

Alendronate, Sodium Salt

sc-202049

Material Safety Data Sheet



The Power to Question

Hazard Alert Code
Key:

EXTREME

HIGH

MODERATE

LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

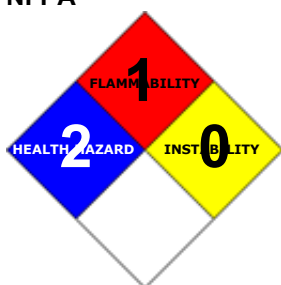
PRODUCT NAME

Alendronate, Sodium Salt

STATEMENT OF HAZARDOUS NATURE

CONSIDERED A HAZARDOUS SUBSTANCE ACCORDING TO OSHA 29 CFR 1910.1200.

NFPA



SUPPLIER

Company: Santa Cruz Biotechnology, Inc.

Address:

2145 Delaware Ave

Santa Cruz, CA 95060

Telephone: 800.457.3801 or 831.457.3800

Emergency Tel: CHEMWATCH: From within the US and
Canada: 877-715-9305

Emergency Tel: From outside the US and Canada: +800 2436
2255 (1-800-CHEMCALL) or call +613 9573 3112

PRODUCT USE

Bone resorption inhibitor used in treatment of osteoporosis. Remedy

SYNONYMS

C4-H13-N-O7-P2.3H2O.Na, C4-H13-N-O7-P2.3H2O.Na, C4H18NNaO10P2, "phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, ", "phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, ", trihydrate, "(4-amino-1-hydroxybutylidene)bisphosphonic acid, monosodium salttrihydrate", "(4-amino-1-hydroxybutylidene)bisphosphonic acid, monosodium salttrihydrate", "alendronate sodium salt", "aminohydroxybutylidene biphosphonate monosodium salt trihydrate", "monosodium (4-amino-1-hydroxybutylidene)bisphosphonate trihydrate", "monosodium (4-amino-1-hydroxybutylidene)bisphosphonate trihydrate", "sodium trihydrogen (4-amino-1-hydroxybutylidene)diphosphate, trihydrate", "sodium trihydrogen (4-amino-1-hydroxybutylidene)diphosphate, trihydrate", "bone resorption inhibitor/ osteoporosis inhibitor", Fosamax, "G-704, 650", MK-217, L-670-452, L-670-452

Section 2 - HAZARDS IDENTIFICATION

CANADIAN WHMIS SYMBOLS



EMERGENCY OVERVIEW

RISK

Harmful if swallowed.

Irritating to eyes and skin.

May cause long-term adverse effects in the aquatic environment.

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED

■ Accidental ingestion of the material may be harmful; animal experiments indicate that ingestion of less than 150 gram may be fatal or may produce serious damage to the health of the individual.

■ The phosphonic acid compounds ATMP, HEDP, DTPMP and their salts can be considered to be of low to moderate acute oral toxicity. ATMP acid was of moderate acute toxicity to mammals. The acute oral LD50 in rat was determined to be 2910 mg active acid/kg bw. In comparison, the tetrasodium and pentasodium salt of ATMP were less acutely toxic with LD50 values of 8610 and 7120 mg active salt/kg bw, respectively. HEDP acid and its salts are of moderate acute oral toxicity LD50's in rats and mice ranging from 1100 to 1878 mg active acid/kg bw. The oral LD50 values of HEDP salts were in a slightly wider range from 581 mg active salt/kg bw to greater than 5000 mg active salt/kg. DTPMP acid and salts are of low toxicity with oral LD50 values from 3870 mg active salt/kg bw to less than 8757 mg active salt/kg bw.

In pharmacology bisphosphonates (also called diphosphonates) are a class of drugs that inhibit osteoclast action and resorption of bone; they are used for the prevention and treatment of osteoporosis, osteitis deformans (Paget's disease of the bone), bone metastasis (with or without hypercalcaemia), multiple myeloma and other conditions that feature bone fragility.

The association between bisphosphonates and severe musculoskeletal pain may be overlooked by healthcare professionals, delaying diagnosis, prolonging pain and/or impairment, and necessitating the use of analgesics. The severe musculoskeletal pain may occur within days, months, or years after starting a bisphosphonates. Some patients have reported complete relief of symptoms after discontinuing the bisphosphonate, whereas others have reported slow or incomplete resolution. The risk factors for and incidence of severe musculoskeletal pain associated with bisphosphonates are unknown.

■ Harmful if swallowed.

EYE

■ The observed eye irritation potential of the phosphonic acid compounds ATMP, HEDP, DTPMP and their salts, ranged from practically non-irritating to severely irritating with irreversible effects.

