signs of local irritation after 90 days of application.
Result : AVERAGE SCORE
No signs of irritation (no specifications)
OTHER EFFECTS: no treatment related effects on the other parameters measured.
Test substance : CAS 56-81-5 (glycerine), purity 99.5% for synthetic and natural glycerine.
Reliability : (2) valid with restrictions
The information in the report is confined to the above.

25.01.2002 (64)

Species : rabbit
Concentration :

Exposure	:	
Exposure time	:	
Number of animals	:	
Vehicle	:	
PDII	:	
Result	:	slightly irritating
Classification	:	
Method	:	other
Year	:	1986
GLP	:	no data
Test substance	:	no data
Remark	:	Literature could not be retrieved.
Source	:	Croda Universal Ltd Goole, North Humberside EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable

25.01.2002 (87)

5.2.2 EYE IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Dose	:	.1 ml
Exposure time	:	
Comment	:	
Number of animals	:	6
Vehicle	:	
Result	:	not irritating
Classification	:	
Method	:	other: Draize (1944)
Year	:	1971
GLP	:	no data
Test substance	:	other TS
Method	:	TEST ANIMALS: - Sex: male - Weight at study initiation: >= 2 kg - Number of animals: 6 ADMINISTRATION/EXPOSURE - Preparation of test substance: undiluted - Amount of substance instilled: 0.1 ml EXAMINATIONS - Scoring system: Draize - Observation at: 1, 24, 72 h and 7 days - Tool used to assess score: at 24, 72 h and 7 days fluorescein examination if no effects were seen at the previous examination The same method was used in 20 different laboratoria.
Result	:	AVERAGE SCORE (24-h median) - Overall irritation score per laboratory: 0-2 (110 is maximum score)
Test substance	:	CAS 56-81-5 (glycerine), purity not indicated.
Reliability	:	(2) valid with restrictions The information in the report is confined to the above.

17.12.2001 (85)

Species	:	rabbit
Concentration	:	undiluted
Dose	:	.1 ml

Exposure time	:	
Comment	:	
Number of animals	:	6
Vehicle	:	
Result	:	not irritating
Classification	:	
Method	:	other: Draize
Year	:	1979
GLP	:	no data
Test substance	:	other TS

Method : TEST ANIMALS:
- Strain: New Zealand White
- Sex: female
- Source: Keene Ridge Farms, Moriarty, NM
- Weight at study initiation: 2-6 kg
- Number of animals: 6

ADMINISTRATION/EXPOSURE
- Preparation of test substance: undiluted
- Amount of substance instilled: 0.1 ml

EXAMINATIONS
- Scoring system: Draize
- Observation at: 1, 24, 48, 72 and 96 h
- Tool used to assess score: fluorescein

Result : AVERAGE SCORE
- Overall irritation score: 0.4 at 1 h, 0 at 24-96 h

REVERSIBILITY: yes, within 24 h

Test substance : CAS 56-81-5 (glycerine), purity not indicated (Glycerol/Water mixture of unknown composition).

Conclusion : Not irritating.

Reliability : (4) not assignable
Secondary literature; the information in the report is confined to the above.

25.01.2002 (72)

Species	:	rabbit
Concentration	:	
Dose	:	
Exposure time	:	
Comment	:	
Number of animals	:	
Vehicle	:	
Result	:	slightly irritating
Classification	:	
Method	:	OECD Guide-line 405 "Acute Eye Irritation/Corrosion"
Year	:	
GLP	:	yes
Test substance	:	no data

Remark : Rabbit strain: New Zealand White; sex: male.
The conjunctiva was slightly to moderately irritated in all rabbits one hour after treatment. Thereafter the irritation diminished and had disappeared at 48 hours after treatment.

Test substance : CAS 56-81-5 (glycerine), purity not indicated.

Reliability : (4) not assignable
The information in the report is confined to the above.

25.01.2002 (65)

Species : rabbit
Concentration :
Dose : .1 ml
Exposure time :
Comment :
Number of animals :
Vehicle :
Result : not irritating
Classification :
Method : other
Year : 1953
GLP : no data
Test substance : other TS

Method : TEST ANIMALS:
- Number of animals: 4

ADMINISTRATION/EXPOSURE:
- Amount of substance instilled: 0.1 mL
- Vehicle: none
- Postexposure period: 48 hours

EXAMINATIONS
- Scoring system: Draize (1944)
- Observation times: 1, 24 and 48 hours
- Tool used to assess score: fluorescein staining

Remark : Comparative acute toxicity of synthetic and natural glycerin.
Result : Irritation was observed with both synthetic and natural glycerol, but was absent at 24 and 48 hours.
Test substance : CAS 56-81-5 (glycerine), purity 99.5% for synthetic and natural glycerine.
Reliability : (2) valid with restrictions
The information in the report is confined to the above.

17.12.2001 (64)

Species : rabbit
Concentration :
Dose :
Exposure time :
Comment :
Number of animals :
Vehicle :
Result : slightly irritating
Classification :
Method : other
Year : 1986
GLP : no data
Test substance : no data

Remark : Literature could not be retrieved.
Source : Croda Universal Ltd Goole, North Humberside
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable

25.01.2002 (87)

Species : rabbit
Concentration :
Dose :
Exposure time :

Comment	:	
Number of animals	:	
Vehicle	:	
Result	:	slightly irritating
Classification	:	
Method	:	other
Year	:	1986
GLP	:	no data
Test substance	:	no data
Remark	:	Literature could not be retrieved.
Source	:	Croda Universal Ltd Goole, North Humberside EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable

25.01.2002 (88)

Species	:	human
Concentration	:	
Dose	:	
Exposure time	:	
Comment	:	
Number of animals	:	
Vehicle	:	
Result	:	not irritating
Classification	:	
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	no data
Remark	:	A strong burning and stinging sensation, with tear production but no injury apparently from contact with the neat chemical. Literature could not be retrieved.
Source	:	Unichema Chemie B.V. Gouda
Reliability	:	(4) not assignable

25.01.2002 (89)

5.3 SENSITIZATION

Type	:	Patch-Test
Species	:	human
Number of animals	:	
Vehicle	:	
Result	:	not sensitizing
Classification	:	
Method	:	other
Year	:	1973
GLP	:	no
Test substance	:	other TS: glycerol. No indication about purity.
Remark	:	Medicolegal aspects of occupational dermatitis survey in a foam rubber factory. Skin patch tests for 48 hours.
Test substance	:	CAS 56-81-5 (glycerine), purity not indicated (unknown mixture of glycerine and water).
Reliability	:	(4) not assignable The information was confined to the above.

17.12.2001 (90)

Type	:	other
Species	:	guinea pig
Number of animals	:	12
Vehicle	:	
Result	:	not sensitizing
Classification	:	
Method	:	other
Year	:	1953
GLP	:	no data
Test substance	:	other TS
Method	:	TEST ANIMALS: - Weight at study initiation: 350-429 g - Number of animals: 12/treatment ADMINISTRATION/EXPOSURE - Induction schedule: 10 times on alternate days - Concentrations used for induction: 0.1 mL of 0.1% solution of natural or synthetic glycerol in isotonic sodium chloride solution. - Challenge schedule: 2 weeks after last induction - Concentrations used for challenge: 0.05 mL of (presumably) 0.1% solution EXAMINATIONS - Grading system: diameter, height and colour of the reaction compared to the reaction at the first sensitizing injection
Remark	:	Comparative acute toxicity of synthetic and natural glycerin. Following 10 injections of 0.1 ml of a 0.1% solution of natural or synthetic glycerin, the investigators noted that a further injection of 0.05 ml of the solutions gave no indications of sensitization to glycerin in any of the 24 adult white male guinea pigs.
Result	:	No response was observed to challenge for either synthetic or natural glycerol.
Test substance	:	CAS 56-81-5 (glycerine), purity 99.5% for natural and synthetic glycerine.
Conclusion	:	Most reliable study available.
Reliability	:	(4) not assignable The information in the report is confined to the above.

17.12.2001 (64)

Type	:	Patch-Test
Species	:	human
Number of animals	:	
Vehicle	:	
Result	:	not sensitizing
Classification	:	
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	other TS: glycerol. No indication about purity.
Remark	:	Out of "several thousand" dermatitis patients who were tested, only two showed reactions in 20-24-hr covered patch tests with 50% glycerol. However, because the purity of the glycerol tested was not given, it is not excluded that the observed effects in two patients could have been caused by an impurity or a contamination of the sample (e.g. propylene glycol or butanetriol). With respect to the very high number of individuals tested and

the concentration of the test compound (50%) one would expect to see more incidences, if glycerol had a relevant allergenic potential (Lit. Henkel, 1992).
Literature could not be retrieved.

Source : Unichema Chemie B.V. Gouda
EUROPEAN COMMISION - European Chemicals Bureau Ispra (VA)

Reliability : (4) not assignable

25.01.2002 (91)

Type : Patch-Test
Species : human
Number of animals :
Vehicle :
Result : ambiguous
Classification :
Method : other
Year : 1979
GLP : no data
Test substance : no data

Remark : Literature could not be retrieved.
Out of "several thousand" dermatitis patients tested, two showed skin reactions in 20 to 24-hr covered patch tests with 50% glycerol and were thus diagnosed as glycerol sensitized. One also reacted with 1% glycerol. Both had regularly used a skin cream containing 10% glycerol.

Source : Croda Universal Ltd Goole, North Humberside
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (4) not assignable

25.01.2002 (92) (93)

5.4 REPEATED DOSE TOXICITY

Type :
Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : inhalation
Exposure period : 14 days
Frequency of treatm. : 5 days/week, 6 hours/day
Post exposure period :
Doses : 1000, 2000 and 4000 mg/m3
Control group : yes, concurrent no treatment
LOAEL : = 1000 mg/m³
Method : other: not indicated
Year : 1992
GLP : no data
Test substance :

Method : TEST ORGANISMS
- Age: not indicated
- Weight at study initiation: not indicated
- Number of animals: 10/sex/treatment
- Source: Charles River Breeding Laboratories

ADMINISTRATION / EXPOSURE
- Exposure period: 14 days, 5 days/week, 6 hours/day (total 10 exposures)
- Route of administration: nose only

- Doses: 0, 1000, 2000 and 4000 mg/m3 (calculated to be equivalent to oral doses 339, 678, 1355 mg/kg bw based on average body weight of 0.425 kg and 6 L/h respiratory volume)
- Particle size: MMAD <1.5 um (respirable)
- Preparation of particles: viscous-liquid aerosol generator
- Air changes: not indicated

CLINICAL OBSERVATIONS AND FREQUENCY:
- Mortality/clinical signs: twice daily
- Body weight: at 2 or 3 days intervals
- Food consumption: weekly
- Haematology: not specified (complete blood count included)
- Biochemistry: blood urea nitrogen, creatinine, glucose, protein, albumin, albumin/globulin, ASAT, ALAT, LDH, gamma glutamyl transferase, cholesterol, triglycerides and phospholipids
- Urinalysis: not conducted

ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Organ weights: lungs, liver, kidneys, brain and heart
- Macroscopic: not specified (complete necropsy)
- Microscopic: respiratory tract (with associated lymphnodes) and gross lesions (all animals); liver, kidneys, heart of control and high dose animals; lungs trachea and anterior nasal cavity were stained with hematoxylin and eosin and duplicate slides with Alcian blue/periodic acid Schiff (Goblet cell changes)

ANALYSES: target concentration and homogeneity of aerosol
- Method: sampling with aerosol monitor and gravimetric and GC analyses
- Sampling times: actual concentration 2 samples per exposure chamber; homogeneity and uniformity in mock exposure before start of the experiment (6 samples) and during animal exposure (10 samples/concentration)

STATISTICAL METHODS: ANOVA, least significant difference

Result : ANALYSES:
- Actual dose level: 1000, 1930 and 3910 mg/m3 (98-100% of target)
- Stability: not reported
- Homogeneity (uniformity): relative standard deviation 1.6-2.5% of mean value

TOXIC RESPONSE/EFFECTS BY DOSE LEVEL:
- Mortality: 2 males at 1000 mg/m3 and 1 male and 1 female at 2000 mg/m3
- Clinical signs: no treatment related effects
- Body weight gain: decreased in males and females at all concentrations (58-28% in females)
- Food consumption: no treatment related effects
- Clinical chemistry: glucose decreased in females at all concentrations (28-19%)
- Haematology: no treatment related effects
- Organ weights: no treatment related effects
- Gross pathology: no treatment related effects
- Histopathology: minimal to midl squamous metaplasia of the epiglottis in males and females at 0, 1000, 1930 and 3910 mg/m3 (1/10, 13/18, 16/19 and 13/14, respectively). Although a dose-related increase in the frequency of squamous metaplasia was not apparent, the frequency of mild metaplasia was greatest at the top dose (7 animals with minimal and 6 with

mild).

STATISTICAL RESULTS: all effects mentioned showed statistical significance, except the decreased weight gain in males

Test substance : CAS 56-81-5 (glycerine), purity >99.8%

Conclusion : LOAEL 1000 mg/m3 based on local effects on the epithelium of the upper respiratory tract.
Most reliable study.
Most reliable study available.

Reliability : (2) valid with restrictions
1 The report is limited to the above mentioned. No individual values were included.
2 The effect on body weight can be attributed to stress due to the nose only exposure and is therefore considered not related to exposure to the test substance
3 The effects on glucose were seen in females only and showed no relationship with concentration. Although a relationship between glycerol exposure and glucose in serum can not be fully excluded, the biological relevance of this effect is considered of minor importance.

