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ENVIRONMENT DIRECTORATE

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Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology

SIDS INITIAL ASSESSMENT PROFILE

CAS NO. 30618-84-9

The Joint Meeting is invited to agree on the declassification of this document, by 11 August 2017.

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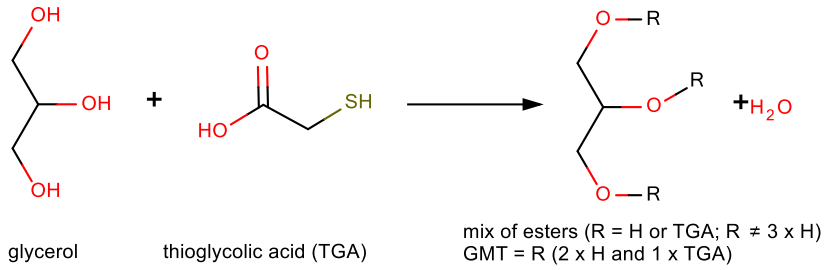
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	30618-84-9
Chemical Name	Acetic acid, mercapto-, monoester with 1,2,3-propanetriol) Glycerol Monothioglycolate (GMT)
Structural Formula	 glycerol thioglycolic acid (TGA) mix of esters (R = H or TGA; R ≠ 3 x H) GMT = R (2 x H and 1 x TGA)

SUMMARY CONCLUSIONS OF THE SIAR

Glycerol monothioglycolate (GMT) is the main constituent of a reaction mass (CAS Registry Name: Acetic acid, mercapto-, monoester with 1,2,3-propanetriol) containing a complex mixture of 1- and 2-monoesters, 1,2- and 1,3-diesters, unreacted glycerol and traces of the triester and thioglycolic acid. A typical commercial product of GMT contains approximately 70% - 80% of the sulfhydryl-group (SH-group). The composition of the product depends on the ratio glycerol to thioglycolic acid of the esterification process. The GMT reaction mass is exclusively used in cosmetic products without any further purification steps. Therefore, the product names were e.g. GMT 70, GMT 75 or GMT 80. To clarify a misunderstanding regarding product names, the two-digit figure within the product names like GMT 80 or GMT 75 does not refer to the exact monoester content of 80% or 75% glyceryl monothioglycolate in the reaction mass, but refers to the overall SH-content of the esters within the reaction mass (sum of mono-, di- and tri-esters). The common name GMT, GMT 75 or GMT 80 as well as the CAS number mentioned in study reports or in the literature always refer to the reaction mass of the esterification process. The constituents and impurities of the reaction mass were therefore always tested together when used in physico-chemical or (eco)toxicological studies. The almost similar physico-chemical properties made it impossible to isolate single constituents from the reaction mass.

Physical-chemical properties

GMT 80 is a viscous, colorless liquid with a melting point of -33 °C, an estimated boiling point of 244 °C and a measured vapor pressure of 1.2 x 10^{-3} Pa (9.3 x 10^{-6} mmHg) at 25 °C. The measured octanol-water partition coefficient (log K_{ow}) of the mono-constituent GMT is 0.45 at 22 °C. This value represents sufficiently the various commercially available reaction masses of GMT and can be used as a surrogate e.g. for environmental endpoints. The water solubility of GMT 80 is > 1000 g/L. Under environmental conditions, there are two relevant types of ionisable groups present in the reaction mass, SH groups and OH groups. At pH of about 8 or less the main constituents of the reaction mass are largely protonated.

Human Health

No data are available on the toxicokinetics, metabolism and distribution of GMT by dermal, oral or inhalation exposure. GMT is expected to be initially hydrolyzed by the acidic pH of the stomach or by ubiquitously expressed carboxylesterases to glycerol and thioglycolate e.g. in the skin. Glycerol is an intrinsic precursor for gluconeogenesis, triglyceride or phospholipid synthesis. The toxicologically relevant metabolite thioglycolate displays a rapid and nearly complete urinary excretion in rabbit, rat and monkey. Only negligible amounts of the thioglycolate where detected in blood or body tissues.

Taken together, bioaccumulation potential of the reaction mass of glycerol and thioglycolic acid and its metabolites is not expected. Dermal absorption of GMT is predicted to be low, based on the ratio of oral to

dermal LD_{50} values (172 mg/kg bw oral compared to >2000 mg/kg bw dermal). No information is available on effects via lactation.

The acute oral [OECD TG 401] LD_{50} in rats is 172 mg/kg bw. Mortalities were observed at all doses ≥ 160 mg/kg bw in both sexes. Clinical signs included subdued behaviour, lethargy and/or prostration with no findings at necropsy. The acute dermal LD_{50} in rats is > 2000 mg/kg bw. Clinical signs included red secretion, abnormal posture, erythema, eschar formation and oedema. No reliable acute inhalation studies are available.

GMT is considered to be slightly irritating to the skin [OECD TG 404] and the eyes [OECD TG 405] of rabbits. A similarly slight irritation to the skin and the eyes has been seen in humans. A sensitisation potential was demonstrated in guinea pigs in one maximization study [OECD TG 406], and the sensitising potential was clearly demonstrated in hairdressers who worked without protective gloves in the past using preparations containing GMT.