ATMP acid tested as neat product was considered to be moderately irritating to rabbit eyes, whereas the tetra- and pentasodium salt which were tested in aqueous solutions containing around 40 % active salt were found to be practically non-irritating. These products were evaluated without immediate rinsing the eye following application. All test animals were free of symptoms by the end of the observation period.

HEDP acid was tested as a formulation containing 60 % active acid and minimal amounts of HCl with and without rinsing immediately after application. In the study without rinsing, the formulation caused severe irritation and persistent effects. Rinsing the eye directly after application, lessened the severity of the response and all effects disappeared by the end of the observations. The HEDP salts were less irritating to the rabbit eyes in studies with pure salts and formulations thereof tested without rinsing. The tetrasodium salt (i.e., tested as solution containing up to 30 % active salt) was only minimally irritating to the rabbits eyes.

In general the same trend as was found with skin irritation was found for eye irritation. The acid compounds were more irritating than tested salts and duration of exposure (i.e., as mimicked by rinsing/non-rinsing immediately after product installation) increased the observed symptoms.

■ There is evidence that material may produce eye irritation in some persons and produce eye damage 24 hours or more after instillation. Severe inflammation may be expected with pain. There may be damage to the cornea. Unless treatment is prompt and adequate there may be permanent loss of vision. Conjunctivitis can occur following repeated exposure.

SKIN

■ The acids and salts of ATMP, HEDP, and DTPMP can be considered to be of low acute dermal toxicity. ATMP acid and its tetra- and pentasodium salt were practically non-toxic with LD50 values exceeding the concentrations tested. Dermal LD50 values were determined to be greater than 6310 mg active acid/kg bw. No dermal toxicity was observed for HEDP acid and its salts at the highest tested concentrations tested of 1650 mg active salt/kg bw. DTPMP compounds.

On the basis of the studies phosphonic acid chelatants and their salts, can generally be considered to be mildly irritating to skin at most. In one study a more severe reaction was observed, when an aqueous solution containing 25 % of ATMP acid was applied to intact rabbit skin for 4 hours under occluded conditions. The same result was obtained when an aqueous solution containing 33 % active tetrasodium salt of HEDP was applied to rabbit skin for 24 hours under occlusive dressing. The longer application time of 24 h caused more irritation than when the acid or salt product was only applied over 4 h where no irritation response was observed in most cases regardless of the strength of the product tested. Applying the neat acid or salt did not seem to produce a consistently greater effect, rather in some cases the neat powder product was less irritating than some tested formulations, indicating reduced potential of the applied powder product for skin reactivity.

■ Open cuts, abraded or irritated skin should not be exposed to this material.

■ Entry into the blood-stream, through, for example, cuts, abrasions or lesions, may produce systemic injury with harmful effects. Examine the skin prior to the use of the material and ensure that any external damage is suitably protected.

■ The material may cause moderate inflammation of the skin either following direct contact or after a delay of some time. Repeated exposure can cause contact dermatitis which is characterized by redness, swelling and blistering.

INHALED

■ Persons with impaired respiratory function, airway diseases and conditions such as emphysema or chronic bronchitis, may incur further disability if excessive concentrations of particulate are inhaled.

■ The material can cause respiratory irritation in some persons. The body's response to such irritation can cause further lung damage.

CHRONIC HEALTH EFFECTS

■ Limited evidence suggests that repeated or long-term occupational exposure may produce cumulative health effects involving organs or biochemical systems.

Long term exposure to high dust concentrations may cause changes in lung function i.e. pneumoconiosis; caused by particles less than 0.5 micron penetrating and remaining in the lung. Prime symptom is breathlessness; lung shadows show on X-ray.

Long term exposure to organophosphonate chelating agents may cause adverse effects.

Rats fed on aminotri(methylenephosphonic acid) (ATMP), for up to 24 months, exhibited reduced body weight and changes in liver, spleen and kidney weights. No adverse histologic, haematologic, biochemical or urinological effects were seen. The "no-effect" level was 150 mg/kg/day. No significant teratogenic or foetotoxic effects were observed in the off-spring of rats and mice exposed to the neutral sodium salt, by gavage. No maternal toxicity was observed at any level. No adverse treatment related effects or reproductive parameters and no pathological or histopathological lesions were observed in either parental animals or pups following dietary exposure of the solid active acid at various times in the mating and birth cycle for three generations.