Flag : Critical study for SIDS endpoint

25.01.2002 (73) (94)

Type :
Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : inhalation
Exposure period : 13 weeks
Frequency of treatm. : 5 days/week, 6 hours/day
Post exposure period :
Doses : 33, 165 and 660mg/m3
Control group : yes, concurrent no treatment
NOAEL : = 167 mg/m³
Method : other: not indicated
Year : 1992
GLP : no data
Test substance :

Method : TEST ORGANISMS
- Age: not indicated
- Weight at study initiation: not indicated
- Number of animals: 15/sex/treatment
- Source: Charles River Breeding Laboratories

ADMINISTRATION / EXPOSURE
- Exposure period: 13 weeks, 5 days/week, 6 hours/day
- Route of administration: nose only
- Doses: 0, 33, 165, 660 mg/m3 (calculated to be equiavlent to oral doses of 11.2, 55.9 and 224 mg/kg bw based on average body weight of 0.425 kg and 6 L/h respiratory volume)
- Particle size: MMAD <2.0 um (respirable)
- Preparation of particles: viscous-liquid aerosol generator
- Air changes: not indicated

CLINICAL OBSERVATIONS AND FREQUENCY:
- Mortality/clinical signs: twice daily
- Body weight: weekly
- Food consumption: weekly

- Haematology: not specified (complete blood count included)
- Biochemistry: blood urea nitrogen, creatinine, glucose, protein, albumin, albumin/globulin, ASAT, ALAT, LDH, gamma glutamyl transferase, cholesterol, triglycerides and phospholipids

ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Organ weights: lungs, liver, kidneys, brain and heart
- Macroscopic: not specified (complete necropsy)
- Microscopic: total of 40 tissues of high dose and control animals; lungs trachea and anterior nasal cavity were stained with hematoxylin and eosin and duplicate slides with Alcian blue/periodic acid Schiff (Goblet cell changes)

Three rats/sex of control and high dose group were killed during week 10, lung lobes were excised and 2 samples/rat were examined by transmission electron microscopy for abnormalities associated with the Clara cells. The same procedure was followed for 3 rats/sex of all groups during terminal necropsy

ANALYSES: target concentration and homogeneity of aerosol
- Method: sampling with aerosol monitor and gravimetric and GC analyses
- Sampling times: actual concentration 2 samples per exposure chamber; homogeneity and uniformity in mock exposure before start of the experiment (6 samples) and during animal exposure (20 samples/concentration)

STATISTICAL METHODS: ANOVA, least significant difference

Result : ANALYSES:
- Actual dose level: 33, 167 and 662 mg/m3 (100-101% of target)
- Stability: not reported
- Homogeneity (uniformity): relative standard deviation <1% of mean value

TOXIC RESPONSE/EFFECTS BY DOSE LEVEL:
- Mortality: none
- Clinical signs: no treatment related effects
- Body weight gain/food consumption: no treatment related effects
- Clinical chemistry: triglycerides decreased in males at 33 (34%) and 167 mg/m3 (22%) only.
- Haematology: no treatment related effects
- Organ weights: no treatment related effects
- Gross pathology: no treatment related effects
- Histopathology: minimal squamous metaplasia of the epiglottis in 2/25, 1/19, 4/20 and 10/21 rats at 0, 33, 167 and 662 mg/m3; 1 male at 662 mg/m3 showed mild squamous metaplasia.
No differences in morphology of the Clara cells in control and high dose rats

STATISTICAL RESULTS: all effects mentioned showed statistical significance (squamous metaplasia only significant at high concentration)

Test substance : CAS 56-81-5 (glycerine), purity >99.8%

Conclusion : NOAEL 167 mg/m3 based on local irritant effects on the upper respiratory tract.
Most reliable study.

Most reliable study available.

Reliability : (2) valid with restrictions
1 The report is limited to the above mentioned. No individual values were included.
2 The effects on triglycerides were seen in males only and showed no relationship with concentration. Although a relationship between glycerol exposure and triglycerides in serum can not be fully excluded, the biological relevance of this effect is considered of minor importance.

Flag : Critical study for SIDS endpoint

25.01.2002 (73) (94)

Type	:	
Species	:	rat
Sex	:	male/female
Strain	:	Long-Evans
Route of admin.	:	oral feed
Exposure period	:	2 year
Frequency of treatm.	:	
Post exposure period	:	
Doses	:	5, 10 and 20% in diet calculated to be equivalent to doses of: males 2000, 4000 and 8000 mg/kg bw, females 2500, 5000 and 10000 mg/kg bw
Control group	:	
Method	:	other: not indicated
Year	:	
GLP	:	
Test substance	:	

Method :

TEST ORGANISMS
- Age: not indicated
- Weight at study initiation: 96-109 g (males), 92-108 g (females)
- Number of animals: 22/sex/treatment, 26/sex for controls
- Source: Institute of Experimental Biology of University of California

ADMINISTRATION / EXPOSURE
- Exposure period: 2 year (1 year for the high dose group)
- Route of administration: oral in diet
- Doses: 5, 10 and 20% in diet; males 2000, 4000 and 8000 mg/kg bw, females 2500, 5000 and 10000 mg/kg bw

CLINICAL OBSERVATIONS AND FREQUENCY:
- Clinical signs: daily in cage and weekly examination outside the home cage
- Mortality: daily
- Body weight: weekly
- Food consumption: weekly
- Haematology: erythrocyte and leucocyte count and haemoglobin after 3, 6, 12, 18 and 24 months
- Urinalysis: albumin, glucose, casts and red and white blood cells after 3, 6, 12, 18 and 24 months (24-48 urine collection)

ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Organ weights: liver, kidneys, heart, spleen and lungs
- Macroscopic: no details provided
- Microscopic: liver, spleen, adrenals, kidney, small intestine, gonads and urinary bladder

OTHER EXAMINATIONS: glycogen and lipid content of the liver of

surviving rats at 0 and 20% glycerol.

ANALYSES: not performed

STATISTICAL METHODS: Chi-sqare test, student t-test, ANOVA (Fisher)

Result : TOXIC RESPONSE/EFFECTS BY DOSE LEVEL:
- Mortality and time to death: not indicated
- Clinical signs: not reported
- Body weight gain: no statistically significant differences between treated and control animals
- Food consumption: slightly increased (significant) in males at 5 and 10% natural glycerin
- Haematology: no treatment related effects
- Urinalysis: albumin: no significant treatment related effects (92% incidence in females at 20% natural glycerin compared to 54-64% in controls); glucose, casts, red and white blood cells: no treatment related effects
- Organ weights: incidental increases and decreases were reported without apparent relationship to treatment
- Gross pathology: no lesions related to treatment.
- Histopathology: Incidental bronchiectasis, pneumonia, pulmonary abcesses, taenia infestation of the liver, hydronephosis and pyelonephritis (total 27 rats were affected).
- Other: liver glycogen and lipid did not significantly differ between 0 and 20% glycerin (liver glycogen natural glycerin 4.2-4.3% and synthetic glycerin 3.7-4.2%)

Test substance : CAS 56-81-5 (glycerine),
Natural glycerine, achieved from market stock, purity not indicated (impurities were fatty acids and esters)
Synthetic glycerin, purity 99.5% (rest mainly water with very small amounts of glycerin polymers and glyceraldehyde)

Conclusion : NOAEL 10000 mg/kg bw based on the absence of treatment related effects in high dose animals.
Most reliable study.
Most reliable study available.

Reliability : (2) valid with restrictions
1 The report was confined to the above.
2 No individual data were included and microscopy was performed on distinct organs only.

Flag : Critical study for SIDS endpoint

25.01.2002 (64)

Type :
Species : rat
Sex : male
Strain : other: Carworth
Route of admin. : oral feed
Exposure period : 4 weeks
Frequency of treatm. :
Post exposure period :
Doses : 20% glycerine in diet (calculated to be equivalent to oral doses of 8824 mg/kg bw/day based on average bodyweight of 0.425 kg and food intake of 18.75 g/d)
Control group : no data specified
Method : other: not indicated
Year :
GLP : no data
Test substance : other TS

Method	:	At the end of 4 weeks, 5 rats of each treatment were killed, liver, lipids and cholesterol were determined and epididymus fat pads were quantitatively excised and weighed.
Result	:	Mentioned criteria, as well as weight gain and food intake (efficiency) revealed no adverse effects attributable to glycerin consumption.
Test substance	:	CAS 56-81-5 (glycerine), purity not indicated.
Reliability	:	(4) not assignable 1. Secondary literature, the information is confined to the above. 2. In comparison with the control diet less glucose monohydrate, sucrose and dextrin and more cellulose was present in the 20% glycerol diet.

16.11.2001 (95)

Type	:	
Species	:	rat
Sex	:	no data
Strain	:	
Route of admin.	:	oral feed
Exposure period	:	8 weeks
Frequency of treatm.	:	
Post exposure period	:	
Doses	:	12 g/10 g diet (calculated to be equivalent to 52941 mg/kg bw based on 18.75 g/d food intake and average bodyweight of 0.425 kg)
Control group	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS

Method	:	Before the start of the experiment 10 rats received a minimum diet (sufficient to maintain their weight) during 5 weeks. Thereafter a supplement of 12 g glycerine/10 g diet was added to the diet of 5 of the rats during 8 weeks, while the other 5 rats remained on the original diet. After these 8 weeks groups were switched.
Result	:	Untreated animals (receiving no glycerine) showed weight loss, while animals receiving glycerine exhibited normal growth.
Test substance	:	CAS 56-81-5 (glycerine), purity not indicated.
Reliability	:	(4) not assignable The information was confined to the above.

11.12.2001 (65)

Type	:	
Species	:	rat
Sex	:	no data
Strain	:	
Route of admin.	:	oral feed
Exposure period	:	25 weeks
Frequency of treatm.	:	
Post exposure period	:	
Doses	:	20 and 41% in diet (calculated to be equivalent to 8824 and 18088 mg/kg bw /day based on 18.75 g/d food intake and average bodyweight of 0.425 kg)
Control group	:	yes, concurrent no treatment
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS

Method	:	30 rats received a glycerine-supplemented diet (20 or 41%) during 25 weeks. After this period rats were necropsied. Kidneys, liver and intestines were examined.
Result	:	No abnormalities, normal growth rate.
Test substance	:	CAS 56-81-5 (glycerine), purity not indicated.
Reliability	:	(4) not assignable The information was confined to the above.

11.12.2001 (65)

Type	:	
Species	:	rat
Sex	:	male/female
Strain	:	
Route of admin.	:	oral feed
Exposure period	:	20 weeks
Frequency of treatm.	:	
Post exposure period	:	
Doses	:	1, 3, 6, 10, 15, 20, 30, 40, 50 and 60% in diet (calculated to be equivalent to oral doses of 441, 1324, 2647, 4412, 6618, 8824, 13235, 17647, 22059 and 26471 mg/kg bw/day based on 18.75 g/d food intake and average bodyweight of 0.425 kg)
Control group	:	yes, concurrent no treatment
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS

Method	:	5 rats/sex/treatment received glycerine in their diet during 20 weeks. Animals were observed daily and body weight was recorded weekly. Hb was determined at regular intervals. Selected animals from each group were tested for effects on excercise, water intake and urinary output. All animals that died and a selection of the survivors were necropsied. Another selection was sacrified and investigated for effects on dry matter, fat and liver glycogen.
Result	:	Decreased growth rate at 40% and above. Pathological effects at 10% and above (dose related) consisting mainly of hydropic and fatty degeneration of liver parenchymous cells.
Test substance	:	CAS 56-81-5 (glycerine), purity not indicated.
Reliability	:	(4) not assignable 1 The information was confined to the above. 2 During the first weeks dead animals were replaced by additional animals.

11.12.2001 (65)

Type	:	
Species	:	rat
Sex	:	no data
Strain	:	
Route of admin.	:	oral feed
Exposure period	:	40 weeks
Frequency of treatm.	:	
Post exposure period	:	
Doses	:	20, 41 and 61% in diet (calulated to be equivalent to oral doses of 8824, 18088 and 26912 mg/kg bw/day based on 18.75 g/d food intake and average bodyweight of 0.425 kg)
Control group	:	yes, concurrent no treatment
Method	:	
Year	:	

GLP :
Test substance : other TS

Method : Glycerine replaced the starch in the diet.
Result : Decreased activity, unkept coat and impaired growth at 61%.
Increased water consumption at 41% (30%) and 61% (230%)-> dose related
Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Reliability : (4) not assignable
The information was confined to the above.

16.11.2001 (65)

Type :
Species : rat
Sex : male/female
Strain :
Route of admin. : oral feed
Exposure period : 1 year
Frequency of treatm. :
Post exposure period :
Doses : 5, 10, 20% in diet (calculated to be euivalent to oral doses of 2206, 4412 and 8824 mg/kg bw day based on 18.75 g/d food intake and average bodyweight of 0.425 kg)
Control group : yes, concurrent no treatment
Method :
Year :
GLP :
Test substance : other TS

Method : 63 rats/sex/treatment received the test substance for 1 year. Data were collected on growth, food intake and caloric efficiency. Clinical investigations on blood and urine were performed. Macroscopic and microscopic examination of all animals at 20% was performed. For the other treatment groups liver, kidneys, spleen, gonads and adrenals were investigated.
Result : No adverse effects.
Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Reliability : (4) not assignable
The information was confined to the above.

11.12.2001 (65)

Type :
Species : rat
Sex :
Strain : Wistar
Route of admin. : oral feed
Exposure period : 20 days
Frequency of treatm. :
Post exposure period :
Doses :
Control group :

Remark : Literature could not be retrieved.
Result : Rats were fed a glycerol containing diet over a period of 20 days. Two control groups were included one receiving normal laboratory diet ad libitum and a pair-fed control (on normal diet). Body weight gain was reduced in glycerol fed animals.
Liver weight was slightly increased compared to controls and kidney weight was strongly increased. Liver and kidney
enzymatic activity was high in glycerol fed rats. At the end of the

experiment 95% of the glycerol was retained and blood and liver glucose were above normal levels. Water intake and urine production were about 5 times higher in animals treated with glycerol compared to controls.

Test substance : CAS 56-81-5 (glycerine), incorporated in diet replacing the carbohydrate of the standard diet

Reliability : (4) not assignable

25.01.2002 (96)

Type :
Species : rat
Sex : male/female
Strain :
Route of admin. : oral feed
Exposure period : 2 years
Frequency of treatm. :
Post exposure period :
Doses : diets containing 5, 10, or 20% glycerin (=calculated to be equivalent to 2206, 4412 and 8824 mg/kg bw/day based on 18.75 g/d food intake and average bodyweight of 0.425 kg)
Control group : yes
Method : other
Year :
GLP : no data
Test substance : other TS

Remark : Literature could not be retrieved.
Result : No deleterious or toxicological effects were noted among the groups of rats fed for two years on diets containing 5, 10 or 20% of either Atlas synthetic glycerin or natural glycerin, or among either of these experimental groups and the controls.
Source : Simel S.p.A. Industria Chimica Cremona
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : CAS 56-81-5 (glycerine), ATLAS synthetic glycerin and natural glycerin.
Reliability : (4) not assignable

25.01.2002 (97)

Type :
Species : rat
Sex : male/female
Strain :
Route of admin. : drinking water
Exposure period : 3 months
Frequency of treatm. :
Post exposure period :
Doses : 1, 2, 5, 10 or 20% solution of glycerin (calculated to be equivalent to 667, 1334, 3335, 6670 and 13340 mg/kg bw/day based on density of 1.26 g/cm3, water intake of 22.5 ml/d and average bodyweight of 0.425 kg)
Control group : yes
Method : other
Year :
GLP : no data
Test substance : no data

Result : Two of the 12 rats receiving 20% glycerin died during the 6th week of the test; the others showed, at this point, disturbance of the development and growth but recovered and grew normally in the further course of the experiment such that at the end of the test period no indication of injury attributable to glycerin ingestion was perceivable.

Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Reliability : (4) not assignable
The information in the report is confined to the above.
16.11.2001 (68) (65) (69)

Type :
Species : Rat
Sex : no data
Strain :
Route of admin. : drinking water
Exposure period : 10 and 17 days
Frequency of treatm. :
Post exposure period :
Doses : 2.5 % in drinking water (calculated to be equivalent to oral doses of 1668 mg/kg bw /day based on density of 1.26 g/cm3, water intake of 22.5 ml/d and average bodyweight of 0.425 kg)
Control group : other: see method

Method : Control animals received 2.5% glucose solution as drinking water.
Result : No effects on body and liver weight.
Significant decrease of cholesterol synthesis and serum cholesterol.
Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Conclusion : Absence of effects on cholesterol synthesis are attributed to an extraordinarily wide within group variance by the author of the report.
Reliability : (4) not assignable
The information in the report is confined to the above.
12.12.2001 (65)

Type :
Species : Rat
Sex : no data
Strain :
Route of admin. : drinking water
Exposure period : 10 days
Frequency of treatm. :
Post exposure period :
Doses : 1.5 and 3% in drinking water (calculated to be equivalent to oral doses of 1000 and 2000 mg/kg bw/day based on density of 1.26 g/cm3, water intake of 22.5 ml/d and average bodyweight of 0.425 kg)
Control group : no data specified

Result : Decreased serum cholesterol levels compared with controls.
Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Reliability : (4) not assignable
The information in the report is confined to the above.
16.11.2001 (65)

Type :
Species : Rat
Sex : Female
Strain :
Route of admin. : drinking water
Exposure period : 6 months
Frequency of treatm. :
Post exposure period :
Doses : 5% in drinking water (calculated to be equivalent to oral doses of 3335 mg/kg bw/day based on density of 1.26 g/cm3, water intake of 22.5 ml/d and average bodyweight of 0.425 kg)

Control group	:	other: tap water
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS
Method	:	5 females (6-8 weeks old) were given natural or synthetic glycerin during 6 months. Animals were weighed weekly. Haematological parameters and Hb were determined monthly. Macroscopic and microscopic investigations were done on heart, lungs, liver, spleen, stomach, intestines, kidneys. thymus, thyroid and adrenals.
Result	:	No effects on growth, red blood cells and haemoglobin. White blood cell counts differed within groups during the study. This was attributed to regular blood sampling procedures. Macroscopic incidental findings were a small thymus in 2 animals and slight interstitial pneumonia in one on natural glycerine and small spleen (with small lymphnodes and moderate hemosiderin deposits) and thymus atrophia in one animal that died on synthetic glycerol. Calcified masses in kidney tubulus between cortex and medulla in 3/5 rats on natural glycerin and 3/5 rats on synthetic glycerin.
Test substance	:	CAS 56-81-5 (glycerine), purity not indicated.
Reliability	:	(4) not assignable The information in the report is confined to the above.

11.12.2001 (73) (65)

Type	:	
Species	:	Rat
Sex	:	male/female
Strain	:	
Route of admin.	:	drinking water
Exposure period	:	96 days
Frequency of treatm.	:	
Post exposure period	:	
Doses	:	0, 1, 2, 5, 10 or 20% aqueous glycerin solution (calculated to be equivalent to oral doses of 667, 1334, 3335, 6670 and 13340 mg/kg bw/day based on density of 1.26 g/cm3, water intake of 22.5 ml/d and average bodyweight of 0.425 kg)
Control group	:	Yes
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	no data
Remark	:	Literature could not be retrieved.
Result	:	Growth of the rats receiving 10% or less of glycerin was normal. The animals receiving 20% glycerin exhibited normal growth for the first few weeks, followed by a temporary impairment. Growth of these rats then returned to normal.
Source	:	Simel S.p.A. Industria Chimica Cremona EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable

25.01.2002 (98)

Type	:	
Species	:	Rat
Sex	:	male/female
Strain	:	

Route of admin.	:	Gavage
Exposure period	:	approx. 1/2 year
Frequency of treatm.	:	
Post exposure period	:	
Doses	:	1.0 ml of a 50% aqueous glycerine solution/100 g bw (equivalent to 6300 mg/kg bw/day based on density of 1.26 g/cm3)
Control group	:	Yes
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	other TS
Result	:	All of the rats developed normally and the mortality of all groups was comparable. After 6, 12 and 18 weeks, rats from each group were sacrificed, dissected and their organs removed for histological examination. No pathological changes were disclosed and determination of liver glycogen revealed normal levels. X-ray examinations carried out on animals of each group at the beginning as well as in intervals of 6 weeks, remained without abnormal findings.
Test substance	:	CAS 56-81-5 (glycerine), purity not indicated.
Reliability	:	(4) not assignable The information in the report is confined to the above.

11.12.2001 (65) (69)

Type	:	
Species	:	Rat
Sex	:	male/female
Strain	:	
Route of admin.	:	gavage
Exposure period	:	50 days
Frequency of treatm.	:	on weekdays
Post exposure period	:	
Doses	:	10 ml/kg bw (= 2520 mg/kg bw based on density of 1.26 g/cm3)
Control group	:	no data specified
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS
Method	:	Observations consisted of mortality, body weight gain, behaviour, liver glycogen. Post mortem examination was done on the endocrine glands, pituitary, adrenal and ovaries. The skeleton was investigated by X-rays.
Result	:	No abormal effects were found.
Test substance	:	CAS 56-81-5 (glycerine), 20% aqueous glycerine solution.
Reliability	:	(4) not assignable The information in the report is confined to the above.

11.12.2001 (65) (69)

Type	:	
Species	:	Rat
Sex	:	male
Strain	:	
Route of admin.	:	gavage
Exposure period	:	44 days
Frequency of treatm.	:	daily
Post exposure period	:	

Doses	:	1, 5, 10 and 20% in water (equivalent to 115, 575, 1150 and 2300 mg/kg bw based on density 1.26 and mean animal weight of 110 g)
Control group	:	yes, concurrent vehicle
Method	:	other: not indicated
Year	:	
GLP	:	
Test substance	:	

Method :

TEST ORGANISMS
- Age: not indicated
- Weight at study initiation: 75-110 g
- Number of animals: 20/treatment

ADMINISTRATION / EXPOSURE
- Exposure period: 44 days
- Route of administration: oral (gavage)
- Doses: 1, 5, 10 and 20% in water (dosing volume 1 mL); about 115, 575, 1150 and 2300 mg/kg bw (based on density 1.26 and mean animal weight of 110 g)

CLINICAL OBSERVATIONS AND FREQUENCY:
Not indicated

ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Macroscopic: no details provided
- Microscopic: liver, kidney and urinary bladder

ANALYSES: not performed

STATISTICAL METHODS: not indicated

Result :

TOXIC RESPONSE/EFFECTS BY DOSE LEVEL:
- Mortality: 15% in treatment and control groups
- Clinical signs: no treatment related effects
- Body weight gain: no differences between treated and control animals
- Histopathology: no findings

Test substance	:	CAS 56-81-5 (glycerine), in water, purity not indicated
Conclusion	:	The data are insufficient to draw a sound conclusion on a NOAEL. No effects were found at doses between 115 and 2300 mg/kg.
Reliability	:	(4) not assignable 1 The report is limited to the above mentioned 2 It is not clear whether or not no histopathalogical findings were observed in the glycerol treated animals, since the report is in fact a study on 1,3-butyleneglycol, using glycerol as controls.

11.12.2001 (99)

Type	:	
Species	:	Rat
Sex	:	male
Strain	:	
Route of admin.	:	gavage
Exposure period	:	21 days
Frequency of treatm.	:	daily
Post exposure period	:	
Doses	:	20% in water (equivalent to 1525 mg/kg bw based on density 1.26 and mean animal weight of 165 g)
Control group	:	yes, concurrent vehicle

Method	:	other: not indicated
Year	:	
GLP	:	
Test substance	:	
Method	:	TEST ORGANISMS - Age: not indicated - Weight at study initiation: 140-160g - Number of animals: 8/treatment ADMINISTRATION / EXPOSURE - Exposure period: 21 days - Route of administration: oral (gavage) - Doses: 20% in water (dosing volume 1 mL); ~1525 mg/kg bw (based on density 1.26 and mean animal weight of 165 g) OBSERVATIONS: - Mortality: frequency not indicated - Body weight on day 0, 3, 6, 9, 12, 15, 18 and 21 - O2-consumption on day 0, 3, 6, 9, 12, 15, 18 and 21 (by method of Loeser (1938))
Result	:	TOXIC RESPONSE/EFFECTS BY DOSE LEVEL: - Mortality: 0/8 controls, 5/8 treated - Body weight gain: no differences between treated and control animals - O2-consumption: decreased on day 3, 9, 18 and 21
Test substance	:	CAS 56-81-5 (glycerine), in water, purity not indicated
Reliability	:	(4) not assignable 1 The report is limited to the above mentioned. The test was set up for the determination of O2-consumption 2 The decreased O2-consumption on day 18 and 21 is considered less reliable, since measurements were performed on only 3 survivors.
11.12.2001		(99)
Type	:	
Species	:	rat
Sex	:	male
Strain	:	
Route of admin.	:	gavage
Exposure period	:	44 days
Frequency of treatm.	:	daily
Post exposure period	:	
Doses	:	10% in water (1260 mg/kg bw based on density 1.26)
Control group	:	yes, concurrent vehicle
Method	:	other: not indicated
Year	:	
GLP	:	
Test substance	:	
Method	:	TEST ORGANISMS - Age: not indicated - Weight at study initiation: 75-100 g - Number of animals: 10/treatment ADMINISTRATION / EXPOSURE - Exposure period: 44 days - Route of administration: oral (gavage) - Doses: 10% in water (dosing volume 1 cm3/100 g bw); 1260 mg/kg bw (based on density 1.26)

OBSERVATIONS:
- Haematology on day 2 and weekly thereafter (Hb, erythrocytes, total and differential leucocytes)

Result : TOXIC RESPONSE/EFFECTS BY DOSE LEVEL:
- Eosinophils increased during week 3 to 6 (attributed to an infection with worms)

Test substance : CAS 56-81-5 (glycerine), in water, purity not indicated
Reliability : (4) not assignable
The report is limited to the above mentioned. The test was set up to determine blood parameters.

11.12.2001 (99)

Type :
Species : rat
Sex : female
Strain :
Route of admin. : gavage
Exposure period : 3 days
Frequency of treatm. : 3 times/day
Post exposure period :
Doses : 950, 1900 and 3800 mg/kg bw
Control group : yes
LOAEL : = 950 mg/kg bw
Method : other: not indicated
Year :
GLP :
Test substance :

Method : TEST ORGANISMS:
- Source: Charles River
- Age: not indicated
- Number: 10/treatment (20 for controls)
- Weight at study initiation: 150-210 g

ADMINISTRATION:
- Doses: 950, 1900 and 3800 mg/kg bw (100, 80, 60, 40, 20%)-Vehicle water
- Controls: water
- Dosing schedule: 3 times daily (sacrificed after second dose on day 3)

OBSERVATIONS: gastro-intestinal irritation, macroscopic and microscopic investigation of stomach and intestinal mucosa

Result : In animals treated with undiluted test substance a dose related increase in the number of animals showing hyperaemia, petechial haemorrhage and erosions was seen. Dilution of the applied test substance lead to reduction of the effects.

Test substance : CAS 56-81-5 (glycerine)(concentration in water 100%, 80%, 60%, 40% and 20%), purity not specified
Conclusion : LOAEL for local irritant effects 950 mg/kg bw
Reliability : (4) not assignable
1 The report is limited to the above mentioned.
2 Only effects on the gastrointestinal tract were reported.

11.12.2001 (100)

Type :
Species : rat
Sex : no data

Strain	:	no data
Route of admin.	:	oral unspecified
Exposure period	:	25 Weeks
Frequency of treatm.	:	with each meal
Post exposure period	:	no data
Doses	:	Approximately 20000 mg/kg bw/d
Control group	:	no data specified
NOAEL	:	ca. 2000 mg/kg bw
Method	:	other
Year	:	1933
GLP	:	no data
Test substance	:	no data
Remark	:	Literature could not be retrieved.
Source	:	Croda Universal Ltd Goole, North Humberside EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable
25.01.2002		
Type	:	
Species	:	rabbit
Sex	:	
Strain	:	
Route of admin.	:	other: see remark
Exposure period	:	30-40 days
Frequency of treatm.	:	
Post exposure period	:	
Doses	:	
Control group	:	
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	other TS
Method	:	4 Rabbits were given either a 50% aqueous solution in saline or saline alone either by stomach tube or from a drinking cup daily.
Remark	:	Literature could not be retrieved.
Result	:	Doses of 10 ml of the glycerin solution daily were well tolerated by the rabbits. Those animals which were autopsied at the end of the experiment showed no gross pathological changes. Neither the plasma nor the red blood cell cholesterol levels showed any consistent changes which could be attributed to the intake of glycerin.
Source	:	Unichema Chemie B.V. Gouda EUROPEAN COMMISION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable
25.01.2002		(101)
Type	:	
Species	:	dog
Sex	:	male/female
Strain	:	
Route of admin.	:	oral feed
Exposure period	:	2 years
Frequency of treatm.	:	
Post exposure period	:	
Doses	:	diets containing 5, 10 and 20% glycerin (no reference values available for conversion to mg/kg)
Control group	:	yes

Method	:	other
Year	:	
GLP	:	no data
Test substance	:	other TS
Remark	:	These studies were conducted to investigate the oral toxicity of Atlas synthetic glycerin compared to natural glycerin. Literature could not be retrieved.
Result	:	The observations failed to reveal any treatment effects from either the Atlas synthetic or the natural glycerin.
Source	:	Unichema Chemie B.V. Gouda
Test substance	:	Atlas synthetic glycerin and natural glycerin.
Reliability	:	(4) not assignable
25.01.2002		(97) (65)
Type	:	
Species	:	dog
Sex	:	no data
Strain	:	
Route of admin.	:	oral feed
Exposure period	:	50 weeks
Frequency of treatm.	:	
Post exposure period	:	
Doses	:	35% in diet (no reference values available for conversion to mg/kg)
Control group	:	
Method	:	other: not indicated
Year	:	
GLP	:	
Test substance	:	
Method	:	TEST ORGANISMS - Age: 5 weeks - Weight at study initiation: ~1.5 kg - Number of animals: 3/treatment (controls were litter mates) ADMINISTRATION / EXPOSURE - Exposure period: 50 weeks - Route of administration: in diet - Doses: 35% in diet (after week 36 intake was reduced to 50-80% of previous) OBSERVATIONS: - Body weight (frequency not indicated) - Erythrocyte counts (frequency not indicated)
Result	:	- Body weight: until week 36 no differences between animals on glycerol rich diet and controls; after week 36 weight loss (16%, 1.8 kg) in dogs on glycerol rich diet (not in controls) - Erythrocyte counts did not reveal any differences between dogs of both groups.
Test substance	:	CAS 56-81-5 (glycerine), purity not specified The test diet contained 35% glycerol and 17% carbohydrate; controls received a diet containing 52% carbohydrate
Conclusion	:	No conclusion can be drawn, because of the limited data available
Reliability	:	(3) invalid 1 The report is limited to the above mentioned 2 The actual dose received by the dogs could not be

calculated by the reviewer, because no information on the dog's body weight and the amount of food provided was included.

11.12.2001 (65) (102)

Type	:	
Species	:	dog
Sex	:	male/female
Strain	:	other: Mongrel
Route of admin.	:	gavage
Exposure period	:	3 days
Frequency of treatm.	:	3 times/day
Post exposure period	:	
Doses	:	950, 1900 and 3800 mg/kg bw
Control group	:	
NOAEL	:	= 950 mg/kg bw
Method	:	other: not indicated
Year	:	
GLP	:	no
Test substance	:	

Method :
TEST ORGANISMS:
- Age: not indicated
- Number: 1/treatment (2 at highest dose)
- Weight at study initiation: 8.9-16 kg

ADMINISTRATION:
- Doses: 950, 1900 and 3800 mg/kg bw (undiluted)
- Controls: water
- Dosing schedule: 3 times daily (sacrificed after second dose on day 3)

OBSERVATIONS: gastro-intestinal irritation, macroscopic and microscopic investigation of stomach and intestinal mucosa

Result :
At 950 mg/kg bw: no abnormalities.
At 1900 mg/kg bw: the mucosa was severly hyperaemic with petechial haemorrhages
At 3800 mg/kg bw: the stomach mucosa was (slightly to) severly hyperaemic with areas with petechial haemorrhages or erosions; duodenum appeared normal or with hyperaemic areas.

