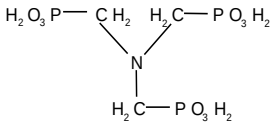
SIDS INITIAL ASSESSMENT PROFILE

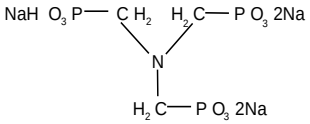
Category Name	ATMP and salts (Phosphonic Acid Compounds Group 1) Amino tris(methylenephosphonic acid) and its sodium salts
Chemical Names and CAS Numbers	

Chemical name	CAS no.	Abbreviation
Amino tris(methylenephosphonic acid	6419-19-8	ATMP
Amino tris(methylenephosphonic acid), xNa Salt	20592-85-2	ATMP-xNa
Amino tris(methylenephosphonic acid), Na Salt	none found	ATMP-Na
Amino tris(methylenephosphonic acid), 2Na Salt	4105-01-5	ATMP-2Na
Amino tris(methylenephosphonic acid), 3Na Salt	7611-50-9	ATMP-3Na
Amino tris(methylenephosphonic acid), 4Na Salt	94021-23-5	ATMP-4Na
Amino tris(methylenephosphonic acid), 5Na Salt	2235-43-0	ATMP-5Na
Amino tris(methylenephosphonic acid), 6Na Salt	15505-05-2	ATMP-6Na

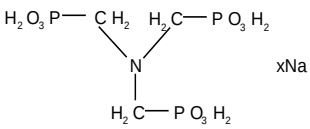
Structural Formula



Amino tris(methylenephosphonic acid)
CAS # 6419-19-8



Amino tris(methylenephosphonic acid), 5Na Salt
CAS # 2235-43-0



Amino tris(methylenephosphonic acid), xNa Salt
CAS # 20592-85-2

SUMMARY CONCLUSIONS OF THE SIAR

Category Rationale

This category covers a phosphonic acid and various sodium salts of that acid. The different salts are prepared by neutralising the acid to a specific pH. Data are available for the acid and some salts. The substances are commercially available as aqueous solutions only and in an environmental context the speciation will be the same. In the present context the effect of the counter-ion (sodium) will not be significant. The properties of the members of the category are consistent across all end points.

The category is expressed as Phosphonic Acid Compounds Group 1 because two other groups have been identified, with close structural analogy to the present one. Group 2 is 1-Hydroxy-1,1-ethane-diphosphonic acid (CAS 2809-21-4) and its sodium and potassium salts; Group 3 is Diethylene triamine penta(methylene phosphonic acid) (CAS 15827-60-8) and its sodium salts.

Human Health

In the rat, ATMP is poorly absorbed from the gut and rapidly eliminated after oral and i.v. administration. Elimination is primarily via the faeces following oral dosing with urine predominating after i.v. dosing. These

differences demonstrate clear differences in systemic disposition of ATMP after enteral or parenteral administration. Bone is the only tissue that exhibits deposition of test substance-derived radioactivity, however this is unlikely to occur to any biologically significant extent in view of the low level of uptake reported.

ATMP is of low acute toxicity in mammals. The acute oral LD_{50} is 2910 mg/kg while the dermal LD_{50} is >6310 mg/kg. The tetrasodium salt of ATMP was of lower toxicity with an oral LD_{50} of ~8610 mg/kg and a dermal LD_{50} of >5740 mg/kg. The pentasodium salt (20592-85-2) was of lower oral toxicity (7120 mg/kg) and dermal toxicity (>6320 mg/kg).

ATMP is a moderately severe eye irritant. The tetra- and pentasodium salts of ATMP are mildly irritating. ATMP can be considered to be non-irritating to the skin. The tetra- and pentasodium salts of ATMP induced very slight skin irritation responses. ATMP is not a skin sensitizer.