Rats fed on ethylenediamine(methylenephosphonic acid) (EDTMP) (300 mg/kg daily for 10 weeks) before mating and up to the end of the mating period, showed reduced body weights, defects in dental enamel on the incisors and significantly reduced liver weights. In an ongoing study, several rats treated with EDTMP (50-333 mg/kg/day) died during the first twelve months and were seen to have osteosarcomas with metastases. Other adverse effects of EDTMP treatment included increased white blood cell counts in mice, anaemia and reduction in erythrocytes, haemoglobin, haematocrit, serum cholesterol, total serum protein and globulin, in rats.

In a one-generation reproductive study the off-spring of rats, fed up to 3000 ppm DTPMPA (diethylenetriaminepentakis(methylenephosphonic acid)), showed no adverse effects although there was a slight decrease in birth weights.

In clinical trials the no-effect level for effects on bone density is 1 mg/day. In preclinical studies, slight focal degeneration (no-observed-effect-level (NOEL) 0.05 mg/kg/day), abnormal endochondral bone maturation (lowest-observed-effect-level (LOEL) 0.01 mg/kg/day) and focal gastritis (NOEL 0.1 mg/kg) were noted in animals. No foetal changes were noted, independent of maternal toxicity, but the pharmacological activity of the material inhibits calcium mobilisation from bone necessary for normal birth (parturition).
Based on mutagenicity and genotoxic studies there does not appear to be a genotoxic risk in man at therapeutic doses.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

HAZARD RATINGS

		Min	Max	
Flammability:	1			
Toxicity:	2			
Body Contact:	2			
Reactivity:	1			
Chronic:	2			

Min/Nil=0
Low=1
Moderate=2
High=3
Extreme=4



NAME	CAS RN	%
sodium alendronate	121268-17-5	>98

Section 4 - FIRST AID MEASURES

SWALLOWED

- IF SWALLOWED, REFER FOR MEDICAL ATTENTION, WHERE POSSIBLE, WITHOUT DELAY.
- Where Medical attention is not immediately available or where the patient is more than 15 minutes from a hospital or unless instructed otherwise:
- For advice, contact a Poisons Information Center or a doctor.
- Urgent hospital treatment is likely to be needed.
- If conscious, give water to drink.
- INDUCE vomiting with fingers down the back of the throat, ONLY IF CONSCIOUS. Lean patient forward or place on left side (head-down position, if possible) to maintain open airway and prevent aspiration.

NOTE: Wear a protective glove when inducing vomiting by mechanical means.

- In the mean time, qualified first-aid personnel should treat the patient following observation and employing supportive measures as indicated by the patient's condition.
- If the services of a medical officer or medical doctor are readily available, the patient should be placed in his/her care and a copy of the MSDS should be provided. Further action will be the responsibility of the medical specialist.
- If medical attention is not available on the worksite or surroundings send the patient to a hospital together with a copy of the MSDS.

EYE

- If this product comes in contact with the eyes:
- Wash out immediately with fresh running water.
- Ensure complete irrigation of the eye by keeping eyelids apart and away from eye and moving the eyelids by occasionally lifting the upper and lower lids.
- If pain persists or recurs seek medical attention.
- Removal of contact lenses after an eye injury should only be undertaken by skilled personnel.

SKIN

- If skin contact occurs:
- Immediately remove all contaminated clothing, including footwear
- Flush skin and hair with running water (and soap if available).
- Seek medical attention in event of irritation.

INHALED

- If fumes or combustion products are inhaled remove from contaminated area.
- Other measures are usually unnecessary.

NOTES TO PHYSICIAN

- for poisons (where specific treatment regime is absent):

BASIC TREATMENT

- Establish a patent airway with suction where necessary.
- Watch for signs of respiratory insufficiency and assist ventilation as necessary.
- Administer oxygen by non-rebreather mask at 10 to 15 l/min.
- Monitor and treat, where necessary, for pulmonary edema .
- Monitor and treat, where necessary, for shock.
- Anticipate seizures .
- DO NOT use emetics. Where ingestion is suspected rinse mouth and give up to 200 ml water (5 ml/kg recommended) for dilution where patient is able to swallow, has a strong gag reflex and does not drool.

ADVANCED TREATMENT

- Consider orotracheal or nasotracheal intubation for airway control in unconscious patient or where respiratory arrest has occurred.
- Positive-pressure ventilation using a bag-valve mask might be of use.
- Monitor and treat, where necessary, for arrhythmias.
- Start an IV D5W TKO. If signs of hypovolemia are present use lactated Ringers solution. Fluid overload might create complications.
- Drug therapy should be considered for pulmonary edema.
- Hypotension with signs of hypovolemia requires the cautious administration of fluids. Fluid overload might create complications.
- Treat seizures with diazepam.
- Proparacaine hydrochloride should be used to assist eye irrigation.

