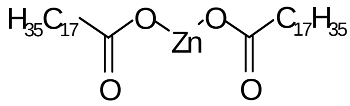
SIDS INITIAL ASSESSMENT PROFILE

CAS Numbers with Chemical Names and Structural Formula			
	7440-66-6	Zinc metal	Zn
	1314-13-2	Zinc oxide	ZnO
	557-05-1/ 91051-01-3	Zinc distearate	
	7646-85-7	Zinc chloride	$ZnCl_2$
	7733-02-0	Zinc sulphate	$ZnSO_4$
	7779-90-0	Trizinc bis (orthophosphate)	$Zn_3(PO_4)_2 \cdot 2\text{-}4H_2O$

SUMMARY CONCLUSIONS OF THE SIAR

Category Justification

The Zincs Category includes six CAS numbers that are similar from a hazard point of view. It is assumed that all zincs either dissociate or form the zinc cation that is responsible for the hazardous effects. In the environment the zinc cation is formed via several speciation or transformation reactions, while furthermore it is assumed that, where appropriate, the counter ion does not significantly attribute to the major effects seen. In the human health assessment of the hazards it is assumed that for systemic toxicity the hazardous properties can be attributed again to the zinc cation and the counter ion be ignored.

Human Health

Being an essential element, zinc plays an important role in many processes in the body. Although zinc deficiency can lead to notable health effects, the risk assessment for an essential element like zinc does not concern deficiencies but excess in exposure over natural background levels.
A lot of information was available for evaluation of the data-rich zinc compounds. The database not only included toxicity data on the six zinc compounds. In case of systemic effects also data on other zinc compounds were used, based on the assumption that after intake the biological activities of the zinc compounds are determined by the zinc cation.
Within certain limits, the total body zinc as well as the physiologically required levels of zinc in the various tissues can be maintained, both at low and high dietary zinc intake. Regulation of gastrointestinal absorption and gastrointestinal secretion probably contributes the most to zinc homeostasis. In spite of this a regular exogenous supply of zinc is necessary to sustain the physiological requirements because of the limited exchange of zinc between tissues.
The Zn^{2+} absorption process in the intestines includes both passive diffusion and a carrier-mediated process. The absorption can be influenced by several factors such as ligands in the diet and the zinc status.
Persons with adequate nutritional levels absorb 20-30% and animals 40-50%. However, persons that are Zn-deficient absorb more, while persons with excessive Zn intake absorb less. For zinc oxide it has been shown that bioavailability is about 60% of that for soluble zinc salts, corresponding to 12-18%.
Although quantitative data on the absorption of zinc following inhalation exposure (especially relevant in

occupational settings) are not available it is concluded that inhalation absorption for the soluble zinc compounds is at maximum 40%, while for the less soluble/insoluble zinc compounds inhalation absorption is at maximum 20%. Some animal data suggest that pulmonary absorption is possible. For dermal exposure (relevant in both occupational and consumer settings) adequate quantitative data on the absorption of zinc are not available. However, it is concluded that the dermal absorption of solution or suspensions of zinc or zinc compounds is 2%, whereas for dust exposure to zinc or zinc compounds this value is 10-fold lower.
Zinc is distributed to all tissues and tissue fluids and it is a cofactor in over 200 enzyme systems. Zinc is primarily excreted via feces, but can also be excreted via urine, saliva, hair loss, sweat and mothermilk.

Zinc metal, zinc oxide, zinc distearate, and zinc phosphate have a low acute toxicity, are not corrosive and irritating to the skin, eyes, or respiratory tract, and are not sensitizing to the skin. In contrast, zinc chloride is corrosive, irritating to the respiratory tract, and acutely toxic after inhalation ($LC_{50} \leq 1975$ mg/m^3, 10 min. exposure time) and ingestion (LD_{50} 1100-1260 mg/kg bw). Zinc sulfate is also acutely toxic after ingestion ($LD_{50} < 2000$ mg/kg bw), as well as severely irritating to the eyes.
When present as ultrafine (≤ 0.1 µm) particles in fumes, zinc oxide may cause metal fume fever upon inhalation. The generation of ultrafine zinc oxide particles occurs only at very specific operations, such as the welding of steel. In humans, the LOAEL for metal fume fever was 5 mg/m^3. This was concluded from a study in which 4 persons were exposed for 2 hours to control furnace gases or ultrafine zinc oxide particles (5 mg ZnO/m^3). Inhalation of zinc chloride fumes also resulted in adverse effects in humans: local effects in the respiratory tract were observed at a LOAEL of 4.8 mg ultrafine zinc chloride/m^3 after an exposure of 30 minutes to zinc chloride fume).

