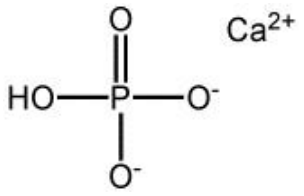
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	7757-93-9
Chemical Name	Calcium hydrogenorthophosphate
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Physical and chemical properties

Calcium hydrogenorthophosphate is an odourless, tasteless, white crystalline powder, with melting point of >450° C . It has a density of 2.92 g/cm^3 and water solubility of 153 mg/L at 20°C, pH 6.5 and is insoluble in ethanol. The boiling point, vapour pressure, dissociation constants and partition coefficients are not applicable to an inorganic salt like calcium hydrogenorthophosphate.

Human Health

Calcium and phosphate play a key role as an essential structural component of the skeleton. Calcium is absorbed from the gastrointestinal (GI) tract in a two-step process. Absorption occurs rapidly from the gut lumen into mucosal cells, and is then extruded into the interstitial fluid, with the first step faster than the second. 1,25-Dihydroxyvitamin D (1,25(OH)2D, the active form of vitamin D) is required for both steps in calcium transport. Fractional calcium absorption varies inversely with dietary calcium intake. During calcium deficiency, the absorption of calcium from diet increases, as a result of serum parathyroid hormone and 1,25(OH)2D action. Calcium in the bloodstream is predominantly associated with albumin. Unabsorbed ingested calcium is excreted in the feces. Renal calcium excretion is a function of the filtered load and the efficiency of reabsorption; the latter of these is regulated by parathyroid hormone. A high sodium diet increases the renal excretion of calcium, as both compete for reabsorption at the same sites in the renal tubules.

About 85% of the roughly 500 to 700 g of phosphate in the body is contained in bone, where it is an important constituent of carbonated hydroxyapatite. In soft tissues, phosphate is mainly found in the intracellular compartment. Inorganic phosphate is a major intracellular anion, but it is also present in plasma. Like calcium, gastrointestinal phosphate absorption is also enhanced by vitamin D. Renal phosphate excretion roughly equals GI absorption to maintain net phosphate balance. Phosphate depletion can occur in a variety of disease states and results in conservation of phosphate by the kidneys. Bone phosphate serves as a reservoir, which can buffer changes in plasma and intracellular phosphate.

The oral LD_{50} values were higher than 2,000 mg/kg bw for female rats [OECD TG 423]. The substance did not cause relevant clinical effects or findings at necropsy. Normal body weight gains were obtained in all animals for the 2nd step of the acute oral study, but there was temporary loss of body weight in one animal for the 1st step and that was recovered on 7 days after administration.

Neat calcium hydrogenorthophosphate was not irritating to rabbit skin. Two older *in vivo* studies indicated that dicalcium phosphate (anhydrous or the dihydrate) was not irritating to the rabbit eye.

Although no good-quality sensitisation studies were found for calcium hydrogenorthophosphate itself, the

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presence of these ions in large amounts in the body, structural considerations, existing data on other calcium and phosphate salts, as well as a good-quality LLNA study on the sodium salt, indicate that calcium hydrogenorthophosphate is highly unlikely to possess any significant sensitisation potential.

In a repeated dose oral toxicity study in rats [OECD TG 407], calcium hydrogenorthophosphate was given by gavage at dose levels of 0, 250, 500 or 1,000 mg/kg bw/day to rats. Ten animals/sex (in the control and top-dose group) and 5 animals/sex (in the low and medium-dose groups) were used. There were no treatment-related changes in clinical signs, body weight, food consumption, urinalysis, hematology, serum biochemistry, necropsy finding and organ weights. Based on these results, it was concluded that the oral administration of calcium hydrogenorthophosphate to rats resulted in no toxicologically significant changes in all items examined. Therefore, under the present experimental conditions, the NOAEL of the test item is considered to be 1,000 mg/kg bw/day for both sexes of rats in this 28-day repeated dose oral toxicity study.

