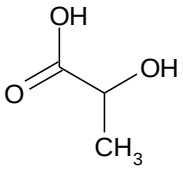
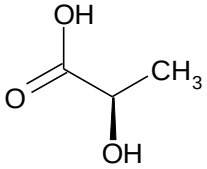
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	50-21-5
Chemical Name	Lactic Acid
Structural Formula	 Lactic Acid  L(+) Lactic Acid

SUMMARY CONCLUSIONS OF THE HAZARD CHARACTERIZATION

NOTE: The conclusions in this document are based on consideration of comments from OECD member countries and the final Hazard Characterization and Robust Summary documents published in August 2008 by the United States in the US HPV Chemicals Program (http://iaspub.epa.gov/oppthpv/hpv_hc_characterization.get_report?doctype=1). The SIDS endpoints requested in the US HPV Chemicals Program are equivalent to those evaluated in the OECD HPV Chemicals Program.

Justification for Supporting Chemical

The sponsored chemical, lactic acid (CAS No. 50-21-5), is the racemic mixture. However, only the natural form of lactic acid—L(+) lactic acid (CAS No. 79-33-4)—is usually manufactured. L(+) Lactic acid is biologically important; therefore, most available hazard data have been developed for the L(+) form. L(+) lactic acid is used as a supporting chemical for racemic lactic acid. The calcium salt (calcium lactate) of lactic acid was also used as a supporting chemical for repeated dose toxicity and carcinogenicity.

Physical-Chemical properties

Lactic acid is a clear to slightly yellow liquid with a melting point of 16.8°C, a boiling point of 258°C at 1,000 hPa, a vapour pressure of 0.004 hPa at 20 ºC, the octanol-water partition coefficient (log K_{ow}) of –0.62 and water solubility of 876 g/L. As the dissociation constant (pKa) is 3.68, lactic acid is anticipated to exist primarily in its dissociated form at environmentally relevant pH.

Human Health

No data were provided for reproductive toxicity and limited data are available for some other endpoints. However, testing was not deemed necessary because the substance is a normal component of human intermediary metabolism.

L(+)-Lactic acid is a natural, functional metabolite in mammals, and serves as mammalian fuel. According to the ″lactate shuttle″ concept, L(+) lactic acid represents a major means of distributing carbohydrate potential energy for oxidation and gluconeogenesis. The concept of a "lactate shuttle" is that during hard exercise, as well as other

conditions of accelerated glycolysis, glycolic flux in muscle involves L(+)-lactic acid formation regardless of the state of oxygenation. The production rate of endogenous L(+)-lactic acid in the resting human is about 1.3 mol (70 kg/bw) 24 h^{-1} (equals 117 g/day).

The acute oral LD_{50} value for L(+)-lactic acid is 3543 – 4936 mg/kg-bw for male and female Charles River rats. Lethargy, ataxia, prostration, irregular breathing, piloerection, squinting, lacrimation, salivation, crusty eyes and muzzle, loose stools, damp or yellow/brown stained fur and moribund were the clinical signs observed as early as 0 – 1 hour after dosing and as late as day 2. Necropsy of animals found dead and the four surviving females at 3162 mg/kg-bw included discoloured lungs; firm texture of lungs; green foci on one lung; several stomach lesions; discoloured liver; white foci on the liver; pale capsular areas, superficial erosion, or mottled liver; discoloured kidney and red-brown exudates in the nasal and/or oral regions. The acute dermal LD_{50} value in male and female New Zealand white rabbits is > 2000 mg/kg bw following 2 hour exposure of L(+)-lactic acid to clipped, abraded skin. No mortality or clinical signs of toxicity were seen. Severe erythema and edema were observed at the application sites of all animals on day 1. Both erythema and edema decreased in severity by observation day 14. Blanching, necrosis, eschar formation, atonia, desquamation and denuded areas were also seen at some application sites. At necropsy, A dark red focus was observed on the lung of one male; no other abnormalities were observed. In a 4-h acute inhalation study in male and female Fischer rats via nose-only exposure to L(+)-lactic acid aerosol, the LC_{50} was > 7.9 mg/L. Rapid breathing, lacrimation, hunched posture, ruffled fur and unkempt appeared with soiled fur were observed in the exposed animals. Female rats appeared lethargic during exposure. By 24 hours, most animals appeared to have recovered from lethargy and unkempt fur. Exposed females (4/5) had ruffled and ungroomed fur until post-treatment day 4. One exposed female died on day-8 post-treatment. No gross lesions were observed at necropsy.

L(+)-Lactic acid is severely irritating and corrosive to rabbit skin [OECD TG 404], slightly irritating to guinea pig skin and not irritating to pig skin. L(+)-Lactic acid is not a dermal sensitiser in guinea pigs [Buehler method].