Test substance	:	CAS 56-81-5 (glycerine) undiluted, purity not specified
Conclusion	:	NOAEL for local irritant effects 950 mg/kg bw
Reliability	:	(4) not assignable 1 The report is limited to the above mentioned. 2 Only effects on the gastrointestinal tract were reported.

11.12.2001 (103)

Type	:	
Species	:	dog
Sex	:	male/female
Strain	:	
Route of admin.	:	oral unspecified
Exposure period	:	4 months
Frequency of treatm.	:	twice weekly
Post exposure period	:	
Doses	:	2.0 ml/kg (= 2520 mg/kg based on density of 1.26 g/cm3)
Control group	:	

Method : One animal/sex/treatment received glycerine during 4 months (after 1 months there was a two-week interruption).

Examinations included growth, weekly urine tests and histological examination of the liver, kidney, spleen, bladder, stomach, intestines, spleen, adrenal, heart, muscle and lungs.

Remark : No information on the formulation administered was provided.
Result : No abnormalities were observed.
Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Reliability : (4) not assignable
The information in the report is confined to the above.

11.12.2001 (65)

Type :
Species : guinea pig
Sex : no data
Strain :
Route of admin. : other: see method
Exposure period : 30-40 days
Frequency of treatm. :
Post exposure period :
Doses :
Control group :
Method : other
Year :
GLP : no data
Test substance : other TS

Method : 10 Guinea pigs were given either a 50% aqueous solution in saline or saline alone either by stomach tube or from a drinking cup daily.
Remark : Literature could not be retrieved.
Result : Guinea pigs receiving more than 5 ml of a 50% glycerin solution (= 6300 mg/kg bw/day based on density of 1.26 g/cm3 and avaerage bodyweight of 500g) daily by stomach tube died with acute symptoms.
Autopsies performed on animals at termination of the experiment revealed no pathological changes. The plasma cholesterol level showed no consistent changes attributable to the intake of glycerin while the red blood count of the guinea pigs (2 exposed via stomach tube, 1 exposed via drinking water) receiving glycerin dropped during the experiment indicating a probable anemic effect of glycerin in the guinea pig.
Source : Unichema Chemie B.V. Gouda
Test substance : CAS 56-81-5 (glycerine), purity not indicated.

11.12.2001 (104)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Ames test
System of testing : TA1535, TA1537, TA98 and TA100
Test concentration : 100, 333.3, 1000, 3333, 10000 µg/plate
Cycotoxic concentr. : >= 10000 µg/plate
Metabolic activation : with and without
Result : negative
Method : other: not indicated
Year : 1983
GLP : no data
Test substance :

Method : SYSTEM OF TESTING

- Species/cell type: TA1535, TA1537, TA98 and TA100
- Metabolic activation system: liver S9 fraction from rats and hamsters treated with Aroclor 1254
- Deficiency: histidine

ADMINISTRATION:
- Dosing: 100, 333.3, 1000, 3333, 10000 µg/plate
- Number of replicates: 3
- Application: preincubation assay
- Positive controls: 2-aminoanthracene (all strains with S9); 4-nitro-o-phenylenediamine (TA98 without S9); sodium azide (TA100 and TA1535 without S9); 9-aminoacridine (TA1537 without S9)
- Negative control: water
- Pre-incubation time: 20 min

CRITERIA FOR EVALUATING RESULTS:
- Statistical method: Margolin (1981) if result is positive

Remark : 1. The test was performed by three different labs. These are the results of the first lab.
2. The test was performed twice and gave exactly the same results.

Result : GENOTOXIC EFFECTS:
- With metabolic activation(rat): negative
- With metabolic activation(hamster): negative
- Without metabolic activation: negative

CYTOTOXIC CONCENTRATION:
- With or without metabolic activation: >= 10000 µg/plate

Test substance : CAS 56-81-5 (Glycerine), purity >99%.
Conclusion : Most reliable study available
Reliability : (2) valid with restrictions
Non-GLP study.
Flag : Critical study for SIDS endpoint
17.12.2001 (105)

Type : Ames test
System of testing : TA1535, TA1537, TA98 and TA100
Test concentration : 100, 333, 1000, 3333, 10000 µg/plate
Cycotoxic concentr. : >= 10000 µg/plate
Metabolic activation : with and without
Result : negative
Method : other: not indicated
Year : 1983
GLP : no data
Test substance :

Method : SYSTEM OF TESTING
- Species/cell type: TA1535, TA1537, TA98 and TA100
- Metabolic activation system: liver S9 fraction from rats and hamsters treated with Aroclor 1254
- Deficiency: histidine

ADMINISTRATION:
- Dosing: 100, 333, 1000, 3333, 10000 µg/plate
- Number of replicates: 3
- Application: preincubation assay
- Positive controls: 2-aminoanthracene (all strains with S9); 4-nitro-o-phenylenediamine (TA98 without S9); sodium azide (TA100 and TA1535 without S9); 9-aminoacridine (TA1537 without S9)
- Negative control: water
- Pre-incubation time: 20 min

CRITERIA FOR EVALUATING RESULTS:
- Statistical method: Margolin (1981) if result is positive

Remark : 1. The test was performed by three different labs. These are the results of the second lab.

Result : GENOTOXIC EFFECTS:
- With metabolic activation(rat): negative
- With metabolic activation(hamster): negative
- Without metabolic activation: negative

CYTOTOXIC CONCENTRATION:
- With or without metabolic activation: >= 10000 µg/plate

Test substance : CAS 56-81-5 (Glycerine), purity >99%.

Conclusion : Most reliable study available.

Reliability : (2) valid with restrictions
Non-GLP study.

Flag : Critical study for SIDS endpoint

21.01.2002 (105)

Type : Ames test

System of testing : TA1535, TA1537, TA98 and TA100

Test concentration : 100, 333, 1000, 3333, 10000 µg/plate

Cycotoxic concentr. : >= 10000 µg/plate

Metabolic activation : with and without

Result : negative

Method : other: not indicated

Year : 1983

GLP : no data

Test substance :

Method : SYSTEM OF TESTING
- Species/cell type: TA1535, TA1537, TA98 and TA100
- Metabolic activation system: liver S9 fraction from rats and hamsters treated with Aroclor 1254
- Deficiency: histidine

ADMINISTRATION:
- Dosing: 100, 333, 1000, 3333, 10000 µg/plate
- Number of replicates: 3
- Application: preincubation assay
- Positive controls: 2-aminoanthracene (all strains with S9); 4-nitro-o-phenylenediamine (TA98 without S9); sodium azide (TA100 and TA1535 without S9); 9-aminoacridine (TA1537 without S9)
- Negative control: DMSO
- Pre-incubation time: 20 min

CRITERIA FOR EVALUATING RESULTS:
- Statistical method: Margolin (1981) if result is positive

Remark : 1. The test was performed by three different labs. These are the results of the third lab.

Result : GENOTOXIC EFFECTS:
- With metabolic activation(rat): negative
- With metabolic activation(hamster): negative
- Without metabolic activation: negative

CYTOTOXIC CONCENTRATION:
- With or without metabolic activation: >= 10000 µg/plate

Test substance : CAS 56-81-5 (Glycerine), purity >99%.

Conclusion : Most reliable study available.

Reliability : (2) valid with restrictions

Non-GLP study.

Flag : Critical study for SIDS endpoint
21.01.2002 (105)

Type : Ames test
System of testing : TA 98, TA 100, TA 1535, TA 1537, TA 1538
Test concentration : 200-1000 ug/plate
Cycotoxic concentr. : no cytotoxicity observed
Metabolic activation : with and without
Result : Negative
Method :
Year : 1988
GLP : no data
Test substance :

Method : SYSTEM OF TESTING
- Species/cell type: Salmonella typhimurium TA98, TA100, TA1535, TA 1537 and TA1538
- Deficiences: histidine
- Metabolic activation system: rat S-9

ADMINISTRATION:
- Dosing: 200, 400, 600, 800 and 1000 ug/plate
- Number of replicates: 3
- Application: preincubation assay
- Positive and negative control groups and treatment:
without S-9: 2-nitrofluorene (TA98, TA1538), sodium azide (TA100, TA1535) and 9-aminoanthracene (TA1537)
with S-9: 2-aminoanthracene
- Pre-incubation time: not indicated

DESCRIPTION OF FOLLOW UP REPEAT STUDY: indepent repeat with TA100 (not reported)

CRITERIA FOR EVALUATING RESULTS:
reproducible, dose-related increase in the number of revertants

Result : - With metabolic activation: negative
- Without metabolic activation: negative

In TA100 the number of revertants was increased compared to solvent controls, without relationship with the applied concentration. Therefore the test was repeated with TA100 at slightly higher glycerol concentrations with a negative result (no data available)

PRECIPITATION CONCENTRATION: not indicated

CYTOTOXIC CONCENTRATION: no cytotoxicity up to 1000 ug/plate

Test substance : CAS 56-81-5 (glycerine), purity >99.5%
Conclusion : Most reliable study available.
Reliability : (2) valid with restrictions
1 The report is limited to the above mentioned. No individual values were included.
2 It is not clear from the report, why 5000 ug/plate was not included as the highest concentration tested. OECD 471 states that in absence of precipitate and/or cytotoxicity the highest test concentration should be 5000 ug/plate.
3 In TA 100 the number of revertants was increased in the initial experiment compared to solvent controls, without relationship with the applied concentration. It is reported that the results of the repeated

experimnt with TA100 confirmed that glycerol is not mutagenic in TA100 (data not shown).

Flag : Critical study for SIDS endpoint
17.12.2001 (106)

Type : HGPRT assay
System of testing : CHO-cells
Test concentration : 100-1000 ug/mL
Cycotoxic concentr. : no cytotoxicity observed
Metabolic activation : with and without
Result : Negative
Method :
Year : 1988
GLP : no data
Test substance :

Method : SYSTEM OF TESTING
- Cell type: CHO-K1-BH4
- Proficiences: HGPRT gene
- Metabolic activation system: rat S-9

ADMINISTRATION:
- Dosing: 100, 200, 400, 600, 800 and 1000 ug/mL
- Number of replicates: not indicated
- Negative control: water (solvent)
- Positive control groups: without S-9 ethyl methanesulphonate; with S-9 dimethylbenzanthracene
- Treatment: 5 hours

CRITERIA FOR EVALUATING RESULTS:
At least a three-fold increase in mutation frequency above controls in a dose dependent manner.

Result : - With metabolic activation: negative
- Without metabolic activation: negative

At 800 and 1000 ug/mL the mutation frequency was increased >= 3 fold (24E-06 and 6E-06, respectively) compared to controls (2E-06).

PRECIPITATION CONCENTRATION: not indiated

CYTOTOXIC CONCENTRATION:
Not observed

Test substance : CAS 56-81-5 (glycerine), purity >99.5%
Conclusion : Most reliable study available.
Reliability : (2) valid with restrictions
1 The report is limited to the above mentioned. No individual values were included.
2 The increased mutation frequency seen at the two highest concentrations (800 and 1000 ug/mL) in absence of a concentration response relationship does not meet the criteria set for a positive response set by the author of the report. 3 It is not clear from the report, why 5000 ug/mL was not
included as the highest concentration tested. OECD 476 states that in absence of precipitate and/or cytotoxicity the highest test concentration should be 5000 ug/mL.

Flag : Critical study for SIDS endpoint
17.12.2001 (106)

Type : Sister chromatid exchange assay
System of testing : CHO cells

Test concentration	:	200-1000 ug/ml
Cycotoxic concentr.	:	no cytoxicity observed
Metabolic activation	:	with and without
Result	:	Negative
Method	:	
Year	:	1988
GLP	:	no data
Test substance	:	

Method :
SYSTEM OF TESTING
- Species/cell type: CHO-cells WBL
- Metabolic activation system: rat S-9
- No. of metaphases analyzed: 50/concentration

ADMINISTRATION:
- Dosing: 200, 400, 600, 800 and 1000 ug/mL
- Number of replicates: 2
- Treatment: 2 hours with S-9; 25.5 hours without S-9
- Negative control: water (solvent)
- Positive control groups: triethylenemelamine(-S9); cyclophosphamide (+S9)

CRITERIA FOR EVALUATING RESULTS:
A reproducible, dose-dependent increase in frequency of SCE's compared to solvent control

Result :
GENOTOXIC EFFECTS:
- With metabolic activation: negative
- Without metabolic activation: negative

CYTOTOXIC CONCENTRATION:
Not cytotoxicity at any of the concentrations tested.

Test substance	:	CAS 56-81-5 (glycerine), purity >99.5%
Conclusion	:	Most reliable study available.
Reliability	:	(2) valid with restrictions The report is limited to the above mentioned. No individual values were included.
Flag	:	Critical study for SIDS endpoint

25.01.2002 (106)

Type	:	Unscheduled DNA synthesis
System of testing	:	Rat hepatocytes
Test concentration	:	100-1000 ug/mL
Cycotoxic concentr.	:	
Metabolic activation	:	
Result	:	Negative
Method	:	
Year	:	1988
GLP	:	no data
Test substance	:	

Method :
SYSTEM OF TESTING
- Radiographic UDS assay in rat hepatocytes

ADMINISTRATION:
- Dosing: 100, 250, 500, 750 and 1000 ug/mL
- Test was performed twice (doses second exp 750 and 1000 ug/mL)
- Negative control: not applicable
- Positive control: methylaminofluorene

CRITERIA FOR EVALUATING RESULTS:
- reproducible dose dependent increase of number of nuclear grains
- Statistical method: ANOVA, followed by Dunnett's test

Result : The number of nuclear grains in controls and treated hepatocytes did not differ significantly. Positive controls were within expected ranges.
Test substance : CAS 56-81-5 (glycerine), purity >99.5%
Conclusion : Most reliable study available.
Reliability : (2) valid with restrictions
The report is limited to the above mentioned. No individual values were included.
Flag : Critical study for SIDS endpoint
25.01.2002 (106)

Type : Chromosomal aberration test
System of testing : CHO cells
Test concentration : 100-1000 ug/mL
Cycotoxic concentr. : no cytotoxicity observed
Metabolic activation : with and without
Result : Negative
Method :
Year : 1988
GLP : no data
Test substance :

Method : SYSTEM OF TESTING
- Species/cell type: CHO-cells WBL
- Metabolic activation system: rat S-9
- No. of cells scored: 100/concentration (50 for positive controls)

ADMINISTRATION:
- Dosing: 100, 200, 400, 600, 800 and 1000 ug/mL
- Treatment: 10 and 14 hours (with S-9) without recovery; 2 hours (without S-9) with 10 and 14 hr recovery
- Negative control: water (solvent)
- Positive control groups: triethylenemelamine(-S9); cyclophosphamide (+S9)

CRITERIA FOR EVALUATING RESULTS:
A statistically significant, reproducible and dose-dependent increase in frequency of cells with aberrations compared to solvent control.