BRONSTEIN, A.C. and CURRANCE, P.L.

EMERGENCY CARE FOR HAZARDOUS MATERIALS EXPOSURE: 2nd Ed. 1994.

Treat symptomatically.

The physicochemical properties of phosphonic acid compounds, notably their high polarity, charge and complexing power, suggests that they will not be readily absorbed from the gastrointestinal tract. This is supported by experimental data which confirm that absorption after oral exposure is low, averaging 2-7% in animals and 2-10% in humans. Faecal elimination of unabsorbed material predominates after ingestion (up to 90% of dose). Renal clearance of any material absorbed from the gut is rapid, with urinary half-lives of 5 hr and 70 hr reported. This second phase of excretion may represent mobilization of material. Initially sequestered by bone, since deposition studies have shown preferential accumulation of these substances in the epiphyseal plate and other regions of the long bones in vivo. Around 25% of material absorbed following an oral dose is excreted unchanged in urine, with the remainder converted to an N-methyl derivative or unidentified product(s). Inconsistent data indicate conversion to carbon dioxide is negligible. More pronounced accumulation is observed in bone after i.v. or i.p. injection, reflecting enhanced bioavailability following exposure by these non-physiological routes. Based on the available data, no major differences appear to exist between animals and humans with regard to the absorption, distribution and elimination of phosphonic acid compounds in vivo.

ATMP acid and ATMP salts are poorly absorbed from the gut and rapidly eliminated after oral and i.v. administration. Faeces represent the principal route of excretion after oral administration with trace amounts present in urine and carcass. Faeces elimination was, in contrast, comparatively insignificant after i.v. injection, with the majority of the dose present either in urine or carcass. Bone is the only tissue that exhibits deposition of test-substance derived radioactivity. Absorption after dermal exposure was very low and only trace amounts were found in urine, faeces and carcass. The main route of excretion was via the urine in the first 24 hours following application.

Gastro-intestinal absorption of HEDP acid and HEDP salts in rat, dog, rabbit and monkey is low, with the majority of the dose excreted in faeces and a substantial amount excreted via the urine. The remainder of the test substance derived radioactivity deposited mainly in the bones. After i.v. or i.p. injection, internal body burdens increased, presumably reflecting greater systemic availability.

Very limited information is available on the absorption, distribution, metabolism and elimination of DTPMP acid and DTPMP salts.

Absorption from the gastrointestinal tract is estimated to be 0.75% after oral doses of 5 and 80 mg. Approximately one-half of the absorbed material is excreted unchanged in the urine in the first two hours (90% of the plasma concentration is eliminated from the plasma within 6 hours). In dogs, additional excretion occurs in several phases with a second phase having a half-life of 1.5 days, the third phase having a half-life of 6-weeks and a fourth phase having a half-life of at least 4 years. The latter phase is thought to represent elimination from the bone and is representative of body burden. The terminal elimination half-life is greater than 10 years in man.

Section 5 - FIRE FIGHTING MEASURES

Vapour Pressure (mmHG):	Negligible
Upper Explosive Limit (%):	Not available.
Specific Gravity (water=1):	Not available
Lower Explosive Limit (%):	Not available

EXTINGUISHING MEDIA

-
- Water spray or fog.
- Foam.
- Dry chemical powder.
- BCF (where regulations permit).
- Carbon dioxide.

FIRE FIGHTING

-
- Alert Emergency Responders and tell them location and nature of hazard.
- Wear breathing apparatus plus protective gloves.
- Prevent, by any means available, spillage from entering drains or water course.
- Use water delivered as a fine spray to control fire and cool adjacent area.
- DO NOT approach containers suspected to be hot.
- Cool fire exposed containers with water spray from a protected location.
- If safe to do so, remove containers from path of fire.
- Equipment should be thoroughly decontaminated after use.

GENERAL FIRE HAZARDS/HAZARDOUS COMBUSTIBLE PRODUCTS

-
- Combustible solid which burns but propagates flame with difficulty.
- Avoid generating dust, particularly clouds of dust in a confined or unventilated space as dusts may form an explosive mixture with air, and any source of ignition, i.e. flame or spark, will cause fire or explosion. Dust clouds generated by the fine grinding of the solid are a particular hazard; accumulations of fine dust may burn rapidly and fiercely if ignited.
- Dry dust can be charged electrostatically by turbulence, pneumatic transport, pouring, in exhaust ducts and during transport.
- Build-up of electrostatic charge may be prevented by bonding and grounding.

