SIDS INITIAL ASSESSMENT PROFILE

CAS No.	7758-87-4
Chemical Name	Tricalcium phosphate
Structural Formula	$2[PO4^{3-}]\ 3[Ca^{2+}]$

SUMMARY CONCLUSIONS OF THE SIAR

Physical and chemical properties

Tricalcium phosphate is amorphous, odourless, tasteless powder substance with a melting point of 1670 °C and density of 3.14 g/cm3. It has a low water solubility of ≤20 mg/L at 20 °C and negligible vapour pressure. The boiling point and partition coefficient for tricalcium phosphate are not applicable to an inorganic salt.

Human Health

Calcium is required for the proper functioning of muscle contraction, nerve conduction, hormone release, and blood coagulation. In addition, proper calcium concentration is required for various other metabolic processes. Calcium stores depend on dietary intake, absorption of gastrointestinal (GI) tract and renal calcium excretion. Phosphorus is one of the most abundant elements in the human body. Most phosphorus in the body is complexed with oxygen as phosphate. Phosphate is absorbed from, and to a limited extend secreted into, the GI tract. Transport of phosphate from the gut lumen is an active, energy-dependent process that is modified by several factors. As an example, vitamin D stimulates phosphate absorption, an effect reported to precede its action on calcium ion transport. In adults, about two thirds of the ingested phosphate is absorbed, and then almost entirely excreted into the urine. In growing children, phosphate balance is positive. Concentrations of phosphate in plasma are higher in children than in adults. Collapse of phosphate balance as 'hyperphosphatemia' decreases the affinity of hemoglobin for oxygen and is hypothesized to explain the physiological 'anemia' of childhood.

In an acute oral toxicity study [OECD TG 423], tricalcium phosphate was administered via gavage to 2 groups of 3 female rats at dose level of 2,000 mg/kg bw. No death and abnormal clinical signs were observed. Body weights increased normally. There were no macroscopic abnormalities at necropsy in the oral study. The acute oral LD_{50} value was >2,000 mg/kg bw for rats. Depending on the relative absorption of calcium versus phosphate, a rise in serum phosphorus could stimulate parathyroid hormone (iPTH) secretion. The absorption and acute metabolic effects of oral tricalcium phosphate (TCP) and calcium carbonate (CC) were evaluated with 10 women, aged 22-40 years. The subjects were fasted overnight for 12 hours, 1,200 mg calcium (as CC or TCP) was ingested. Serum and urine calcium, phosphorus, and creatinine, urine cyclic adenosine monophosphate (cAMP) were determined. iPTH levels following TCP were also measured. Calcium absorption was determined by the postload rise in urine calcium above baseline. Urine calcium excretion increased significantly and was accompanied by significant rises in serum calcium after both preparations. Following tricalcium phosphate administration, serum and urine phosphorus increased. Urinary cAMP did not change after either preparation, and iPTH levels fell after oral tricalcium phosphate. Tricalcium phosphate administered orally is absorbed and does not stimulate parathyroid gland function. No acute inhalation and dermal toxicity studies were available.

No experimental data are available for skin and eye irritation in animals. Trisodium phosphate has however skin and eye irritation properties, therefore it can be anticipated that tricalcium phosphate may also have skin and eye irritant properties.

There were no experimental data available for skin sensitization in animals.

In a repeated dose oral toxicity study according to the OECD Guideline 422, tricalcium phosphate was administered via gavage at dose levels of 0, 250, 500 and 1,000 mg/kg bw/day to male rats from 2 weeks before mating to the end of the mating period, for at least 28 days, and to females from 2 weeks before mating to day 4 of lactation including the mating and gestation periods. Ten animals/sex/dose were assigned to the main group and 6 animals/sex/dose were used in the recovery group. No death was observed in either sex. There were no treatment-related changes in clinical signs, body weight, food consumption, urinalysis, hematology, serum biochemistry, necropsy finding and organ weights. At histopathological examination, slight tubular

degeneration/regeneration was observed in kidney in males and mineralization in kidney in females at 1,000 mg/kg bw/day. However, these findings were not considered to be toxicologically significant, since no treatment-related changes were observed in serum biochemistry due to kidney dysfunction. Based on these results, the NOAEL for repeated dose oral toxicity was considered to be 1,000 mg/kg bw/day in both sexes (the hightest dose tested).