Result : GENOTOXIC EFFECTS:
- With metabolic activation: negative
- Without metabolic activation: negative

In the initial assay with metabolic activation a statistically significant increase in the number of aberrations compared to controls was seen only at 200 ug/mL
(recovery period 10 hr)

PRECIPITATION CONCENTRATION: not indicated

MITOTIC INDEX:
without S-9 (10 hr): 84-97% of control
without S-9 (14 hr): 78-101% of control
with S-9 (10 hr rec.): 59-92% of control (no relationship with concentration)
with S-9 (14 hr rec): no decrease observed

CYTOTOXIC CONCENTRATION:
No cytotoxicity observed with concentrations tested.

Test substance : CAS 56-81-5 (glycerine), purity >99.5%
Conclusion : Most reliable study available.
Reliability : (2) valid with restrictions
1 The report is limited to the above mentioned. No individual values were included.
2 The isolated increase in number of aberrations seen at 200 ug/mL (+S-9) is considered of no biological relevance, since there was no relationship with the concentration tested.
3 It is not clear from the report, why 5000 ug/mL was not included as the highest concentration tested. OECD 473 states that in absence of precipitate and/or cytotoxicity the highest test concentration should be 5000 ug/mL.
Flag : Critical study for SIDS endpoint
25.01.2002 (106)

Type : Ames test
System of testing : Salmonella typhimurium strain TA-100
Test concentration : 0.1 and 1 mmol per plate
Cycotoxic concentr. :
Metabolic activation : with and without
Result : Negative
Method : Other
Year : 1979
GLP : no data
Test substance : no data

Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Reliability : (4) not assignable
The information in the report is confined to the above.
16.11.2001 (107)

Type : Ames test
System of testing : Salmonella typhimurium strain TA100
Test concentration : 0.5 mg/plate
Cycotoxic concentr. :
Metabolic activation : with and without
Result : Negative
Method :
Year :
GLP : no data
Test substance : other TS

Remark : The liver microsomal fraction was from PCB-induced rats.
Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Reliability : (4) not assignable
Secondary literature with information essentially confined to what is included in the current summary.
16.11.2001 (108)

Type : Bacillus subtilis recombination assay
System of testing : Bacillus subtilis H17 and M45
Test concentration :
Cycotoxic concentr. :
Metabolic activation :
Result : Positive
Method :
Year :

GLP :
Test substance :

Method : Cells were incubated for 30 min. in presence of the test substance. After treatment viable cells were counted.
Test substance : CAS 56-81-5 (glycerine), purity not indicated
Reliability : (4) not assignable
Only a short abstract is available.
It can not be excluded that interference of the test substance with the cell surface may have influenced the study outcome.
16.11.2001 (109)

Type : Escherichia coli reverse mutation assay
System of testing : various
Test concentration :
Cycotoxic concentr. :
Metabolic activation : with and without
Result : negative
Method : other
Year : 1985
GLP : no data
Test substance : no data

Remark : Literature could not be retrieved.
Source : Croda Universal Ltd Goole, North Humberside
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
25.01.2002 (110) (111)

Type : Ames test
System of testing : Salmonella typhimurium strain TA-100
Test concentration : 0.1 and 1 mmol per plate
Cycotoxic concentr. :
Metabolic activation : with and without
Result : negative
Method :
Year :
GLP :
Test substance :

Remark : Literature could not be retrieved.
Source : Wolff Walsrode AG Walsrode
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
25.01.2002

Type : Ames test
System of testing : TA92, TA94, TA98, TA100, TA1535 and TA1537
Test concentration : <= 50 mg/plate
Cycotoxic concentr. :
Metabolic activation : with and without
Result : negative
Method : other: not indicated
Year :
GLP : no data
Test substance : other TS

Method : SYSTEM OF TESTING
- Species/cell type: TA92, TA94, TA98, TA100, TA1535 and TA1537

- Deficiency: histidine
- Metabolic activation system: Rat liver S9 mix (polychlorinated biphenyls induced)

ADMINISTRATION:
- Dosing: 6 concentrations <= 50 mg/plate
- Number of replicates: 2
- Application: preincubation assay
- Negative control: phosphate buffer
- Pre-incubation time: 20 min

CRITERIA FOR EVALUATING RESULTS: The result was considered positive if the number of revertant colonies found was twice or more that of the control.

Result : GENOTOXIC EFFECTS:
- With metabolic activation: negative
- Without metabolic activation: negative

Test substance : CAS 56-81-5 (glycerine), purity 99.4%

Reliability : (4) not assignable
1. The information in the report is confined to the above. The article is a review article of more than 200 investigated substances.
2. The strains used are no standard strains as recommended by the OECD.
3. No standard positive controls were included. It is not clear whether the positive results obtained with some of the tested compounds were achieved with the same batch of bacteria as glycerine.

15.11.2001 (112)

Type : Chromosomal aberration test
System of testing : CHO cells
Test concentration : 1 mg/ml
Cycotoxic concentr. :
Metabolic activation : without
Result : negative
Method : other: not indicated
Year :
GLP : no data
Test substance : other TS

Method : SYSTEM OF TESTING
- Species/cell type: CHO cells
- No. of metaphases analyzed: 100

ADMINISTRATION:
- Dosing: 1 mg/ml and two doses at lower concentrations (maximum dose based on 50% growth reduction at 1.0 mg/ml)
- Negative control: untreated and solvent-treated (physiol. saline) cells
- Incubation time: 24 and 48 h (last 2 h in presence of colcemid)

CRITERIA FOR EVALUATING RESULTS: negative if incidence was less than 4.9%, equivocal if it was between 5.0 and 9.9%, and positive if it was more than 10.0%

Result : GENOTOXIC EFFECTS:
- Without metabolic activation: negative (only 48 h result reported)

FREQUENCY OF EFFECTS: 2.0% of polyploid cells and 1.0% of cells with structural aberrations at 1.0 mg/ml

Test substance : CAS 56-81-5 (glycerine), purity 99.4%

Reliability : (4) not assignable
1. The information in the report is confined to the above. The article is a

review article of more than 200 investigated substances.
2. No standard positive controls were included. It is not clear whether the positive results obtained with some of the tested compounds were achieved with the same batch of bacteria as glycerine.

15.11.2001 (112)

Type	:	Ames test
System of testing	:	TA98, TA100, TA1535, TA1537 and TA1538
Test concentration	:	1 - 10000 µg/plate
Cycotoxic concentr.	:	
Metabolic activation	:	no data
Result	:	negative
Method	:	other: Ames
Year	:	1975
GLP	:	no data
Test substance	:	other TS

Method : SYSTEM OF TESTING
- Species/cell type: TA98, TA100, TA1535, TA1537 and TA1538
- Deficiency: histidine
- Metabolic activation system: rat liver homogenate

ADMINISTRATION:
- Dosing: 1 - 10000 µg/plate
- Positive controls: N-methyl-N'-nitro-N-nitrosoguanidine (TA100 and TA1535); 2-aminofluorene (TA98, TA100 and TA1538); 9-aminoacridine (TA1537)

Result : GENOTOXIC EFFECTS:
- negative

Test substance : CAS 56-81-5 (glycerine), purity not indicated (glycerine/water mixture of unknown composition).

Reliability : (4) not assignable
1 Secondary literature; the information in the report is confined to the above mentioned.
2 Although it was indicated that a test with metabolic activation was included, it could not be established whether a test without metabolic activation was included also.

11.12.2001 (86)

Type	:	
System of testing	:	Human lymphocytes
Test concentration	:	200 mmol/l = 18.4 g/l
Cycotoxic concentr.	:	no cytotoxicity observed
Metabolic activation	:	
Result	:	
Method	:	
Year	:	1982
GLP	:	
Test substance	:	other TS

Method : Lymphocyte proliferative growth was stimulatated with PMA during 3 days. Cells were incubated in presence of [3H]thymidine for 20 hours. The effect of a number hydroxyl radical scavengers on [3H]thymidine incorporation was determined.

Result : Glycerine was found to inhibit [3]thymidine incorporation (16.4% of control).

Test substance : CAS 56-81-5 (Glycerine), purity not indicated.

03.01.2002 (113)

5.6 GENETIC TOXICITY 'IN VIVO'

Type	:	Dominant lethal assay
Species	:	rat
Sex	:	male/female
Strain	:	
Route of admin.	:	
Exposure period	:	
Doses	:	10, 100 and 1000 mg/kg bw
Result	:	ambiguous
Method	:	
Year	:	1985
GLP	:	no data
Test substance	:	

Method : Male rats (number not indicated) were treated with glycerine (most probably injected in the abdomen). Thereafter the animals were mated with 11-12 untreated females/treatment. Two weeks after mating females were sacrificed and the number of implantation sites, foetal loss, live foetuses and anomalous foetuses was established.

Result : Implantation sites: 101, 104 and 91 at 10, 100 and 1000 mg/kg bw respectively (controls 116)
Foetal loss: 11, 20 and 59% at 10, 100 and 1000 mg/kg bw respectively (controls 8%)
Live foetuses: 90, 83 and 37 at 10, 100 and 1000 mg/kg bw respectively (controls 107)
Anomalies: none in glycerine treated and control animals

Test substance : CAS 56-81-5 (Glycerine), purity not indicated.

Conclusion : Glycerine may have a potential mutagenic effect on gender cells, which results in post-implantation deaths. The effect however, did not reach statistical significance.

Reliability : (4) not assignable
1 The report is limited to the above.
2 No positive control group was included. The study did not use an adequate number of animals. Group sizes of 30-50 are recommended in the OECD guideline (478).
3 Because the purity of the test substance is not mentioned, it is feasible that some undiluted contamination is responsible for the observed effect. In a two generation study no effects on pregnancy were found at doses upto 2000 mg/kg bw.

24.01.2002 (114)

Type	:	other: chromosome aberration test
Species	:	rat
Sex	:	male
Strain	:	
Route of admin.	:	other: injection in the abdomen
Exposure period	:	
Doses	:	1000 mg/kg bw
Result	:	negative
Method	:	
Year	:	1985
GLP	:	no data
Test substance	:	

Method : 10 male rats received 1000 mg/kg bw glycerine in water or isotonic salt solution (dosing volume 2 mL). After 50 hours animals were killed and chromosome preparations were prepared from marrow cells from the femoral bone. Cytogenic analysis was performed in 50 metaphases.

Result	:	Number of cells with aberrations 2.2% (0% in concurrent controls) Number of cells with gaps 1.6% (0% in concurrent controls) Polyploid cells 3.2% (0% in concurrent controls)
Test substance	:	CAS 56-81-5 (Glycerine), purity not indicated.
Conclusion	:	Glycerine did not induce a statistically significant increase in chromosomal aberrations when compared to control values.
Reliability	:	(4) not assignable The report is limited to the above. No positive control group was included.

24.01.2002 (114)

5.7 CARCINOGENICITY

Species	:	mouse
Sex	:	
Strain	:	other: ddY
Route of admin.	:	drinking water
Exposure period	:	
Frequency of treatm.	:	
Post exposure period	:	
Doses	:	5% solution
Result	:	
Control group	:	yes
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	no data
Remark	:	The promoting effect of glycerol on the pulmonary tumorigenesis in ddY mice induced by 4-nitroquinoline (4NQO; 0.3 mg/mouse= about 10 mg/kg bw; s.c.). Literature could not be retrieved.
Result	:	The incidence of pulmonary tumor-bearing mice as well as the mean number of induced tumors per mouse were significantly enhanced in mice given glycerol for 4-25 weeks after 4NQO treatment, compared with mice given 4NQO alone.
Reliability	:	(4) not assignable

25.01.2002 (115)

Species	:	mouse
Sex	:	male
Strain	:	other: ddY
Route of admin.	:	drinking water
Exposure period	:	1-4 weeks
Frequency of treatm.	:	
Post exposure period	:	
Doses	:	5% in drinking water
Result	:	
Control group	:	other: see method
Method	:	
Year	:	1987
GLP	:	no data
Test substance	:	other TS
Method	:	TEST ORGANISMS - Age: 6 weeks - Number of animals: 20 males/treatment ADMINISTRATION / EXPOSURE

- Single s.c. injection of 4NQO (10 mg/kg bw) on day 1 followed by treatment with glycerol during, 1, 2, 3 or 4 weeks
- Dose: 5% in drinking water (~8350 mg/kg bw)
- Vehicle (4NQO): olive oil and cholesterol (20:1)
- Controls: untreated, 4NQO treated (single) and glycerol treated (4 weeks)
- Observation period: 25 weeks

Examinations:
- Mortality
- Body weight
- No./size of pulmonary tumours
- Tumour histopathology

STATISTICAL METHODS: Student's t-test, chi-square test

Result : Mortality: 2 animals in the group that was treated with glycerine for 3 weeks and 1 animal in the group that was treated with glycerine for 4 weeks. These animals showed rapidly growing subcutaneous sarcomas at the injection site from week 16-20 (invading into pleural and peritoneal cavities and liver).

Body weight: tendency to increase with increasing exposure time to glycerine (not significant)

Pulmonary tumours:
- No. of tumour bearing mice:
controls (not receiving 4NQO) 1/20
controls (receiving 4NQO) 8/20
treatment (1 week glycerine) 11/20
treatment (2 weeks glycerine) 11/19
treatment (3 weeks glycerine) 7/18
treatment (4 weeks glycerine) 15/19
- Mean number of tumours/mouse: significantly increased after 4 weeks of glycerine
- The number of tumour-bearing mice was identical between untreated controls (1/20) and animals receiving glycerine only for 4 weeks.
- Tumour volume: tendency to increase with increasing exposure time to glycerine (not significant)

Other tumours: 3 control mice receiving 4NQO developed sarcomas at the injection site in week 22. Necropsy revealed metastases to the lungs and liver.

Histopathology:
Most tumours were papillary or solid ones. In some papillary tumours atypical cells with polygonal nuclei (hyperchromasia) were observed.

Test substance : CAS 56-81-5 (Glycerine), purity not indicated.

Conclusion : The data suggest that glycerine modulates the initial process of tumourgenesis by 4NQO.

Reliability : (4) not assignable
The information was confined to the above.

25.01.2002 (116)

Species : mouse
Sex : male
Strain : other: ddY
Route of admin. : drinking water
Exposure period : 25 weeks
Frequency of treatm. :
Post exposure period :
Doses : 5% in drinking water
Result :

Control group : other: see method
Method :
Year : 1986
GLP : no data
Test substance : other TS

Method : TEST ORGANISMS
- Age: 6 weeks
- Number of animals: 20 males/treatment

ADMINISTRATION / EXPOSURE
- Single s.c. injection of 4NQO (10 mg/kg bw) on day 1 followed by treatment with glycerol from week 5-30.
- Dose: 5% in drinking water (~8350 mg/kg bw)
- Vehicle (4NQO): olive oil and cholesterol (20:1)
- Controls: untreated, 4NQO treated (single) and glycerol treated (25 weeks)
- Observation period: 30 weeks

Examinations:
- Mortality
- Body weight
- No. of pulmonary tumours
- Tumour histopathology

STATISTICAL METHODS: not specified

Result : Mortality: 2 animals in the group receiving 4NQO only showing fibrosarcomas at the injection site (week 25-28).

