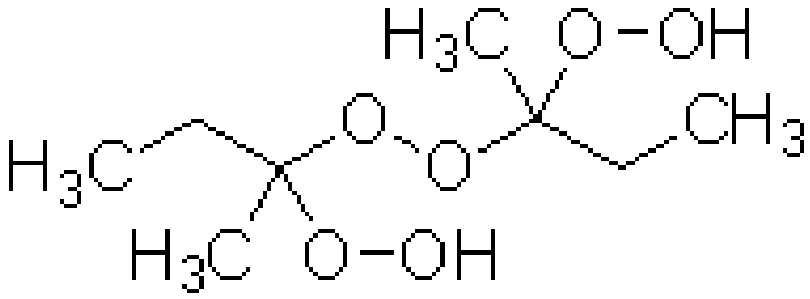
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	1338-23-4
Chemical Name	2-Butanone, peroxide (MEKP)
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

2-Butanone, peroxide (Methyl Ethyl Ketone Peroxide; MEKP) is a shock and heat sensitive substance. It is only available in the presence of diluents which are used in the manufacturing process to reduce the potential explosion hazard of MEKP. Most studies used a commercial product made of about 40% MEKP and 60% dimethyl phthalate. The typical purity for MEKP as a marketed substance is 17 – 35%. Purity greater than 35% has not been reported, and can be considered a maximum. MEKP is a mixed product consisting of dimers (50%), trimers (25%), and monomeric peroxy compounds. Currently the primary diluent used for commercial MEKP is 2,2,4-Trimethyl-1,3-pentanediol diisobutyrate (CAS No. 6846-50-0; 23 -70%).

Human Health

There are no available toxicokinetic, metabolism or distribution data for MEKP. A number of standard acute toxicity studies are available in rats and mice via the inhalation and oral routes of exposure. The acute inhalation of MEKP is most commonly associated with observations of ocular and respiratory irritation, salivation, erythema, decreased motor activity, and respiratory congestion. The 4 hour inhalation LC_{50} of a blend of 7 manufactured MEKP samples in rats was determined to be > 200 mg/L (ca. >28,080 ppm). The 4 hour inhalation observable LC_{50} for non-blended MEKP products range from 15.4 mg/L (2162.2 ppm; male rats) to 53.6 mg/L (female rats; 7525.4 ppm). The acute oral LD_{50} of MEKP ranges from 681 mg/kg bw (for a 42% sample in dimethyl phthalate) to 1017 mg/kg bw (40% MEKP sample in corn oil). Observed clinical signs range from none to mydriasis, bradypnea, dyspnea, hypoactivity, flaccidity, ataxia, sedation, hypothermia, prostration and death. MEKP is a moderate to severe dermal irritant, extremely irritating and corrosive to the eye, and is a respiratory irritant. MEKP is not a skin sensitizer.

In a combined reproductive/developmental toxicity screening study (OECD TG 421, described below), MEKP (32% with a mixture of diluents) was administered orally by gavage to 12 male rats per dose group for up to 29 days and to 12 female rats per dose group for up to 45 days if mated or for 52 days if not mated. The NOAEL for systemic toxicity was 50 mg/kg bw/day. Systemic toxicity was observed at 100/75 mg/kg bw/day as mortality/moribundity, reductions in body weight and food consumption, and macroscopic and microscopic findings in the stomach.

Following dermal application of MEKP to the skin of 10 male and 10 female rats per dose group for 13 weeks, a NOAEL was not reached, with hyperkeratosis occurring in rats at 1.07 mg/animal (ca. 3.2-8.4 mg/kg bw/day in males; ca. 5.2-9.9 mg/kg bw/day in females; estimated based on day 1 and last day of study group mean body weights). A LOAEL of 50.6 mg/kg bw/day was identified in rats (thick, crusty skin at the application site in several animals at the lowest dose tested) following application of MEKP (45% in diluent) to the skin of five males and five females per dose group for 2 weeks. Dermal application of MEKP (45% in dimethyl phthalate) to the skin of 10 male and 10

female mice per treatment group for 13 weeks resulted in a LOAEL of 0.357 mg/animal (ca. 10.6-14.8 mg/kg bw/day in males; ca. 12.7-18.1 mg/kg bw/day in females; estimated based on day 1 and last day of study group mean body weights) (minimal to mild acanthosis at the lowest dose tested). A LOAEL of 112.5 mg/kg bw/day (thickened, crusty, hardened skin, and, in some animals, sloughed, including at the lowest dose tested) was identified in mice following application of MEKP (45% in dimethyl phthalate) to the skin of five males and five females per dose group for 2 weeks. The results of these studies suggest that significant amounts of MEKP in DMP do not become systemically available and that, as expected, the primary toxicity associated with contact with these chemicals is limited to the application site.