In an *in vitro* bacterial reverse mutation test, tricalcium phosphate was not considered to be mutagenic both with and without metabolic activation in multiple strains of *Salmonella typhimurium* and *Escherichia coli* strain [OECD TG 471]. In a chromosomal aberration test, tricalcium phosphate did not exhibit clastogenic effects in with or without metabolic activation. There was no increase as compared with the negative control. Based on these results, tricalcium phosphate was considered to be non genotoxic *in vitro* [OECD TG 473]. No *in vivo* genotoxicity studies were available.

There was no reliable data for carcinogenic activity of tricalcium phosphate.

The reproductive toxicity of the tricalcium phosphate has been well investigated in a reproductive and developmental toxicity screening test in rats [OECD TG 422]. Tricalcium phosphate was administered via gavage at dose levels of 0, 250, 500 and 1,000 mg/kg bw/day to male rats from 2 weeks before mating to the end of the mating period, for at least 28 days, and to females from 2 weeks before mating to day 4 of lactation including the mating and gestation periods. Ten animals/sex/dose were assigned to the main group and 6 animals/sex/dose were used for the recovery group. No death was observed in either sex. There were no treatment-related changes in clinical signs, body weight, food consumption, necropsy finding and organ weights. There were no treatment-related adverse effects on reproductive parameters, including precoital time, mating index, fertility index and pregnancy index. No treatment-related effects on F1 pups were observed in the number of corpora lutea, gestation length, delivery index, number of live and dead pups at birth, litter size, percentage of live and dead pups to implantations, sex ratio, viability index and body weights of pups on post-natal day 0 and 4. There were no externally malformed neonates in any groups. Therefore, the NOAEL for reproductive toxicity and developmental toxicity are considered to be 1,000 mg/kg bw/day

Tricalcium phosphate does not present a hazard for human health due to 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

Environmental fate analysis based on log K_{ow} and log K_{oc} is not applicable for inorganic substances such as tricalcium phosphate. Photodegradation and biodegradation are not applicable to metal-containing inorganic substances like tricalcium phosphate. The current state of the science does not allow for the unambiguous interpretation of the significance of various measures of bioaccumulation (e.g., BCF, BAF) for metal-containing 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} > 2.14 mg/L (highest concentration measured in solution)
Invertebrate [*Daphnia magna*]	48 h EC_{50} > 5.35 mg/L (highest concentration measured in solution)
Algae [*Pseudokirchnerella subcapitata*]	72 h ErC_{50} > 1.56 mg/L (growth rate) (highest concentration measured in solution) 72 h EbC_{50} > 1.56 mg/L (area under growth curve method) (the highest concentration measured in solution)

This chemical does not possess properties indicating a hazard to the environment based on its low hazard profile (no aquatic toxicity at the limit of water solubility) . Adequate screening-level data are available to characterize the environmental hazard for the purposes of the OECD HPV Programme.

Exposure

In the Republic of Korea, the production, use and import volume of tricalcium phosphate was 21,600, 1,546 and 76 tonnes in 2006, respectively. Tricalcium phosphate is used as a raw material for formula feed, enrichment agent with P and Ca of livestock, food/foodstuff additives and dispersing agents for styrene acrylonitrile resin etc. in the sponsor country.

In the sponsor country, tricalcium phosphate is handled in a closed system. No monitoring data are available from the wastewater. The dust containing tricalcium phosphate in production and processing sites is controlled

by ventilation systems and PPEs (personal protective equipments) in the Republic of Korea. The 8hr-TWA concentrations of dust for workplaces in tricalcium phosphate were 0.61～1.82 mg/m3, which were less than occupational exposure limit of 10 mg/m3. Occupational exposure is considered to be negligible in the sponsor country.

Tricalcium phosphate can be absorbed into the body by ingestion. The consumer could be exposed to small quantities of tricalcium phosphate in the consumption of food and by using some food/foodstuff additives. Consumer exposure is considered to be minimal in the sponsor country.