SIDS INITIAL ASSESSMENT PROFILE

CAS No.	79-21-0
Chemical Name	Peracetic acid
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Peracetic acid (PAA) is commercialised as an equilibrium aqueous solution in which peracetic acid is in equilibrium with hydrogen peroxide, acetic acid and water. The concentration of peracetic acid, hydrogen peroxide and acetic acid can reach levels of about 40, 30 and 40 %, respectively, in certain equilibrium solutions. Nearly all toxicity studies, related with human health and environment, were done with equilibrium solutions. PAA is also commercialised as a distilled product containing primarily peracetic acid and water. Distilled PAA solutions are unstable under ambient conditions and re-equilibrate under formation of hydrogen peroxide and acetic acid. By cooling below 0 °C the hydrolysis reaction is slowed down. The amount of peracetic acid in these aqueous solutions ranges from about 0.15 to 40 %. All peracetic acid solutions are clear, colourless liquids with a pungent vinegar-like odour and the pH of these solutions is less than 1.5. Peracetic acid solutions have oxidising properties. Peracetic acid can be degraded to hydrogen peroxide and acetic acid. The hazards of hydrogen peroxide (CAS. 772-84-1) are described in the SIAP which was agreed at SIAM 9 (1999).

Human Health

An *in vitro* dermal penetration assay at 37 °C using 0.8 % PAA (non corrosive) indicated a low dermal uptake of peracetic acid through the intact skin of pigs. When the skin of rats was exposed to a corrosive concentration of ^{14}C-labelled PAA a considerable uptake of ^{14}C was found but it is unknown if the ^{14}C was present as peracetic acid, acetic acid or CO_2. It is expected that corrosive concentrations of PAA would compromise the normal barrier function of the skin.

Two reliable *in vitro* studies, using different analytical methods, showed a rapid degradation of peracetic acid in rat blood. When rat blood was diluted 1000 times, the half-life of peracetic acid was < 5 minutes. In undiluted blood the half-life is expected to be several seconds or less. For this reason the distribution of peracetic acid is probably very limited and it is not expected to be systemically available after exposure to peracetic acid solutions. Degradation products have not been identified during the kinetic studies. However, based on the structure of the substance the following degradation products are expected: acetic acid, oxygen, hydrogen peroxide and water. Hydrogen peroxide is also presumed to be rapidly degraded into oxygen and water.

The results of acute toxicity tests are expressed on the component peracetic acid, which was calculated based on the composition of the product used for the acute tests. The available acute inhalation studies with aerosols and vapour revealed an 4h-LC_{50} ranging from 76 to >241 mg/m^3. The acute dermal toxicity of PAA solutions was tested in rats and rabbits. No sign of dermal toxicity was observed when rats were exposed to solutions of 0.15-15%, while LD_{50} values of 56.1 and 228.8 mg PAA/kg bw were reported for rabbits for concentrations of 4.9 and 11.7 % PAA, respectively. The dermal toxicity depends on the degree of skin damage caused by the different PAA solutions, since the corrosive properties of PAA solutions may compromise the integrity of the skin. In oral toxicity studies LD_{50} values ranged between 9.0 and 202.8 mg/kg bw based on the component peracetic acid. Sporadic contact with even dilute solutions with the oesophagus could lead to deaths due to corrosion of the tissue and could explain the variability in the LD_{50}.

The pathology and symptoms were similar across all studies, indicating irritation and corrosion of tissues in contact with the test material.

PAA solutions should be considered as corrosive (within 3 minutes) at concentrations of 10 % and higher when applied to the skin of rabbits. PAA was generally corrosive to rabbit skin at a concentration of 5 % if contact lasted 45 minutes or longer. Concentrations of less than 0.34 % PAA were only slight irritants or non-irritants, depending on the exposure duration of the skin. PAA was corrosive at concentrations of 0.34 % and higher when tested in the rabbit eye. Slight or no eye irritation was found at concentrations of 0.15 % or less PAA. Incidental human findings on skin and eye irritation are supporting the animal studies. Peracetic acid gave a positive response in Alarie assay in the mouse, with an RD50 value (concentration producing a 50 % decrease in the respiratory rate) of 12 and 17 mg/m^3 (peracetic acid in vapour mixture from the formulation and peracetic acid only). Human data support the sensory irritating properties of peracetic acid.

No skin sensitisation was observed in three Bühler tests in guinea pigs with different formulations of PAA. The exposure concentration of peracetic acid ranged from 0.15 to 1.2 % during the tests. Additionally, long term experience with production and use of PAA has shown that PAA has no sensitisation potential.