In a bacterial reverse mutation assay [OECD TG 471] with multiple strains of *Salmonella typhimurium* and one strain of *Escherichia coli*, calcium hydrogenorthophosphate was negative both with and without metabolic activation. In an *in vitro* chromosomal aberration test [OECD TG 473], it was also negative with and without metabolic activation. Based on these results, calcium hydrogenorthophosphate is considered to be non genotoxic *in vitro.* In addition, tricalcium phosphate, a similar substance to calcium hydrogenorthophosphate was not mutagenic in bacteria and did not cause chromosome aberration in hamster lung cells.

No data were available for the carcinogenicity of calcium hydrogenorthophosphate.

Calcium hydrogenorthophosphate has been investigated in a reproductive and developmental toxicity screening test [OECD TG 421]. Rats (13/sex/dose) were treated by gavage at doses of 0, 250, 500 or 1,000 mg/kg bw/day. Males were dosed once daily for two weeks each prior to, during and post mating, and females were dosed once daily for two weeks prior to mating, throughout gestation and four days after delivery. During the observation period, there were no dose related effects on clinical signs, body weights, food consumption, mating, gestation, delivery, organ weights, necropsy and histopathology in parents. No dose-related changes in clinical signs, body weights, viability index, external malformations and sex ratios were noted in pups. Based on the results of this study, no dose-related effects were noted in reproductive function of parents and in pups in the 1,000 mg/kg bw/day dosed group. The reproductive and developmental NOAEL was considered to be 1,000 mg/kg bw/day for parents of both sexes and pups, respectively.

Calcium hydrogenorthophosphate has a low hazard profile for human health. Adequate screening-level data are available to characterize the human health hazard for the purposes of the Cooperative Chemicals Assessment Programme.

Environment

Environmental fate analysis based on log Kow and log Koc is not applicable to inorganic substances such as calcium hydrogenorthophosphate. Photodegradation and biodegradation are not applicable to inorganic substances. The current state of science does not allow for the unambiguous interpretation of the significance of various measures of bioaccumulation (e.g., BCF, BAF) for inorganic substances.

The substance has a significant eutrophication potential, similar to that of inorganic phosphate.

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

Fish [*Oryzias latipes*] 96 h LC_{50} >100 mg/L (nominal) [pH 7.18 to 7.97]
> 13.5 mg/L (highest concentration measured in solution)
Invertebrate [*Daphnia magna*] 48 h EC_{50} >100 mg/L (nominal) [pH 7.80 to 8.14]
> 2.9 mg/L (highest concentration measured in solution)
Algae [*P. subcapitata*] 72 h E_rC_{50} >100 mg/L (growth rate, nominal) [pH 8.30 to 9.06]
> 4.4 mg/L (growth rate, highest concentration measured in solution)
72 h E_yC_{50} >100 mg/L (yield, nominal) [pH 8.30 to 9.06]
> 4.4 mg/L (yield, highest concentration measured in solution)

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Calcium hydrogenorthophosphate has a low hazard profile for the environment. Adequate screening-level data are available to characterize the environmental hazard for the purposes of the Cooperative Chemicals Assessment Programme.

Exposure

In the Republic of Korea (sponsor country), the production, use and import volumes of calcium hydrogenorthophosphate were 1,292, 796 and 20,292 tonnes in 2006, respectively. In European Nordic countries estimated use volumes of calcium hydrogenorthophosphate were approx. 400, 6,500 and 3,600 tonnes in 2007, 2008 and 2009, respectively.

Calcium hydrogenorthophosphate is mainly used as a disinfectant in toothpaste products, in pharmaceuticals, pigments, paints, and as ink additives and food/foodstuff additives in the sponsor country. It is also used for control of acidity in powdered drink mixes and as a leavening agent in bread, cake mixes, and self-rising flour. The general public may be exposed to small quantities of calcium hydrogenorthophosphate by the consumption of food and some food/foodstuff additives.

In use facilities of the sponsor country, calcium hydrogenorthophosphate is handled in closed systems. No monitoring data were available for the workplace. Occupational exposure is managed with local ventilation systems and personal protective equipment such as dust masks, gloves and goggles. Occupational exposure is considered to be negligible in the sponsor country.

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