Repeated exposure in the diet to 500 mg/kg bw/day of the acid for 2 years resulted in no toxicological effects of concern. The systemic NOAEL for this good quality study conducted to OECD guideline 453 is therefore considered to be >500 mg/kg bw/day. Information available on the tetrasodium salt is less robust but similarly indicates that it is of low oral toxicity following repeat exposure with a NOAEL of >600 mg active acid/kg bw/day derived from a 28 day study or >175 mg/kg bw/d derived from a 90 day study.

Neither the acid nor a sodium salt induced gene mutations in bacteria. ATMP induced gene mutations in mouse lymphoma cells but this effect was not seen when a neutralized test solution was tested up to the solubility limit and is therefore considered to be an artefact of pH. The pentasodium salt of ATMP did not induce chromosome damage either *in vitro* or *in vivo*. Both the acid and the salts are therefore considered to lack genotoxic potential. This is confirmed by a carcinogenicity study. ATMP was not carcinogenic to rats treated with dose levels up to 500 mg/kg in the diet for 24 months.

ATMP is not selectively toxic to the male or female reproductive system, with a NOAEL of 275 mg/kg bw/day for males and 310 mg/kg bw/day for females. While no reproductive toxicity data were located for the salts, physico-chemical considerations suggest these will resemble those of the parent acid. ATMP and its salts are not fetotoxic or teratogenic in the rat or mouse with a consistent NOAEL of 1000 mg/kg body weight/day in both species.

Overall the NOAEL for ATMP is > 500 mg/kg bw/day, based on a chronic toxicity study.

Conclusion for Human Health

The chemicals in this category possess properties indicating a hazard for human health (ATMP is a moderately severe eye irritant). Although these hazards do not warrant further work as they are related to pH effects and chelation properties, they should nevertheless be noted by chemical safety professionals and users.

Environment

ATMP is a polyphosphonic acid of molecular weight 299. The phosphonic acid function is a strong acid, and it is frequently produced as a salt for reasons of ease of use. It can form stable complexes with polyvalent metal ions. As a consequence of the ionisation over typical pH ranges, it is of high water solubility ($\geq$ 500 g/l) and low octanol-water partition coefficient (Log Kow = -3.53). Its vapour pressure is very low (1.9×10^{-10} Pa (estimated)). At pH 7, ATMP in water will be almost fully ionised four times, with a majority of the molecules ionised five times.

There is a possibility that the emission of a phosphonic acid could locally decrease the pH in the aquatic environment. In the normal use of these substances, their pH, concentration and water quality have to be monitored very carefully. Therefore, a significant decrease of the pH of the receiving water is not expected. Furthermore, the substances are usually used as salts with near-neutral pH, and their effects on pH are further buffered by the presence of metal ions. Generally the changes in pH of the receiving water should stay within the natural range of the pH, and for this reason, adverse effects on the aquatic environment are not expected due to release of the phosphonic acids.

ATMP and its salts may enter the environment via normal use in water treatment applications. It is predicted and has

been shown to be adsorbed by inorganic matrices (measured Koc = 11740), and therefore adsorption to sewage sludge and soil is strong. ATMP and its sodium salts are not readily or inherently biodegradable in laboratory studies carried out under standard conditions. Although these data suggest the potential for persistence, there is, however, evidence of partial degradation by abiotic processes in natural waters, and biodegradation following acclimation, or under conditions of low inorganic phosphate. In the presence of commonly found metal ions possessing redox properties, such as iron, metal-catalysed degradation and photodegradation can be rapid, which promotes further biodegradation. ATMP is not bioaccumulative (measured BCF <25).

As complexing agents, these substances could remobilise metals in the environment; however, their high degree of adsorption to sediments suggests that this is unlikely to occur.