To investigate the repeated dose toxicity, a GLP guideline study was done with rats, which were exposed by gavage for 13 weeks to 5 % PAA diluted to various concentrations (0.018 % to 0.55 % of the component peracetic acid). At 0.75 mg/kg/day transient or intermittent loud breathing was observed in two females but the effect was not considered adverse. Based on the results of this study the NOAEL was 0.75 mg/kg bw/day (component peracetic acid). The only observed effects were local effects that are concentration related. It is therefore reasonable to define a No Observed Adverse Effect Concentration rather than a classical NOAEL. Based on the component peracetic acid, the NOAEC for local effects was 0.055 %.

Gene mutation assays in bacteria tests, with and without metabolic activation, showed negative results. Two DNA repair tests in human foetal lung cells did not indicate a genotoxic potential of PAA. In the *in vitro* chromosome aberration test, positive findings were obtained only at cytotoxic concentrations. Under *in vivo* conditions, PAA (4.5 and 5.17% product) did not produce micronuclei in two mouse micronucleus tests after oral administration. In two *in vivo/ex vivo* assays of unscheduled DNA synthesis in rats after oral administration, PAA did not show significant genotoxicity potential. Overall these data do not raise concern with regard to the mutagenic and genotoxic potential of PAA However, peracetic acid is not systemically available and this could explain the lack of *in vivo* mutagenicity, but site of contact effects cannot be excluded completely. No valid carcinogenicity study with PAA is available.

No valid data on fertility are available. However, in a well documented GLP and guideline study aqueous dilutions of 5 % PAA were administered daily by gavage to Sprague-Dawley rats for 13 weeks. No effects of peracetic acid on the reproductive organs of both sexes following macroscopic *post mortem* examinations and microscopic examinations (histopathology) were notable during the study. Because peracetic acid is rapidly degraded in blood, distribution to reproductive organs is not anticipated, and therefore it is unlikely to be a reproductive toxicant. In addition, the degradation product hydrogen peroxide did not indicate any effect in the reproductive organs during a 90-day drinking water study and furthermore, a rapid degradation was presumed resulting in a lack of systemic availability.

In a well documented GLP and guideline developmental toxicity study performed with 32-38 % PAA, pregnant Wistar rats were administered dose levels of 100, 300 or 700 mg peracetic acid/l (corresponding to 12.5, 30.4 and 48.1 mg peracetic acid/kg bw/day) via the drinking water from day 5 to 20 of gestation. No teratogenic effect was evident up to and including the high dose level of 700 mg peracetic acid/l (48.1 mg peracetic acid/kg bw/day). Dose and treatment-related maternal toxicity was observed, considering water and food consumption, above 100 mg/l (12.5 mg PAA/kg bw). At 700 mg peracetic acid/l (48.1 mg/kg bw) this resulted in severe reductions in drinking water and food consumption and in absolute body weight as well as by a drastic reduction in overall body weight gain and in body weight gain corrected for uterine weight. At the high dose level, fetal weight was statistically significantly reduced (5 %) but litter size at this dose level was about 13 % higher than in controls. However, it is doubtful if the reduction of

5% is biologically relevant The overall NOAEL for foetal toxicity is therefore 300 mg/l (30.4 mg PAA/kg bw) based on a statistically significantly lower body weight and an increased incidence of poor and/or hypertrophic ossification (bone formation) in the presence of severe maternal effects (maternal NOAEL = 100 mg/l or 12.5 mg PAA/kg bw/day).

Environment

Peracetic acid is an organic substance which is completely miscible with water (water solubility of 1000 g/l at 20 °C) and which displays oxidising properties. Pure peracetic acid is not available because it is explosive. For this reason it is technically not possible to perform an experimental study according to the guidelines to determine the melting point, boiling point and vapour pressure of pure peracetic acid. Based on modelling, the melting point, boiling point and vapour pressure were estimated to be -42 °C, about 105 °C and 32 hPa (at 25 °C), respectively. The log Pow was reported to be -0.52 (measured value) and the Henry Law's constant is 0.22 $Pa \cdot m^3/mol$. The pKa of peracetic acid is 8.2 at 20 °C and therefore the substance is mainly present in the environment as peracetic acid at a neutral pH (pH = 7), while peracetate would mainly be present if the pH is significantly higher than 8.2.