In three bacterial reverse mutation assays, MEKP produced a weak mutagenic response in a single bacterial tester stain (TA1535) in the presence of metabolic activation. MEKP induced chromosome aberrations, exchange of sister chromatids and DNA mutations (mutation assay) in in vitro mammalian test systems. MEKP is genotoxic.

There are no reliable data to indicate whether MEKP is carcinogenic in animals.

In the combined reproductive/developmental toxicity screening study (OECD TG 421), rats were exposed to 0, 25, 50 and 100/75 mg/kg bw/day MEKP (32% in diluent) by oral gavage for at least 14 days prior to mating. Males continued to receive the test article throughout mating and through the day prior to euthanasia for a total of 28 to 29 doses. Females continued to receive MEKP throughout mating, gestation, and lactation day 2 for a total of 39 to 45 doses. The highest dose was lowered to 75 mg/kg/day after 2 days due to the lethal effects in 1 male and 2 female animal. No specific signs of reproductive or developmental toxicity were seen. The NOAEL for reproductive toxicity was 75 mg/kg bw/day (no effect at highest dose tested). The NOAEL for general toxicity was 50 mg/kg bw/day (statistically significant decrease in male and female body weights) and the NOAEL for developmental toxicity was 50 mg/kg bw/day (statistically significant decrease in neonatal body weights). No specific signs of reproductive toxicity were seen in dermal toxicity studies with rats and mice; the NOAEL for reproductive effects are 107 mg/animal (rat) and 35.7 mg/animal (mouse), respectively

Environment

MEKP is only available in the presence of diluents added to reduce the potential explosion hazard; it is not possible to isolate the substance for testing. The use of diluent to stabilize MEKP interferes with the determination of physico-chemical properties and so values are estimated. MEKP is a mixed product consisting of dimers (50%), trimers (25%), and monomeric peroxy compounds that exist in equilibrium; modeling was performed on each component and a range provided. The estimated melting point range of MEKP is 39.63– 126.1°C and the estimated boiling point range is 242.9-351.2°C. MEKP is only available in the presence of diluents to reduce potential explosion hazard, such that determination of the melting point and boiling point is not applicable. The self accelerating decomposition temperature for MEKP ranges from 63-85°C. The estimated vapor pressure range is 0.84 -1.61x10^{-5} hPa at 25°C. The estimated water solubility range of MEKP is 1.4x10^{+5} - 2.7 mg/L; the estimated log Kow range is -0.429– 4.3; and the estimated log Koc range is 13.2– 3.3x10^{+5}. MEKP is a strong oxidizing agent. MEKP is hydrolytically stable over a range of environmentally relevant pH and temperature conditions (half-lives of 204, 1155, and 224 hours at 25°C and pH 4.0, 7.0 and 9.0, respectively) following OECD TG 111. The overall reaction half-life in air is estimated to range from 13.93 -10.3 hrs; however, based on results of fugacity modeling MEKP is not expected to distribute significantly to air and the results of this modeling may not be relevant . MEKP is not expected to directly photolyze due to the lack of absorption in the environmental UV spectrum. Level III Fugacity modeling, using loading rates for Air, Soil, and Water of 1000 kg/h for each medium, shows the following percent distribution range: Air = 0.06– 3.2e-5%; Soil = 54.6-8.1%; Water = 45.3- 87%; Sediment = 0.08– 4.9%. MEKP is likely readily biodegradable (87% biodegradable over 28 days). Bioaccumulation is not anticipated as the estimated BCF for MEKP is 3.16.