In a combined repeated-dose/reproductive/developmental toxicity screening test [OECD TG 422] GMT 80 was administered by gavage to rats (10/sex/dose) for up to fifty-four consecutive days, at dose levels of 15, 50 and 150 mg/kg bw/day. The study showed no effects on male rats but resulted in mortality in female rats (5 of 10 found dead or sacrificed in extremis) at 150 mg/kg bw/day. Females at this dose also had reduced body weights and body weight gains. The NOAEL for systemic toxicity is 150 mg/kg bw/day (highest dose tested) for males and 50 mg/kg bw/day in females due to mortality at 150 mg/k bw/day.

In a bacterial reverse mutation assay/Ames test with multiple strains of Salmonella typhimurium [OECD TG 471], GMT (67.9% SH content) was negative both with and without metabolic activation. In an *in vitro* chromosomal aberration test in human lymphocytes, GMT 80 was negative with and without metabolic activation [OECD TG 473]. A mouse lymphoma assay [OECD TG 476] of GMT 80 using the heterozygous L5178Y $TK^{+/-}$ cell line in the absence and presence of metabolic activation was negative. Based on these results, GMT is considered to be non genotoxic in vitro.

No data are available for the carcinogenicity of GMT.

Reproductive toxicity data are available for GMT 80 via the oral route. In the OECD TG 422 study described above, no effects on fertility or histopathology and weight of reproductive organs were observed. In addition, no treatment-related developmental effects were seen. The maternal toxicity NOAEL is 50 mg/kg bw/day based on mortality seen at the highest dose as described above. Due to significant mortality in the dams, limited numbers of litters were available for evaluation and therefore, reproductive and developmental effects could not be fully evaluated. The maternal toxicity observed above 50 mg/kg bw/day, is the critical and limiting factor to obtain NOAELs for the reproductive and developmental toxicity endpoints. In this regard, the NOAEL for reproductive and developmental toxicity is 50 mg/kg bw/day and no LOAEL for these endpoints could be established.

GMT possesses properties indicating a hazard for human health (acute oral toxicity, skin sensitisation, repeated-dose toxicity). Adequate screening-level data are available to characterise the human health hazard for the purposes of the OECD Cooperative Chemicals Assessment Programme.

Environment

A hydrolysis test conducted with GMT 80 [OECD TG 111] showed hydrolysis at pH 4 ($t_{1/2}$ > 1 year), pH 7 ($t_{1/2}$ = 223 h)) and pH 9 ($t_{1/2}$ = 17h) at 25 °C. Therefore, hydrolysis can be expected under normal environmental conditions. In the atmosphere, indirect photo-oxidation by reaction with hydroxyl radicals is predicted to occur with a half-life of 2.5 hours. A Closed Bottle Test according to OECD TG 301D resulted in 46% biodegradation after 28 days. A Zahn-Wellens Test according to OECD TG 302B resulted in 97% biodegradation after 14 days. GMT is, therefore, not readily biodegradable but is inherently biodegradable.

GMT is expected to be solely in the water phase. A Henry's law constant of 1.5 x 10^{-6} Pa x m^3/mol at 25 °C suggests that volatilization of GMT from the water phase is not expected to be high. A K_{oc} of ≤ 10 was estimated based on the log K_{ow} and indicates a low potential for accumulation in soil.

The bioaccumulation potential is low based on a BCF value of 3.16 L/kg wet weight estimated with BCFWIN.

The following acute toxicity test results have been determined for aquatic species:

Fish [*Oncorhynchus mykiss*] 96 h LC_{50} = 35 mg/L (measured)

Invertebrate [*Daphnia magna*] 48 h LC_{50} = 11 mg/L (measured)

Algae [*Pseudokirchnerella subcapitata*] 72 h ErC_{50} growth rate = 11 mg/L (measured)

72 h EC_{50} biomass = 4.6 mg/L (measured)

GMT possesses properties indicating a hazard for the environment (acute aquatic toxicity between 10 and 100 mg/L). GMT is not readily biodegradable and has low potential for bioaccumulation. Adequate screening-level data are available to characterise the hazard for the environment for the purposes of the OECD Cooperative Chemicals Assessment Programme.

Exposure

Since 2007, GMT is commercially produced with an annual production volume of less than 450 tonnes worldwide. GMT is mainly produced by esterification of glycerol (CAS No. 56-81-5) and thioglycolic acid (CAS No. 68-11-1). The result is a complex mixture of 1- and 2-monoesters, 1,2- and 1,3-diesters, traces of the triester and unreacted glycerol and thioglycolic acid. The GMT reaction mass is exclusively used in cosmetic formulations without any further purification steps.

The GMT esterification process is manufactured in closed systems, which limits occupational exposure during manufacture. However, during use at hair salons, (GMT is only used in cosmetic hair-care products like permanent wave and hair straightening preparations) exposure is possible. Consumer exposure may occur through the skin during use of cosmetic products. The main source of GMT exposure to the environment is municipal sewage treatment plants. However, there is only minor direct environmental exposure to GMT as a commercial end-product because as part of a cosmetic preparation it is first hydrolyzed and then ultimately oxidized during the use pattern of the cosmetic product. The last step of a permanent wave or hair straightening preparation is the fixation of the new shape of the hair, for instance with a diluted solution of H_2O_2.