In repeated dose toxicity studies with rats and mice, oral zinc exposure resulted in copper deficiency and pathological changes in the pancreas and the spleen as the most sensitive effects, with a NOAEL of 13.3 mg Zn^{2+}/kg bw/day. In studies with human volunteers, women appeared to be more sensitive than men to the effects of repeated zinc supplementation. In women, supplementation at a level of 150 mg Zn^{2+}/day (2.5 mg/kg bw/day, based on a body weight of 60 kg; LOAEL) resulted in clinical signs such as headache, nausea and gastric discomfort, and in indications for disturbance of copper homeostasis. The NOAEL in women supplemented with zinc was 50 mg Zn^{2+}/day (0.83 mg/kg bw/day). The background intake of zinc via food is approximately 10 mg/day.

The results of in vitro genotoxicity studies indicate that zinc has genotoxic potential *in vitro*. However, there is no clear evidence from *in vivo* genotoxicity studies that zinc is genotoxic *in vivo*. There is also no clear experimental or epidemiological evidence for a direct carcinogenic action of zinc, albeit that zinc deficiency or supplementation may influence carcinogenesis given that promoting and inhibiting actions have been reported.

Available data in experimental animals on zinc excess indicate that adverse effects on fertility and fetal development may occur at dose levels (200 mg Zn^{2+}/kg bw/day) at which other effects such as perturbation of parental and fetal copper homeostasis are evident. The only available data in humans indicate that additional zinc up to 0.3 mg Zn^{2+}/kg bw/day during pregnancy did not result in adverse reproductive or developmental effects. In analogy with the findings in animals, where reproductive toxicity was observed at higher dose levels than those at which other effects were already present, it was considered unlikely that in humans reproductive effects will occur at exposure levels at which clinical signs are not manifest.

Environment

The zinc compounds from the Zinc Category are all solids. Melting points are higher than 130ºC and boiling points higher than 732ºC. Vapour pressure for the zinc metal is 31 Pa (at 450ºC) and for zinc chloride 1.33 hPa (at 428ºC). From the category members, zinc chloride has the highest water solubility (4,320 g/L), followed by zinc sulphate (220 g/L), zinc oxide (<1.6 mg/L) and zinc distearate (0.97 mg/L). Zinc phosphate and zinc metal are insoluble in water. An octanol-water partition coefficient is only available for zinc distearate (log Kow of 1.2).

The chronic ecotoxicity data, if based on the total zinc concentrations (i.e. added plus background concentration), have been transformed into the added zinc concentrations, to allow the use of the "added risk approach". The "added risk approach" allows one to cope with essentiality and natural background concentrations in the environment. In this approach both the PEC and the PNEC are determined on the basis of the added amount of zinc, resulting in an

"*added* Predicted Environmental Concentration" (PEC_{add}) and "*added* Predicted No Effect Concentration" ($PNEC_{add}$), respectively.
Chemical and biological processes will affect the speciation of zinc in the environment. Bioavailability of zinc in water, soil and sediment and its implications for the hazard and exposure assessment has been dealt with via bioavailability correction factors (water and soil) and the Acid Volatile Sulphide (AVS)-method (sediment).

For the aquatic environment, the following values for pH, hardness, DOC (dissolved organic carbon) and background zinc concentrations have been used for ecotoxicity data selection: pH between 6 and 9, total hardness between 24 and 250 mg/l as $CaCO_3$, DOC < 2 mg/l (only used for reconstituted waters) and minimal background zinc concentration for soluble zinc around 1 µg/L. These abiotic conditions are known to affect bioavailability and, implicitly, the hazard assessment of zinc in surface water (see above). The selected abiotic ranges are based on current OECD test guidelines for aquatic toxicity testing and relevance for the EU region; other regions may select other ranges for their hazard assessment.