The 96-hour LC_{50} of MEKP (diluent: dimethyl phthalate) for *Poecilia reticulata* is 44.2 mg/L. The 48-hour EC_{50} of MEKP (diluent: dimethyl phthalate) is 39 mg/L for *Daphnia magna.* MEKP (diluent: dimethyl phthalate) toxicity to *Pseudokirchneriella subcapitata* provided a 72-hour EC_{50} of 3.2 and 5.6 mg/L for biomass and growth rate, respectively. In each case, the toxicity of MEKP in dimethyl phthalate was similar or more toxic than dimethyl phthalate alone, suggesting the diluent is not affecting the interpretation of these results.

Exposure

MEKP is a reactive substance that is consumed during use. MEKP is only available in the presence of diluents and in 2005, the worldwide production volume was equivalent to 7168 tonnes of neat material. Applications include polymerization initiators for acrylics, polymerization of unsaturated polyester, vinyl ester, styrenic and other resins with vinyl unsaturation. MEKP is also used for the manufacture of paints, plastics and rubber. MEKP is sold to and used primarily by industrial customers. A few organic peroxide manufacturers sell MEKP to other manufacturers who make products for markets such as auto body patching compounds.

Releases to the environment can occur during handling in industrial settings. However, environmental exposure is limited due to engineering controls (closed system) during its manufacture. In addition, most residual MEKP is removed by environmental controls such as waste water treatment systems. During processing there is some reuse and recycling of containers, minimizing release of residual MEKP.

Potential industrial worker exposure is limited to use in a supervised industrial setting for spray applications and transfer from small packages (mostly one gallon), in which they are shipped to a charge tank, reactor or mixing vessel. The industries in which these peroxides are used are subject to federal and/or state Occupational Safety and Health Administration regulations that define the measures and equipment required to minimize worker exposure to chemicals. OSHA has set a permissible exposure limit (PEL) ceiling limit of 0.7 ppm (5 mg/m^3). The National Institute for Occupational Safety and Health (NIOSH) ceiling limit is 0.2 ppm (1.5 mg/m^3) which the American Conference of Governmental Industrial Hygienists (ACGIH) also uses as the ceiling limit for its Threshold Limit Values (TLV) and Biological Exposure Indices (BEI). The most likely potential routes of exposure would be skin contact from liquid peroxide splash and the contact from the mixed spray from spray operations, which is minimized by the use of personal protective equipment (e.g. goggles, gloves). An additional route of exposure includes the potential for inhalation during supervised industrial for spray applications. Inhalation exposures will be minimized by the use of personal protective equipment. Once decomposed to free radicals, i.e., to initiate polymerization or curing, the MEKP as made and "listed" no longer exists. The end use product (articles produced with MEKP as a catalyst in the polymerization process) may contain low ppm of MEKP; it is bound within the final product and will not be released. In the United States, MEKP is subject to the Emergency Planning and Community Right-to-Know Act (EPCRA) and Section 112(r) of the Clean Air Act. No data are available for 2004 on releases to the environment in the U.S. Environmental Protection Agency (EPA) Toxic Releases Inventory (TRI). MEKP is classified as a hazardous waste regulated under the Resource Conservation and Recovery Act (RCRA) (40 CFR 261) by the U.S. EPA.

Consumer exposure to MEKP is expected to be minimal during normal use. A few organic peroxide manufacturers sell MEKP to other manufacturers who make products for markets such as auto body patching compounds. A formulated MEKP product is for use in a two-part system. The retail customer mixes a small amount of the MEKP with the resin to cure the resin. Once the MEKP has been combined with the resin, residual MEKP is not released from the final product, and is therefore not available for consumer exposure.

RECOMMENDATION AND RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health: The chemical is currently of low priority for further work. The chemical possesses properties indicating a hazard for human health (irritation at the point of contact, genotoxicity *in vitro* and repeated-dose toxicity). Based on data presented by the Sponsor country, relating to production in one country (which accounts for >59% of global production) and relating to use pattern in one country, exposure to humans is anticipated to be low, and therefore this chemical is currently of low priority for further work. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor country.

Environment: The chemical is currently of low priority for further work. The chemical possesses properties indicating a hazard for the environment (acute toxicity to aquatic organisms between 1 and 100 mg/L). However, the chemical is of low priority for further work for the environment because of its likely

ready biodegradation (87% biodegradable over 28 days, 40% MEKP in dimethyl phthalate) and its limited potential for bioaccumulation.

The dominant hazard of this substance is its shock and heat sensitivity.