ATMP and its salts are of low acute toxicity to fish, acute LC_{50} values determined in short-term and prolonged-term exposure tests are all equal to or in excess of 250 mg/l. ATMP also has low chronic toxicity to fish with a 60-day NOEC of 23 mg/l having been determined in an early-life stage test ATMP and its salts are of low to moderate acute toxicity to aquatic invertebrates. The lowest reliable acute toxic concentration determined for ATMP is a 48-h EC_{50} of 94 mg/l for the marine copepod *Acartia tonsa*. A sub-lethal test with the oyster, *Crassostrea virginica*, yielded a 96-hour EC50 for effects on shell growth of 201 mg/l and a chronic test with Daphnia magna yielded a 28-day NOEC of >25 mg/l, suggesting that ATMP has low chronic toxicity to aquatic invertebrates. A further chronic study in *Daphnia magna* of unassignable validity (Klimisch code 4) gave a 21-day NOEC of 3.0 mg/l and LOEC of 10 mg/l (based on nominal concentrations).

ATMP is of low acute toxicity to the marine sediment living amphipod *Corophium volutator* (10-day LC_{50}: >5000 mg/kg dw) and to sewage sludge micro-organisms (*Pseudomonas putida* 30-min EC_0: ≥500 mg/l).

The effects of ATMP observed in tests with algae are likely to be a consequence of nutrient limitation caused by complexation and not true toxicity. Thus, a 96-hour E_bC_{50} for *Selenastrum capricornutum*[1] of 12 mg/l and a 96-hour E_rC_{50} for *Skeletonema costatum* of 80 mg/l are likely to over-estimate the true toxicity. NOECs of ≤20 mg/l (most commonly in the range 10-20 mg/l), determined in studies for which reliability could not be assessed and which might also be subject to the effects of complexation, indicate that ATMP is likely to be of low chronic toxicity to algae.

ATMP is considered to be of low toxicity to terrestrial plants (*Avena sativa* 9-day EC_{50}: >1000 mg/l), although the reliability of the study on which this conclusion is based is uncertain. ATMP is also of low acute toxicity to birds when administered via the dietary exposure route (*Anas platyrhynchos* and *Colinus virginianus* 14-day LC_{50}: >565 mg/kg bw).

[1]Now known as *Pseudokirchneriella subcapitata*

Conclusion for the Environment

ATMP and its salts possess properties indicating a hazard for the environment (EC_{50} in the range 10 – 100 mg/l for algae). However these hazards do not warrant further work as they are related to acute toxicity, pH effects and metal chelation, which may become evident only at very high exposure levels. The substances are not readily biodegradable but have a low bioaccumulation potential.

Exposure

Current worldwide production of ATMP, HEDP and DTPMP (and their salts) is estimated to be in the range of 50,000 to 100,000 metric tonnes annually. The major uses of ATMP and its salts are as an additive in water treatment, where its ability to both complex with metal ions, and to prevent crystalline scale deposition in solution and onto surfaces through adsorption, are utilised. The substances are also used in detergent and cleaning applications, and in the paper, textiles and photographic industries, and also in off-shore oil well applications.

The major route of environmental exposure is expected to be release, often via wastewater treatment plants, to rivers. Agricultural land could be exposed via spreading of sewage sludge. Oil well use would lead to direct exposure of the marine environment. In rivers, they are expected to partition predominantly to sediment.

Human exposure in manufacturing and formulating is possible, but due to the use of personal protective equipment, limited to accidental situation. Where exposure can occur, dermal exposure is the most likely route of exposure. In these cases PPE is recommended. The concentration of the substance in the product, together with PPE/engineering controls are important factors in the assessment of risk associated with the hazardous properties (mainly corrosivity/irritancy). Where concentrated solutions are handled, engineering controls and PPE are used to control exposure and reduce the risk from the corrosive/irritant properties. In downstream uses, where consumer exposure is possible, much more dilute concentrations are used, which significantly reduces or removes the likelihood of corrosivity/irritancy effects.

Consumer exposure is being assessed in more detail as part of the HERA project (HERA, in progress www.heraproject.com/).