The lowest $L(E)C_{50}$ values expressed as soluble metal (mg Zn^{2+}/L) were found to be 0.136 mg/L for the algae *Selenastrum capricornutum*, 0.07 mg/L for the crustacea *Daphnia magna* and 0.14 mg/L for the fish *Oncorhynchus mykiss*.
The lowest "species mean" NOEC of 17 µg/l, for *Pseudokirchneriella subcapitata*, formerly known as *Selenastrum capricornutum*, is based on the geometric mean value of 25 NOEC values from different tests (endpoint growth).
The lowest NOEC for sediment-dwelling organisms (benthic macro-invertebrates) is 488 mg/kg dwt, based on tests in sediment-water systems with Zn-spiked sediment.

For terrestrial microbial processes a lowest NOEC of 17 mg/kg d.w. was found in two respiration tests. For the group plants/invertebrates a lowest NOEC of 32 mg/kg d.w. was found in an invertebrate test species, *Folsomia candida*, and in plant tests with *Trifolium pratense*, *Vicia sativa* and *Hordeum vulgare.* The selected tests with terrestrial organisms typically refer to the EU region; other regions may select other criteria for their hazard assessment.
The bioaccumulation potential of zinc in herbivorous and carnivorous mammals, but also in several invertebrates, will be low (homeostasis). Secondary poisoning and the related issues bioaccumulation and biomagnification are therefore considered less relevant for zinc.

Exposure

Zinc is an essential and naturally occurring element in the environment. Zinc in fresh water or seawater can occur in both suspended and dissolved forms and is partitioned over a number of chemical species. The natural zinc concentrations in soils are highly variable and dependent on the native soil material and the soil characteristics, especially the clay and organic matter content. Zinc in soil is distributed between a number of fractions.

Emissions to the environmental compartments are possible from the production, the use and waste phase of the substances. Zinc and zinc compounds are used in a great number of applications, ranging from steel coating (galvanizing) to cosmetics. It is emphasized that zinc may enter the environment via a variety of point and diffuse sources: a.o. industry, mining, agriculture, historical pollution, etc.

The total production volume of primary zinc metal in the EU in 1995 was about 2,193,000 tonnes. In the Western World the mine production of zinc was 4,730,000 tonnes in 1990, while 1,940,000 tonnes of zinc were produced from secondary sources.
Zinc is a compound that is incorporated in a great number of regional or national monitoring programs. Zinc monitoring data for surface water, soil and sediment could therefore be collected for a number of EU countries.

Exposure in the workplace is limited to the inhalation and dermal route, assuming that oral exposure is prevented by personal hygienic measures. Zinc compounds are used in several consumer products, e.g., in applications of metallic zinc (watering-cans, buckets, nails, gutters, etc.), in paints, cosmetics (eye shadow, sunscreen, deodorant, dandruff shampoo), and drugstore products (baby care ointment, gargle, eye drops). Zinc compounds are also used in dietary supplements, which consumers can buy over the counter. Zinc and zinc compounds are released to the environment through waste water and air effluents at the sites where they are produced and processed. Humans may thus be exposed to these compounds indirectly via the oral and inhalation route. The background intake of zinc via food, due to the natural occurrence of zinc in the environment, is approximately 10 mg/day. This appeared to be the most important exposure to zinc, compared to which the intake via drinking water and ambient air is negligible.

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

Human Health: The chemicals in this category possess properties indicating hazards for human health (acute inhalation toxicity, corrosive to skin and eyes, respiratory irritation (zinc chloride), eye irritation (zinc sulfate) and metal fume fever (zinc oxide).

A risk assessment was performed in the context of the EU Existing Substances Regulation. For human health risks were identified regarding occupational exposure to two members of the Zinc category:

- zinc oxide: metal fume fever due to acute inhalation exposure could not be excluded in a certain occupational exposure scenario, and systemic effects after repeated dermal exposure at the workplace could not be excluded in other scenarios.
- Zinc chloride: where acute local effects to the respiratory tract could not be excluded in a certain occupational exposure scenario.

In the EU an risk reduction strategy is currently under discussion. Other member countries are invited to perform an exposure assessment and if necessary a risk assessment for human health.

Environment: The chemicals in this category possess properties indicating hazard for the environment (aquatic toxicity). Based on the wide spread use of these chemicals, member countries are invited to perform an exposure assessment and if necessary a risk assessment.