Based on the high water solubility, low vapour pressure and low octanol-water partition coefficient, peracetic acid is expected to partition almost exclusively to the aquatic compartment (99.95 %). In air the half-life of peracetic acid is 22 minutes. The abiotic degradation of peracetic acid increases with temperature and pH. At a temperature of 25 °C and at pH of 4, 7 and 9, the degradation half-life value were 48, 48 and < 3.6 hours respectively. Peracetic acid was readily biodegradable during a biodegradation test when an inhibition of the micro-organisms (biocidal effect) was prevented. Peracetic acid will be degraded in a sewage treatment plant if the influent concentration is not extremely high (e.g. > 100 ppm). If effluents generated during the production or use of PAA are treated by a waste water treatment plant, no emission of peracetic acid to the aquatic environment is expected.

Several studies on acute toxicity to aquatic species are available for all trophic levels. The pH of the test solutions was not adapted during the studies because a decrease of the pH was not found. In most cases the endpoints of the aquatic toxicity tests were based on nominal concentrations. The 96-h LC_{50} values for fish ranged between 0.9 and 3.3 mg/l in most freshwater species. The 48-h EC_{50} for *D. magna* ranged between 0.5 and 1.0 mg/l. Based on the representative standard toxicity tests, the lowest 72-h NOEC of 0.084 mg/l was found for *Pseudokirchneriella subcapitata* (formerly known as *Selenastrum capricornutum*). The lowest EC_{50} value of 0.18 mg/l was found during a 120-h growth inhibition test with *P. subcapitata*. . To determine the toxicity for microorganisms, two respiration inhibition tests with activated sludge of predominantly domestic sewage treatment plants were conducted. The EC_{50} after 3 hours was 5.1 and 38.6 mg peracetic acid/l (based on nominal concentrations), respectively. In general, the aquatic tests with fish, invertebrates and algae were reproducible if concentrations were expressed as peracetic acid irrespective of the concentrations of hydrogen peroxide and acetic acid. Thus, the peracetic acid concentration alone may explain the toxicity of PAA formulations.

Exposure

The global number of production sites is estimated to be 40-100 and the majority of the production sites are located in Europe.

The equilibrium peracetic acid consumption (as such) in 2004 was estimated to be:
- 40,000 – 80,000 tonnes in Europe
- less than 20,000 tonnes in the USA and
- less than 10,000 tonnes in the rest of the world.

The quantities of equilibrium peracetic acid, given above, are mainly used for disinfection. Neither use of peracetic acid for chemical synthesis nor *in situ* generation of peracetic acid is included.

Major uses of peracetic acid are in chemical synthesis, disinfection and bleaching. Low concentrations (1-15 %) are used as sanitisers, disinfectants and sterilants in agriculture, food, beverage and medical

industries. High-strength equilibrium (> 15 %) and distilled peracetic acid products are in general employed as oxidising agents in the manufacture of organic chemicals and pharmaceuticals. Distilled peracetic acid is also used as bleaching agent in TCF cellulose pulp production processes replacing chlorine dioxide. Peracetic acid seems to be used in certain European countries in consumer products, which are used for example for hard surface disinfection.

Peracetic acid is also generated *in situ* when products, containing an activator (e.g. tetra-acetyl ethylenediamine, TAED) and a persalt (sodium perborate or sodium percarbonate), are dissolved in water. These products could be laundry detergents but they could also be used for surface disinfection (e.g. hospitals, farms). World-wide consumption in chemical synthesis including captive use (internal use by a company) and *in situ* generation has been estimated at 45,000-50,000 tonnes peracetic acid (100 %) in 1998.

During use of peracetic acid the substance may be released to the aquatic environment Also *in situ* formation may result in an exposure of the aquatic environment. However, if the effluents are treated by wastewater treatment plants no emission of peracetic acid to the aquatic environment is expected.

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

Human health

The chemical is of low priority for further work. The chemical possesses properties indicating a hazard for human health (acute toxicity, corrosive to skin and eyes, respiratory tract irritation, repeated dose toxicity based on local effects); however, these hazards do not warrant further work as they are related to local effects. They should, nevertheless, be noted by chemical safety professionals and users.

Environment

The chemical is a candidate for further work. The substance has properties indicating a hazard for the environment (aquatic toxicity < 1 mg/l for fish, aquatic invertebrate and/or algae based on peracetic acid). Member countries are invited to perform an exposure assessment and, if necessary, a risk assessment (mainly needed for sites without a biological waste water treatment plant).

Note: In the EU the active substance peracetic acid has been notified for the Biocidal Products Directive (98/8/EC). Therefore a comprehensive risk assessment is already ongoing for the biocidal applications of peracetic acid in the EU (submission of complete dossiers in 2007 and 2008). This includes not only a detailed exposure assessment but also a detailed evaluation of the need for further toxicity testing.