Body weight: no treatment related effects

Pulmonary tumours:
- No. of tumour bearing mice:
controls 2/20
controls (receiving glycerine) 2/20
treatment (receiving 4NQO only) 51/20
treatment (NQO + glycerine) 17/20
- Mean number of tumours/mouse: significantly increased after NQO + glycerine (2.9/mouse versus 0.1-0.45/mouse in the other groups). Treatment with glycerine alone did not result in an increase in number of tumour-bearing mice above that observed in untreated controls.

Other tumours: Additional 2 mice receiving 4NQO only developed fibrosarcomas at the injection site (no lung tumours).

Histopathology:
In NQO treated mice all tumours were idetified as type II adenomas.
In NQO + glycerine treated animals 52 tumours were identified as type II adenomas and 6 as Clara cell adenomas.

Test substance : CAS 56-81-5 (Glycerine), purity not indicated.
Reliability : (4) not assignable
The information was confined to the above.

25.01.2002 (117)

Species : mouse
Sex : male
Strain : other: ddY
Route of admin. : drinking water
Exposure period : 4-25 weeks
Frequency of treatm. :

Post exposure period :
Doses : 5% in drinking water
Result :
Control group : other: see method
Method :
Year : 1986
GLP : no data
Test substance : other TS

Method : TEST ORGANISMS
- Age: 6 weeks
- Number of animals: 10 males/treatment

ADMINISTRATION / EXPOSURE
- Single s.c. injection of 4NQO (10 mg/kg bw) on day 1 followed by treatment with glycerine for 4-25 weeks.
- Dose: 5% in drinking water (~8350 mg/kg bw)
- Vehicle (4NQO): olive oil and cholesterol (20:1)
- Controls: untreated, 4NQO treated (single) and glycerol treated (25 weeks)
- Observation period: 25 weeks

Examinations:
- No. of pulmonary tumours
- Tumour histopathology

STATISTICAL METHODS: not specified

Result : Pulmonary tumours:
- No. of tumour bearing mice:
controls 0/10
controls (glycerine 25 weeks) 0/10
controls (receiving 4NQO) 1/10
treament (4 weeks glycerine) 8/10
treament (25 weeks glycerine) 8/9
treament (glycerine week 4-25) 7/10

- Mean number of tumours/mouse (significant increase after NOQ + glycerine):
controls 0
controls (glycerine 25 weeks) 0
controls (receiving 4NQO) 0.1
treament (4 weeks glycerine) 3.5
treament (25 weeks glycerine) 2.3
treament (glycerine week 4-25) 1.9

Histopathology:
All tumours were adenomas.

Test substance : CAS 56-81-5 (Glycerine), purity not indicated.
Reliability : (4) not assignable
The information was confined to the above.

08.01.2002 (118)

Species : rat
Sex : male/female
Strain :
Route of admin. : oral feed
Exposure period : 2 yr
Frequency of treatm. :
Post exposure period :
Doses : 5 or 10 g/kg (24 males and 24 females)

Result	:	
Control group	:	
Method	:	
Year	:	1953
GLP	:	no data
Test substance	:	no data
Remark	:	Not all literature could be retrieved.
Result	:	No increase in tumour incidence.
Source	:	Unichema Chemie B.V. Gouda EUROPEAN COMMISION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable
25.01.2002		(119) (64)
Species	:	rat
Sex	:	male/female
Strain	:	Long-Evans
Route of admin.	:	oral feed
Exposure period	:	
Frequency of treatm.	:	
Post exposure period	:	
Doses	:	5, 10 and 20% in diet
Result	:	
Control group	:	
Method	:	
Year	:	1953
GLP	:	
Test substance	:	
Method	:	TEST ORGANISMS - Age: not indicated - Weight at study initiation: 96-109 g (males), 92-108 g (females) - Number of animals: 22/sex/treatment, 26/sex for controls - Source: Institute of Experimental Biology of University of California ADMINISTRATION / EXPOSURE - Exposure period: 2 year (1 year for the high dose group) - Route of administration: oral in diet - Doses: 5, 10 and 20% in diet; males 2000, 4000 and 8000 mg/kg bw, females 2500, 5000 and 10000 mg/kg bw CLINICAL OBSERVATIONS AND FREQUENCY: - Clinical signs: daily in cage and weekly examination outside the home cage - Mortality: daily - Body weight: weekly ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC): - Organ weights: liver, kidneys, heart, spleen and lungs - Macroscopic: no details provided - Microscopic: liver, spleen, adrenals, kidney, small intestine, gonads and urinary bladder ANALYSES: not performed STATISTICAL METHODS: Chi-sqare test, student t-test, ANOVA (Fisher)
Result	:	TOXIC RESPONSE/EFFECTS BY DOSE LEVEL:

- Mortality and time to death: not indicated
- Clinical signs: not reported
- Body weight gain: no statistically significant differences between treated and control animals
-Histopathology: Malignant neoplasms in 5/26, 1/22, 5/22, 0/22, 0/21, 5/22 and 0/22 animals in control and at 5%, 10%, 20% natural glycerol and at 5%, 10%, 20% synthetic glycerol, respectively.
Benign neoplasms im 0/26, 2/22, 1/22, 0/22, 4/21, 4/22 and 1/22 animals in controls and at 5%, 10%, 20% natural glycerol and at 5%, 10%, 20% synthetic glycerol, respectively.
Among the benign tumours 3 rats were found with pheochromacytomas and 2 with granulosa cell tumours.

Test substance : CAS 56-81-5 (glycerine),
Natural glycerine, achieved from market stock, purity not indicated (impurities were fatty acids and esters)
Synthetic glycerin, purity 99.5% (rest mainly water with very small amounts of glycerin polymers and glyceraldehyde).

Conclusion : No increased incidence in tumour incidence follwing treatment with glycerol.

Reliability : (2) valid with restrictions
The report was confined to the above.

Flag : Critical study for SIDS endpoint

29.01.2002 (64)

5.8.1 TOXICITY TO FERTILITY

Type	:	Two generation study
Species	:	rat
Sex	:	male/female
Strain	:	
Route of admin.	:	gavage
Exposure period	:	8-12 weeks (starting before mating and continuing, in females, until weaning).
Frequency of treatm.	:	daily
Premating exposure period		
Male	:	8 weeks
Female	:	8 weeks
Duration of test	:	
No. of generation studies	:	
Doses	:	20% in water, about 2 g/kg/day
Control group	:	yes, concurrent vehicle
Method	:	
Year	:	1953
GLP	:	no data
Test substance	:	

Method : TEST ORGANISMS
- Age: not indicated
- Weight at study initiation: not indicated
- Number of animals: 10/sex/treatment for Parent and F1

ADMINISTRATION / EXPOSURE
- Test durations: until F2-generation was 100 days of age
- Premating period: 8 weeks
- Exposure period: 12 weeks (until weaning of F1)
- Route of administration: oral (gavage, dose volume 10 mL/kg)
- Doses: 20% solution in water, ~2000 mg/kg bw

MATING PROCEDURES: not indicated (starting when females were between 170 and 215 g)

STANDARDIZATION OF LITTERS: not performed

PARAMETERS ASSESSED:
- Clinical observations: frequency not indicated
- Estrous cycle: in F1 and F2 between 60 and 100 days
- Body weight: in F1 and F2 during day 15 and 60 at 2-day intervals
- Sperm examination: not performed

ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Organ weights F1 and F2: pituitary, thyroid, adrenals, ovaries, testicles
- Histopathology F1 and F2: endocrine system organs on 26 animals

Result : No effects were found on the reproductive efficiency of the parents, nor on the growth, fertility and reproductive performance of the untreated F1 generation, and no histological changes occurred in the tissues of both the F1 and F2 generation.
Onset of oestrus cycle and weight and microscopy of the endocrine organs were comparable to control values for both F1 and F2 animals.
In the parent generation all 10 females became pregnant (litter size 9.0, controls 8.1) and in the F1 9/10 females became pregnant (litter size 8.7, controls 8.1).

Test substance : CAS 56-81-5 (glycerine), 20% solution in water

Conclusion : Most reliable study available.

Reliability : (2) valid with restrictions
1 The report was essentially confined to the above mentioned.
2 Although the study used a significantly high dose level (~2 g/kg bw/day), the significance attached to this study is somewhat limited by the use of 10 females per dose level.

Flag : Critical study for SIDS endpoint

18.12.2001 (120)

Type : Fertility
Species : rat
Sex : male
Strain : Sprague-Dawley
Route of admin. : other: intratesticular
Exposure period :
Frequency of treatm. : on day 1 and 7
Premating exposure period
Male :
Female :
Duration of test : 14 days
No. of generation studies :
Doses : 50 uL glycerol solution
Control group : yes, concurrent vehicle
Method : other: not indicated
Year : 1984
GLP : no
Test substance :

Method : TEST ORGANISMS
- Age: 48 days, 69 days and 90-95 days (3 separate experiments)
- Weight at study initiation: not indicated
- Number of animals: 14, 8 and 8

ADMINISTRATION / EXPOSURE
- Exposure: twice (7 days apart)
- Route of administration: intratesticular injection (right testis treated, left testis control)
- Doses: not indicated (50 uL)

OBSERVATIONS:
- Testes weight (14 days after first injection)
- Spermatogenesis (14 days after first injection)

STATISTICAL METHOD:
Student's t-test

Result : Testis weight (treated side) significantly decreased compared to controls for all ages
Spermatogenesis: treatment resulted in complete loss of spermatogenic cells

Test substance : CAS 56-81-5 (glycerine), solution in water and ethanol (amounts not specified),purity not specified

Reliability : (4) not assignable
1 The information is confined to the above mentioned.
2 The relevance of the exposure route is considered to be low. After oral exposure no effects were observed according to the author of the report.

25.01.2002 (121)

Type : Fertility
Species : rat
Sex : male
Strain : Sprague-Dawley
Route of admin. : other: intratesticular
Exposure period :
Frequency of treatm. : single dose
Premating exposure period
Male :
Female :
Duration of test : 73 days
No. of generation studies :
Doses : 200 uL
Control group : yes, concurrent vehicle
Method : other: not indicated
Year : 1984
GLP : no
Test substance :

Method : TEST ORGANISMS
- Age: 48-101 days
- Weight at study initiation: 342-372 g
- Number of animals: 12/treatment

Animals were allowed to mate three times between day 15 and 73

ADMINISTRATION / EXPOSURE
- Exposure: single
- Route of administration: intratesticular injection (left testis treated, right testis control)
- Doses: 200 uL

OBSERVATIONS: interim kills of 3-5 animals on day 7, 15 and 73:
- Histopathology/weight of testis, seminal vesicles, prostate and epididymides
- No. of sperm/epididymis

STATISTICAL METHOD:
Student's t-test

Result : WEIGHTS: Weight of testis significantly decreased at all sampling times; no effect on weight of prostate and seminal vesicles; weight of the epididymides significantly decreased after 73 days.
SPERM: No. of sperm cells significantly decreased after 15 days and almost no sperm cells after 73 days
HISTOPATHOLOLOGY:
Day 7: nucleated bodies in seminiferous tubules (almost no spermatogenic cells), normal germ cells and Leidig cells
Day 15 and 73: few nucleated bodies in seminiferous tubules (almost no spermatogenic cells), normal Leidig cells. No resumption of spermatogenesis

Test substance : CAS 56-81-5 (glycerine), solution in water (7:3), purity not specified

Conclusion : Intratesticular injection of glycerine inhibits spermatogenesis strongly over a prolonged period of time.

Reliability : (4) not assignable
1 The information is confined to the above mentioned.
2 The relevance of the exposure route is considered to be low. After oral exposure no effects were observed according to the author of the report
3 Additional in vitro testing showed no decreased ability to metabolise progesterone compared to controls.

25.01.2002 (121)

Type : Fertility
Species : rat
Sex : male
Strain : Sprague-Dawley
Route of admin. : other: intratesticular
Exposure period :
Frequency of treatm. : single
Premating exposure period
Male :
Female :
Duration of test : 20-21 weeks
No. of generation studies :
Doses : 200 uL/testis
Control group : yes, concurrent vehicle
Method : other: not indicated
Year : 1984
GLP : no
Test substance :

Method : TEST ORGANISMS
- Age: 86-90 days
- Weight at study initiation: not indicated

- Number of animals: 8/treatment, 8 for water treated controls

ADMINISTRATION / EXPOSURE
- Exposure: single
- Route of administration: intratesticular injection
- Doses: 200 uL

PROCEDURE:
Starting at 14 days after injection animals were allowed to mate with a virgin female for a period of 5 days (females were added in week 2, 3, 4, 5 and 6). 3 treated and 4 control animals were kept until week 21 and were allowed to mate during week 20 and 21.

OBSERVATIONS:
- Mating behaviour
- After each mating period: no. mated, no. pregnant and no. of foetuses by examination of the uterus contents of the females 10 days after cohabitation

Result : Mating behaviour and the number of matings did not differ between treated and control animals.
Pregnancy rate decreased markedly by the third mating period (week 4) (2/8 females pregnant compared to 7/8 in controls).
From week 5 onwards no pregnancies were observed in females mated with treated males.
The mean number of foetuses/mated female in controls was 10-13. In treated animals this number was 11 (week 2), 8 (week 3) and 2 (week 4).

Test substance : CAS 56-81-5 (glycerine), solution in water and ethanol (amounts not specified),purity not specified

Conclusion : Treatment with glycerine did not affect sexual behaviour. However, fertility was affected strongly and prolonged.

Reliability : (4) not assignable
1 The information is confined to the above mentioned.
2 The relevance of the exposure route is considered to be low. After oral exposure no effects were observed according to the author of the report.