The repeated-dose toxicity was evaluated as follows: Experiment I: F344 rats (5/sex/dose) were administered calcium lactate via drinking water at 0, 0.3, 0.6, 1.25, 2.5 and 5% (corresponding to 0, ~30, 60, 125, 250 and 500 mg/kg-bw/day) for 13 weeks. In all groups, basic diet (CRF-1) was given ad libitum. No mortalities occurred. A slight decrease in body weight gain (less than 10%) compared to controls was observed at all concentrations. Changes in some haematological and biochemical parameters were observed. On histological examination, however, no severe toxicological findings were noted in any of the treated groups. Experiment II: Rats were fed synthetic diet B, containing 0, 5, 10, 20 or 30 % calcium lactate. At the highest dose, body weight-gain was decreased compared to the control group. Histological examination revealed nephrocalcinosis in all groups, including the control group and the degree of occurrence was dose-dependent. Females exhibited this lesion to a greater extent than males. In a follow-up study, rats were given CRF-1 or synthetic diet B for 8 weeks. Nephrocalcinosis was observed only in the group given diet B. It was concluded that the nephrocalcinosis observed in Exp. II was dependent on the low Ca/P ratio (less than 1) of the synthetic diet B. The NOAEL was 500 mg/kg bw/day (highest dose tested).

In an Ames test with multiple strains of *Salmonella typhimurium*, L(+) lactic acid was negative both with and without metabolic activation and up to concentrations of 10,000 □g/plate. Positive controls were tested concurrently and responded appropriately. In an *in vitro* chromosomal aberration test using Chinese hamster ovary cells, L(+) lactic acid did not induce clastogenic activity with and without metabolic activation when the medium was neutralized to physiological pH 6.4. Pseudo-positive reactions were seen as a result of low pH. Limited details were available regarding this study. Overall, L(+) lactic acid was not mutagenic.

F344 rats (50/sex/dose) were given calcium lactate in the drinking water at levels of 0, 2.5 or 5% for 2 years. The high-dose animals (males and females) showed a significant reduction in mean body weight gain. There was no evidence of organ-specific toxicity and there was no evidence of carcinogenicity. Limited data are available regarding this study.

No data were provided for the reproductive toxicity endpoint. In a developmental toxicity study, lactic acid was neither toxic to dams or offspring when administered orally to pregnant CD-1 mice via gavage at doses of 0 or 570 mg/kg bw/day during days 6-15 of gestation. The NOAEL for maternal and developmental toxicity was 570 mg/kg bw.

Lactic acid does not present a hazard for the human health based on its low hazard profile. Adequate screening-level data are available to characterize the human health hazard for the purposes of the OECD HPV Programme.

Environment

Lactic acid is not susceptible to hydrolysis under environmental conditions. In the atmosphere, indirect photo-oxidation by reaction with hydroxyl radicals is predicted to occur with a calculated half-life of 22 hours. A biodegradation test resulted in 67% biodegradation in 20 days; therefore, lactic acid is readily biodegradable under aerobic conditions.

A level III fugacity model calculation with equal and continuous distributions to air, water and soil compartments suggests that lactic acid will partition primarily into water (46.3%) and soil (50.5%), with minor distribution to the air (3.2%) and sediment (0.07%). A Henry's law constant of 9.6 x 10^{-9} atm-m^3/mol (9.74 x 10^{-6} hPa-m^3/mol) by VP/WSol estimation method at 25 ºC suggests that volatilisation of lactic acid from the water phase is expected to be low.

The bioaccumulation potential seems to be low based on a log K_{OW} of -0.62, supported by an estimated BCF value of 3 (BCFBAF v 3.0).The following acute toxicity test results for L(+)-lactic acid have been determined for aquatic species:

Fish (Zebrafish; *Brachydanio rerio*)	OECD TG 203	96 h LC_{50} = 320 mg/L*
Fish (Bluegill sunfish; *Lepomis macrochirus*)	OECD TG 203	96 h LC_{50} = 130 mg/L*
Invertebrate (*Daphnia magna*)	OECD TG 202	48 h EC_{50} = 240 mg/L*
Algae (*Pseudokirchneriella subcapitata*)	OECD TG 201	70-h EC_{50} (growth) = 3500 mg/L 70-h EC_{50} (biomass) > 2800 mg/L

*The test solutions were not neutralized.

Lactic acid does not present a hazard for the environment based on its low hazard profile. Adequate screening-level data are available to characterize the hazard for the environment for the purposes of the OECD HPV Programme.

Exposure

Lactic acid and its supporting chemical L(+) lactic acid have an aggregated production volume in the range from 51 million to 110 million pounds (23133 to 49895 tonnes). These chemicals are used as solvents, pH-regulating agents or intermediates in a variety of industries, including the manufacturing of basic organic chemicals, paints and coatings, soaps and cleaning agents as well as textiles and fabrics. Both chemicals are used in commercial settings or consumer products. Lactic acids are naturally occurring in foods, and are used as an acidulant in foods, mordant in printing woolen goods, solvent, and in textile, leather and many other applications.

L(+)-Lactic acid is a natural, functional metabolite in mammals, and serves as mammalian fuel; therefore, humans and animals will be exposed internally to lactic acid.

Environmental exposure to lactic acid is expected based on environmental release information from manufacturing, processing and uses.

Exposures of the general population, workers, consumers and children to lactic acid is also expected based on the wide variety of uses including commercial and consumer uses.