25.01.2002 (121)

Type : Fertility
Species : rat
Sex : male
Strain :
Route of admin. : other: intratesticular
Exposure period :
Frequency of treatm. :
Premating exposure period
Male :
Female :
Duration of test :
No. of generation studies :
Doses : 862 mg/kg (1 day prior to mating)
Control group :
Method :
Year : 1984
GLP : no data
Test substance : no data

Remark	:	Literature could not be retrieved. Study type: TDL0 Paternal effects (Spermatogenesis).
Result	:	Intratesticular injection of glycerol solution suppresses spermatogenesis (meiosis) without any evidence of toxic or endocrine effects.
Source	:	Simel S.p.A. Industria Chimica Cremona EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable

25.01.2002 (122)

Type	:	Fertility
Species	:	monkey
Sex	:	male
Strain	:	
Route of admin.	:	other: intratesticular
Exposure period	:	
Frequency of treatm.	:	
Premating exposure period		
Male	:	
Female	:	
Duration of test	:	
No. of generation studies	:	
Doses	:	119 mg/kg (1 day prior to mating)
Control group	:	
Method	:	
Year	:	1989
GLP	:	no data
Test substance	:	no data

Remark	:	Study type: TDL0 Paternal effects (Spermatogenesis; Testes, epididymus, sperm duct). Literature could not be retrieved.
Result	:	Intratesticular injection of glycerol solution suppresses spermatogenesis (meiosis) without evidence of toxic or endocrine side effects.
Source	:	Unichema Chemie B.V. Gouda EUROPEAN COMMISION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable

25.01.2002 (123)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	rat
Sex	:	female
Strain	:	Wistar
Route of admin.	:	gavage
Exposure period	:	day 6 to day 15 of gestation inclusive
Frequency of treatm.	:	daily
Duration of test	:	20 days
Doses	:	13.1-1310 mg/kg bw
Control group	:	other: sham treated
NOAEL maternal tox.	:	= 1310 mg/kg bw
NOAEL teratogen.	:	= 1310 mg/kg bw
Method	:	other: not indicated
Year	:	1974
GLP	:	no
Test substance	:	

Method : TEST ORGANISMS
- Age: adult
- Mean weight at study initiation: 214-230 g
- Number of animals: 25-28 females/treatment

ADMINISTRATION / EXPOSURE
- Test duration: 20 days
- Exposure period: day 6-15 of gestation inclusive
- Definition of day 0: observation of vaginal sperm plug
- Route of administration: oral (gavage)
- Doses: 13.1, 60.8, 282 and 1310 mg/kg bw (dosing volume <6 mL/kg)
- Vehicle: none

MATING PROCEDURES: most probably 1 male/1 female

PARAMETERS ASSESSED DURING STUDY:
- Mortality/clinical observations: daily
- Body weight: on day 0, 6, 11, 15 and 20
- Food consumption: daily
- Examination of uterine content: no. of implantation sites, resorptions and live and dead foetuses
- Examination of foetuses: body weight, sex, external abnormalities, visceral (1/3 of foetuses) and skeletal (2/3 of foetuses) examination

ORGANS EXAMINED AT NECROPSY: urogenital tract

STATISTICAL METHODS: not indicated

Result : MATERNAL TOXIC EFFECTS BY DOSE LEVEL:
- Mortality: none
- Body weight: no treatment related effects
- Food consumption: no data
- Clinical signs: not reported
- Number pregnant per dose level: 23/25, 24/25, 22/28, 22/25 and 21/25 for controls and at 13.1, 60.8, 282 and 1310 mg/kg bw
- Number aborting: none
- Number of implantations: 11.3, 10.8, 12.3, 11.8 and 11.1 for controls and at 13.1, 60.8, 282 and 1310 mg/kg bw
- Number of resorptions (no of dams involved): 2, 1, 1, 2 and 2 for controls and at 13.1, 60.8, 282 and 1310 mg/kg bw

FETAL DATA:
- Litter size and weights: No treatment related effects
- Number viable: 10.8, 11.1, 11.2, 11.0 and 10.2 per litter for controls and at 13.1, 60.8, 282 and 1310 mg/kg bw
- Sex ratio: no treatment related effects
- External abnormalities: none reported
- Visceral abnormalities: none
- Skeletal abnormalities: delayed ossification in all treatment groups and controls without relationship to treatment

Test substance : CAS 56-81-5 (glycerine) (syrup), purity not specified

Conclusion : Most reliable study available.

Reliability : (2) valid with restrictions
1 No data on uterus weights, no of corpora lutea and food consumption were included in the report.
2 No analyses of the test substance concentration were included.
3 For foetal external, visceral and skeletal examinations only summary tables were included.

Flag : Critical study for SIDS endpoint
25.01.2002 (124)

Species : Mouse
Sex : Female
Strain : CD-1
Route of admin. : Gavage
Exposure period : day 6 to day 15 of gestation inclusive
Frequency of treatm. : Daily
Duration of test : 17 days
Doses : 12.8-1280 mg/kg bw
Control group : other: sham treatment
NOAEL maternal tox. : = 1280 mg/kg bw
NOAEL teratogen. : = 1280 mg/kg bw
Method : other: not indicated
Year : 1974
GLP : No
Test substance :

Method : TEST ORGANISMS
- Age: adult
- Mean weight at study initiation: 28.1-33.2 g
- Number of animals: 25 females/treatment

ADMINISTRATION / EXPOSURE
- Test duration: 17 days
- Exposure period: day 6-15 of gestation inclusive
- Definition of day 0: observation of vaginal sperm plug
- Route of administration: oral (gavage)
- Doses: 12.8, 59.4, 276 and 1280 mg/kg bw
- Vehicle: none

MATING PROCEDURES: most probably 1 male/1 female

PARAMETERS ASSESSED DURING STUDY:
- Mortality/clinical observations: daily
- Body weight: on day 0, 6, 11, 15 and 17
- Food consumption: daily
- Examination of uterine content: no. of implantation sites, resorptions and live and dead foetuses
- Examination of foetuses: body weight, sex, external abnormalities, visceral (1/3 of foetuses) and skeletal (2/3 of foetuses) examination

ORGANS EXAMINED AT NECROPSY: urogenital tract

STATISTICAL METHODS: not indicated

Result : MATERNAL TOXIC EFFECTS BY DOSE LEVEL:
- Mortality: none
- Body weight: no treatment related effects
- Food consumption: no data
- Clinical signs: not reported
- Number pregnant per dose level: 22/25, 23/25, 20/25, 22/25 and 21/25 for controls and at 12.8, 59.4, 276 and 1280 mg/kg bw
- Number aborting: none
- Number of implantations: 11.1, 11.6, 12.0, 11.5 and 10.9 for controls and at 12.8, 59.4, 276 and 1280 mg/kg bw
- Number of resorptions (no of dams involved): 5, 6, 9, 4 and 9 for controls and at 12.8, 59.4, 276 and 1280 mg/kg bw

FETAL DATA:
- Litter size and weights: No treatment related effects
- Number viable: 10.8, 11.1, 11.2, 11.0 and 10.2 per litter for controls and at 12.8, 59.4, 276 and 1280 mg/kg bw
- Sex ratio: no treatment related effects
- External abnormalities: none reported
- Visceral abnormalities: none
- Skeletal abnormalities: delayed ossification in all treatment groups and controls without relationship to treatment

Test substance : CAS 56-81-5 (glycerine) (syrup), purity not specified
Conclusion : Most reliable study available.
Reliability : (2) valid with restrictions
1 No data on uterus weights, no of corpora lutea and food consumption were included in the report.
2 No analyses of the test substance concentration were included.
3 For foetal external, visceral and skeletal examinations only summary tables were included.
Flag : Critical study for SIDS endpoint
25.01.2002 (124)

Species : Rabbit
Sex : Female
Strain : other: Dutch-belted
Route of admin. : Gavage
Exposure period : day 6 to day 18 of gestation inclusive
Frequency of treatm. : Daily
Duration of test : 29 days
Doses : 11.8-1180 mg/kg bw
Control group : other: sham treated
NOAEL maternal tox. : = 1180 mg/kg bw
NOAEL teratogen. : = 1180 mg/kg bw
Method : other: not indicated
Year : 1974
GLP : No
Test substance :

Method : TEST ORGANISMS
- Age: adult
- Mean weight at study initiation: 2.09-2.38 kg
- Number of animals: 15-20 females/treatment

ADMINISTRATION / EXPOSURE
- Test duration: 29 days
- Exposure period: day 6-18 of gestation inclusive
- Route of administration: oral (gavage)
- Doses: 11.8, 54.8, 254.5 and 1180 mg/kg bw (dosing volume <6 mL/kg)
- Vehicle: none

MATING PROCEDURES: artificial insemination

PARAMETERS ASSESSED DURING STUDY:
- Mortality/clinical observations: daily
- Body weight: on day 0, 6, 12, 18 and 29
- Food consumption: daily
- Examination of uterine content: no. of corpora lutea, implantation sites, resorptions and live and dead foetuses
- Examination of foetuses: body weight, sex, external

abnormalities on day 29, neonatal survival, visceral and skeletal examination on day 30

ORGANS EXAMINED AT NECROPSY: urogenital tract

STATISTICAL METHODS: not indicated

Result : MATERNAL TOXIC EFFECTS BY DOSE LEVEL:
- Mortality: 1 animal at 54.8 mg/kg bw, 2 at 254.5 mg/kg bw and 1 at 1180 mg/kg bw
- Body weight: no treatment related effects, significant decrease only at 254.5 mg/kg bw (14%) compared to controls.
- Food consumption: no data
- Clinical signs: not reported
- Number pregnant per dose level: 14/15, 12/15, 10/18, 13/20 and 13/15 for controls and at 11.8, 54.8, 254.5 and 1180 mg/kg bw
- Number aborting: 2 at 254.5 mg/kg bw
- Number of corpora lutea: 9.7, 11.7, 5.6, 8.2 and 11.2 for controls and at 11.8, 54.8, 254.5 and 1180 mg/kg bw
- Number of implantations: 6.1, 5.1, 5.4, 7.3 and 6.4 for controls and at 11.8, 54.8, 254.5 and 1180 mg/kg bw
- Number of resorptions (no of dams involved): 5, 2, 4, 2 and 6 for controls and at 11.8, 54.8, 254.5 and 1180 mg/kg bw

FETAL DATA:
- Litter size: No treatment related effects
- Fetal weight: decreased(14%) at 254.5 mg/kg bw compared to controls.
- Number viable: 5.1, 4.7, 4.8, 5.9 and 5.5 per litter for controls and at 11.8, 54.8, 254.5 and 1180 mg/kg bw mg/kg bw
- Sex ratio: no treatment related effects
- External abnormalities: none reported
- Visceral abnormalities: no treatment related effects
- Skeletal abnormalities: delayed ossification increased at 254.5 mg/kg bw (without relationship to treatment)

Test substance : CAS 56-81-5 (glycerine), purity not indicated.
Conclusion : Most reliable study available.
Reliability : (2) valid with restrictions
1 No data on uterus weights and food consumption were included in the report.
2 The number of pregnant females at 54.8 mg/kg bw is lower than required by OECD 414 (1981).
3 No analyses of the test substance concentration were included.
4 For foetal external, visceral and skeletal examinations only summary tables were included.
Flag : Critical study for SIDS endpoint
25.01.2002 (124)

Species : other: FETAX
Sex :
Strain :
Route of admin. :
Exposure period :
Frequency of treatm. :
Duration of test :
Doses :
Control group :
Method : other: ASTM E1439-91
Year : 1999
GLP :
Test substance :

Method : In this report an interlaboratory validation study of the FETAX-assay was included. This validation is part of the ASTM process to evaluate the repeatability and reliability of the FETAX assay. In this test three laboratories tested 12 coded chemicals (one of which was glycerol) with and without Aroclor 1254 induced microsomes.

All tests were performed in accordance with the ASTM standard guide. For each test duplicate test concentrations (10x2) were included. In each laboratory each test was performed three times, so 9 tests were performed in total.

To judge the developmental hazard the teratogenic index was calculated (TI=96h LC50/96 h EC50 malformation) and it was checked wheteher significant growth inhibition was found at concentrations <30% of the 96-h LC50 (with microsomes).

Developmental hazard for mammalian species is predicted when the mean TI (with microsomes) exceeds 1.5 and the minimal concentration that inhibits growth (MCIG with microsomes) exceeds 30% of the LC50.

Statistical method: Probit analysis (Litchfield-Wilcoxon), trimmed Spearman Karber, Steel and Torrie.

Result : All results included here are related to the tests with the inclusion of microsomes (for detailed results see section 4.9).

Mean TI: 1.66; individual laboratories showed mean values of 0.97, 1.67 and 2.33.
For all tests the MCIG > 30% of the LC50.

Additionally results of mammalian developmental toxicity tests were obtained from the National Toxicology Program, the available scientific literature, two general papers on developmental toxicity screening tests and/or two reference source books. Only refereces to oral administration in mouse, rabbit and rat were employed. Based on these references glycerol was indicated as non-teratogen and therefore the FETAX assay was falsely positive.

Conclusion : In the FETAX test glycerol gave an ambiguous result.
In mammalian experiments (literature) glycerol was not teratogenic.

Reliability : (4) not assignable
1. FETAX (Frog Embryo Teratogenesis Assay-Xenopus) is a 96 hours whole-embryo developmental assay that can be used in detecting mammalian toxicants when an in vitro metabolic activation system is employed.
2. The report is actual a publication on the validation of the FETAX-assay and shows that the assay is falsely positive in the case of glycerol. The literature that is checked for information on the mammalian teratogenicity of glycerol is the following:
A. Shepard T.H., Catalog of Teratogenic Agents, 4th edition, 1983.
B. Lewis R.J., Reproductive Active Chemicals- a reference guide, 1991
C. Hardin B.D. et al., Evaluatuion of 60 chemicals in preliminary developmental toxicity test, Teratogen. Carcinog. Mutagen. 7: 29-48, 1987
D. Kavlock et al., Further evaluation of an in vivo teratology screen. teratogen. carcinog. Mutagen. 7: 7-16, 1987.
Since the reliability of the previous mentioned publications cannot be checked, the reliability is set at 4.

20.12.2001 (63)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

Type of experience : other: Consumer exposure

Result : Dermal consumer exposure

Cosmetics
Consumers can be exposed to numerous cosmetic products containing glycerol such as soaps, bath and shower foams, creams, lotions and deodorants. Creams, lotions and deodorants are expected to remain on the skin for a longer time than the other products mentioned.

Paints, printing inks and resins
Other products containing glycerol, which can result in dermal contact, are the paints, printing inks and resins (like gums). It is anticipated that the maximum concentration of glycerol in these products in 20%.

Migration from Paper and Plastic Articles
Glycerol is also used in papers as softener or flexibiliser. Since the substance is incorporated in the paper matrix migration of the substance is expected to be low (no migration studies are available). Glycerol is also used in cellulose films. From this product glycerol may also migrate. However, the uptake is expected to be low. Both scenarios have not been considered further.

Oral intake by consumers

The following product groups are identified containing glycerol: pharmaceuticals, cosmetics (i.e. toothpaste), cellulose films (edible - meat casings, sausage skins) and food and drinks.

For sausages, the skin is probably 1% of the sausage (in weight) and the skin consists of maximal 5% of glycerol.

Food and drinks
Glycerol is present in the following food and drink products: bakery products, beverages, sweets and candies, flavours, soft drinks concentrates, humectants for edible purposes. Substantial reviews on the safety of glycerol have been prepared by international organisations like the WHO, JECFA and the European SCF.

Inhalation by consumers

Due to the fact that consumer products containing glycerol are almost exclusively liquids, creams or the substance is contained in a matrix, dust formation and hence inhalation is not considered as a relevant exposure path for the public.

The only identified exposure is due to inhalation of cigarette smoke. Cigarettes (1 gram each) contain maximally 5% glycerol, which is probably inhaled by the smoker (uptake 100%).

05.12.2001

Type of experience : other: Worker exposure

Result : Occupational exposure

Occupational exposure to glycerol can occur during production of this substance, during formulation or transformation into other product or during use of product where glycerol is present. The dermal route is considered to be the most relevant exposure route.

Dermal exposure of workers

Paints
To assess the exposure of workers to paint it is assumed that 8 hours a day a worker is painting. The exposure is estimated with Derwin v1.42 to be 0.19 mg cm-2 day-1. Since both hands are exposed of the painter, the exposure is 440 cm2 * 0.19 mg cm-2 day-1 = 84 mg day-1
Using the mass of the painter (70 kg), the uptake is 1.2 mg kg-1 day-1.

25.01.2002

Remark : Literature could not be retrieved.
Result : Fertility study of 64 male employees engaged in the manufacture of glycerol.
Compared with a control group of 63 workers, no significant differences were found in several sperm quality parameters of which sperm counts/mL and percent normal forms are considered to be most reliable.
Source : Unichema Chemie B.V. Gouda
EUROPEAN COMMISION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
25.01.2002 (125)

Remark : Literature could not be retrieved.
Result : A total of 179 cases with various intracranial disorders was treated by intravenous administration of 10-15% solution in an attempt to control cerebral edema.
There was no evidence of significant adverse findings attributable to the administration of glycerol.
Source : Unichema Chemie B.V. Gouda
EUROPEAN COMMISION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
25.01.2002 (126)

Result : Two cases of adverse effects after oral administration of glycerine in patients.
A 82-year old female (hypertensive, mentally senile) received 200 ml 50% glycerine orally for primary angle closure glaucoma. This woman developed headache, shaking of the arm, quivering of the eyes and nausea.
A 68-year old female (diabetic) received 280 ml 50% glycerine orally within a period of 3 days. This glycerine was felt responsible for the ensuing severe diabetic acidosis.

24.09.2001 (127)

Method : 14 volunteers (10 men, 4 women) drank orange juice mixed with 30 mL of 95% glycerol after each of the 3 daily meals.
Result : No overt signs of toxicity or effect on food consumption
24.09.2001 (128) (102)

Method : 37 Cases (human) of cerebral edema caused by acute cerebral infarction, were treated daily with 1.2 g/kg of glycerin i.v. or 1.5 g/kg orally. Seventeen other patient with cases of edema of the central nervous system were similarly treated.
Result : During treatment, mortality of the group with cerebral infarction was 11%, howerver these deaths were not related to glycerin administration. Neurological improvement occurred in all other cases during and at the end of 4 days of treatment. No toxic effects were observed which were attributable to glycerin administration.
14.11.2001 (127) (129)

Method : Skin patch test in 15 workers with glycerol diluted 500 to 1000 times with water.
Result : Negative
24.09.2001 (90)

Result : 1. Acute ingestion of glycerol in male subjects led to an increase in plasma glycerides, the same procedure in women led to no significant change in the glyceride concentration.
2. When glycerol was ingested chronically (42 days), both men and women showed increased serum glyceride concentration, the increase was significantly greater in men, however.
24.09.2001 (130)

Remark : In case control studies a possible association between exposure to hydrocarbons (one example mentioned is glycerol) and tubular necrosis, chronic tubulointerstitial damage and glomerulonephritis is found. The development of glomerulonephritis appears to mainly a immune mediated disease.
No study with glycerol exposure was reported, only general hydrocarbon exposure or other specific substances were mentioned.
24.09.2001 (131) (132)

Result : A case of acute colonic ischemia following a glycerin enema in preparation for coronary artery bypass surgery was reported.
24.09.2001 (133)

Result : Free glycerol is present in human plasma, and its excretion in the urine stops if levels fall below 1 mg/ml plasma.
Source : Croda Universal Ltd Goole, North Humberside
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
16.05.1994 (134) (135)

Remark : Literature could not be retrieved.
Result : The Joint FAO/WHO Expert Committee on Food Additives considered that glycerol was of such low toxicity that it was acceptable for use without a formal acceptable daily intake figure being specified.
Source : Croda Universal Ltd Goole, North Humberside
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
16.11.2001 (136)

Type of experience : other: human; skin irritation

Remark : Literature could not be retrieved.
Result : In "several thousand" dermatitis patients, 20 to 24-hr covered skin contact with a 50% solution was non-irritating.
Source : Unichema Chemie B.V. Gouda
EUROPEAN COMMISION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
25.01.2002 (137)

Remark : Literature could not be retrieved.
Result : Slightly irritating after 48 hours application of 0.05 ml on human skin in a closed patch test. Further the investigators observed a maximum score for irritation of 4 on a scale of 9 at day 14 during a 21 day application of a 10% solution on human skin.
Source : Unichema Chemie B.V. Gouda
EUROPEAN COMMISION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
25.01.2002 (138)

Remark : Literature could not be retrieved.
Result : A strong burning and stinging sensation, with tear production but no injury apparently from contact with the neat chemical.
Source : Unichema Chemie B.V. Gouda
EUROPEAN COMMISION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
25.01.2002 (89)

05.12.2001

5.11 ADDITIONAL REMARKS

Type : adsorption

Remark : Glycerol is readily absorbed after ingestion.
Literature could not be retrieved.
Source : Unichema Chemie B.V. Gouda
EUROPEAN COMMISION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
25.01.2002 (139)

Type : Biochemical or cellular interactions

Remark : Because glycerol in mouse studies was found to enhance

pulmonary tumorgenesis, it was tested for its ability to induce active oxygen formation in lung macrophages treated with 4-nitroquinoline.
No effect on active oxygen species formation was found.
24.09.2001 (140)

Type : Biochemical or cellular interactions

Remark : Glycerol-related lung tumorgenesis enhancing effects found in tests with mice were inhibited by vitamine E treatment and promoted by treatment with iron. This suggests a mechanism of oxidative stress in the nuclei.
16.11.2001 (141)

Type : Biochemical or cellular interactions

Method : Male mice were treated with a single s.c. injection of 4NQO alone (n=9) or followed by glycerine (5% solution in drinking water) during 1, 7 or 28 days (3 mice each).
30 minutes before animals were killed they were injected with a BrdU solution in their tail vein. BrdU uptake in epithelial cell of the distal airways was determined using anti-BrdU antibodies.
Result : No significant difference in number of BrdU positive cells between 4NQO and 4NQO/glycerol treated mice.
Conclusion : Any tumour promoting effect of glycerol may occur independently from pulmonary cell kinetics.
07.01.2002 (116)

Type : Cytotoxicity

Remark : In concentrations exceeding 20 % glycerol is toxic to bacteria due to dehydration.
Literature could not be retrieved.
Source : Unichema Chemie B.V. Gouda
EUROPEAN COMMISION - European Chemicals Bureau Ispra (VA)
14.11.2001 (142)

Type : Distribution

Remark : Glycerol is distributed over the extracellular space.
24.09.2001 (143)

Type : Excretion

Remark : Glycerol is removed from the body by the liver (80-90%) and the kidneys (10-20%).
24.09.2001 (143)

Type : Metabolism

Remark : Rapid transformation takes place either to carbon dioxide or to esters with free fatty acids.
Literature could not be retrieved.
Source : Unichema Chemie B.V. Gouda
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
25.01.2002 (139)

Type : Metabolism

Remark : Glycerine constitutes approx. 10% of the amount of fat present in human food. Aside from furnishing energy by contributing to the general pool of oxidizable organic compounds it has no special role in nutrition.
Glycerine is well absorbed from the intestinal tract of rats and dogs. Phosphorylation of glycerine to alpha-glycerophosphate takes primarily place in liver and kidneys. Once glycerine is incorporated into the carbohydrate metabolic pathway it can form glucose and glycogen in addition to being oxidized for energy via the tricarboxylic acid cycle. Further exogenous glycerine also participates in lipogenesis.
Literature could not be retrieved.

Source : Unichema Chemie B.V. Gouda

Reliability : (4) not assignable

25.01.2002 (144) (145) (67)

Type : Metabolism

Remark : 1. Glycerol metabolism is regulated by the enzymes glycerol kinase, (cytosolic) NAD+-dependent G3P dehydrogenase and (mitochondrial) FAD-linked G3P dehydrogenase.
2. Glycerol is readily absorbed in the intestine, slower absorption also occurs in the stomach. Max. serum level is attained within 15 min. following an oral dose of 5 g.
3. A safe oral dose in humans is 1 g/kg bw every 6 hours. A single intravenous dose of 50 g in a 5% solution can be administered without adverse symptoms.

24.09.2001 (146)

Type : Metabolism

Remark : In lean persons (short fasting) 38% of plasma glycerol (0.054 umol/ml) was turned into glucose and 2.2% into CO2;
In lean persons (long fasting) 76% of plasma glycerol (0.142 umol.ml) was turned into glucose and 5.4% into CO2;
In obese persons (short fasting) 56% of plasma glycerol (0.105 umol/ml) was turned into glucose and 3.1% into CO2;
In obese persons (long fasting) 96% of plasma glycerol (0.180) was turned into glucose and 4.4% into CO2;

Turnover rates of glycerol are directly proportional to plasma glycerol. The major role of glycerol in the body is as a precursor of glucose.

24.09.2001 (147)

Type : Metabolism

Remark : 1. Continuous intravenous administration of glycerol at 1g/kg bw did not result in increased serum insulin.
2. Glycerol turnover rate is fairly constant at 0.74 g/kg/hour.

24.09.2001 (67)

Type : Metabolism

Remark : In vitro experiments with rat liver homogenates showed that glycerol inhibits the incorporation of acetate into cholesterol.
In vivo experiments with rats showed a significant effect of glycerol on cholesterol synthesis and level. In four out of five experiments cholesterol

levels were reduced; it cannot be stated unequivocally however, that glycerol is
hypocholesteremic.
24.09.2001 (148)

Remark : Glycerol has a hemolytical potency. With 0.002 ml Glycerol/ml blood hemolysis in a 10% extent was observed for bovine erytrocytes.
Pharmacodynamics: glycerol acts as a contact laxative.
Literature could not be retrieved.
Source : Unichema Chemie B.V. Gouda
Reliability : (4) not assignable
25.01.2002 (149) (139)

Remark : Glycerol may have protective effects against tobacco smoke induced cancer.
When glycerol was added to tobacco smoke condensate in acetone solvent, the topical carcinogenicity and the ability to produce epithelial hyperplasia in mice was reduced.
16.11.2001 (150)

Remark : 1. The route of administration is of influence on the toxicity of glycerol in humans. Toxic effects, apart from nausea and vomiting, do not occur after oral administration. Toxic effects reported after intraperitoneal and subcutaneous administration are albuminuria, hemoglobinuria, anemia and renal damage.
2. Glycerol has a dehydration effect on the central nervous system. Intraocular pressure begins to fall at plasmaconcentrations of 10 mmoles per liter.
3. Concentration and dilutant used are also of influence on toxicity. Use of saline as dilutant diminishes the toxic effects of glycerol.
16.11.2001 (143)

Remark : 1. Subcutaneous injection of glycerol solutions leads to rapid haemoglobinaemia (detectable with the naked eye), followed by haemoglobinuria, in the rat and rabbit. The severity of haemoglobinaemia depends on the total dose of glycerol, not on its concentration. 0.2 cc/kg bw was the lowest effective dose in rats. Guinea-pig and mouse are less sensitive to subcutaneous glycerol injection.
2. Intravenous injection of up to 20 times the lowest effective subcutaneous dose produces no haemolysis in rats.
14.11.2001 (151)

Remark : Subcutaneous injection of 1.75 mL of 50% glycerol/100g bw in rats caused severe haemolysis followed by necrosis of the tubular portions of the nephrons, but no apparent damage to the glomeruli. Effects were reversible within 6-12 weeks.
11.12.2001 (152)

Remark : Intraperitoneal administration

Rats injected intraperitonealy with 1 ml 100% glycerol/100g bw had severe convulsions and died within 2 hours after injection.
Rats injected with 1 ml 50% glycerol/100g bw also had severe convulsions and most of them died within 4 hours.
Other signs of toxicity were haemoglobinuria, fluid in the peritoneal cavity, dehydrated tissues and renal damage (necrosis of epithelium of the proximal tubules, presence of eosinophilic casts in the loops of Henle, distal convoluted tubules and collecting tubules).

Subcutaneous administration of 1 ml 100% glycerol or 50%/100 g bw to rats produced haemoglobinuria, severe oedema at the site of injection, extremely hydrated tissues and renal tubular necrosis; in some animals at 100% glycerol mild convulsions were reported.

Intravenous injection of both 100% glycerol and 50% glycerol at 1 ml/100g bw to rats led to severe convulsions and death in all animals (unless kept alive by dextrose-saline injection). Other signs included haemoglobinuria and occasionally renal damage.

11.12.2001 (153)

Remark : Intramuscular injection of 50% glycerol in the hind limb of rats at 10 ml/kg bw led to decreased renal bloodflow and oliguria, associated with a reduction of glomerular filtration.

11.12.2001 (154)

Remark : Glycerol injected intraperitoneally or taken per os causes hyperglycemia in fasted rabbits.

16.11.2001 (155)

Remark : Subcutaneous injections of strong solutions of glycerol in rats produce haemolysis and renal tubular necrosis. '
Similar doses given intravenously produce neither of these effects.
Similar doses given intraperitoneally produce renal tubular necrosis but no haemolysis.

16.11.2001 (156)

Remark : A preload of glycerol (30 kcal) was given to 12 healthy, non-obese subjects. Effects on food intake were recorded, blood glucose, glycerol and free fatty acids (FFA) were measured.
Plasma glycerol was increased before the meal and food intake was lowered when a glycerol preload was taken. No effects on other parameters.

11.12.2001 (157)

Remark : 1. The acute ingestion of glycerol (1 ml/kg bw) in male subjects led to an increase in plasma glycerides after 4 hours, the same procedure in women led to no significant change in the glyceride concentration.
2. When glycerol was ingested chronically (1 ml/kg/day, 42

days), both men and women showed increased serum glyceride concentration. The increase was significantly greater in men, however.

11.12.2001 (130)

Remark : Glycerol has a dehydrating action on cerebral edema when blood glycerol level reaches 10 mM (920 mg/l).

11.12.2001 (67)

Remark : Patients with acute cerebral ischemia may benefit from an infusion with 10% glycerol; this may improve cerebral oxidative phosphorylation or provide the brain with an additional energy source.

11.12.2001 (158)

Remark : A three year old boy showed a unique intolerance to glycerol: 1-5 hrs after oral administration of glycerol in doses of 0.5-1.0 g/kg he had euphoria, mental confusion, drowsiness, nausea and vomiting, on one occasion the glycerol also provoked hypoglycemia; intravenously administered glycerol induced an immediate loss of consciousness with spontaneously recovery after 30 min., there were no changes in blood glucose values.

11.12.2001 (159)

Remark : Intravenous administration of 20% glycerol lowers acute elevations of intracranial pressure in children with intracranial hypertension. In two cases (of 152) transient hematuria and hemoglobinemia were seen.

11.12.2001 (160)

Remark : Female rats received a single i.p. injection of 3.5 mL glycerol (12.5% solution)/ kg bw. Urinary output, creatinine clearance , blood pressure, intrarenal blood flow and kidney histopathology were investigated during a 6 hour observation period. Urinary output and creatinine clearance were decreased. No effects on blood pressure and blood flow through the kidney became apparent. Incidental slight renal damage (necrosis of proximal tubular cells) was seen.

11.12.2001 (161)

Remark : Generally recognised as safe as a miscellaneous and/or general food additive under US FDA CFR 21 SS 182.1320 (Glycerin).
Literature could not be retrieved.

Source : Croda Universal Ltd Goole, North Humberside
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (4) not assignable
25.01.2002

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