- Powder handling equipment such as dust collectors, dryers and mills may require additional protection measures such as explosion venting.

Combustion products include: carbon monoxide (CO), carbon dioxide (CO₂), nitrogen oxides (NO_x), phosphorus oxides (PO_x), other pyrolysis products typical of burning organic material.

FIRE INCOMPATIBILITY

- Avoid contamination with oxidizing agents i.e. nitrates, oxidizing acids, chlorine bleaches, pool chlorine etc. as ignition may result.

PERSONAL PROTECTION

Glasses:

Chemical goggles.

Gloves:

Respirator:

Particulate

Section 6 - ACCIDENTAL RELEASE MEASURES

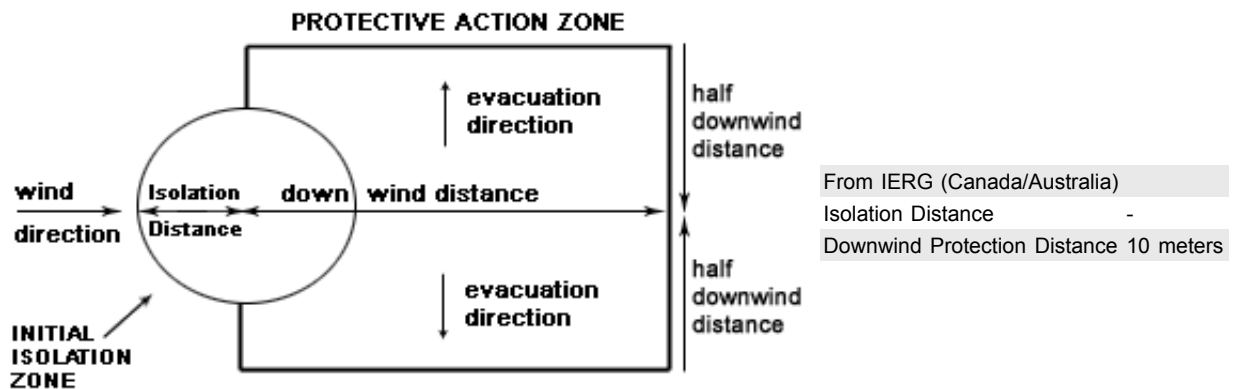
MINOR SPILLS

- Environmental hazard - contain spillage.
- Clean up waste regularly and abnormal spills immediately.
- Avoid breathing dust and contact with skin and eyes.
- Wear protective clothing, gloves, safety glasses and dust respirator.
- Use dry clean up procedures and avoid generating dust.
- Vacuum up or sweep up. NOTE: Vacuum cleaner must be fitted with an exhaust micro filter (HEPA type) (consider explosion-proof machines designed to be grounded during storage and use).
- Dampen with water to prevent dusting before sweeping.
- Place in suitable containers for disposal.

MAJOR SPILLS

- Environmental hazard - contain spillage.
- Moderate hazard.
- CAUTION: Advise personnel in area.
- Alert Emergency Responders and tell them location and nature of hazard.
- Control personal contact by wearing protective clothing.
- Prevent, by any means available, spillage from entering drains or water courses.
- Recover product wherever possible.
- IF DRY: Use dry clean up procedures and avoid generating dust. Collect residues and place in sealed plastic bags or other containers for disposal. IF WET: Vacuum/shovel up and place in labelled containers for disposal.
- ALWAYS: Wash area down with large amounts of water and prevent runoff into drains.
- If contamination of drains or waterways occurs, advise emergency services.

PROTECTIVE ACTIONS FOR SPILL



FOOTNOTES

1 PROTECTIVE ACTION ZONE is defined as the area in which people are at risk of harmful exposure. This zone assumes that random changes in wind direction confines the vapour plume to an area within 30 degrees on either side of the predominant wind direction, resulting in a crosswind protective action distance equal to the downwind protective action distance.

2 PROTECTIVE ACTIONS should be initiated to the extent possible, beginning with those closest to the spill and working away from the site in the downwind direction. Within the protective action zone a level of vapour concentration may exist resulting in nearly all unprotected persons becoming incapacitated and unable to take protective action and/or incurring serious or irreversible health effects.

3 INITIAL ISOLATION ZONE is determined as an area, including upwind of the incident, within which a high probability of localised wind reversal may expose nearly all persons without appropriate protection to life-threatening concentrations of the material.

4 SMALL SPILLS involve a leaking package of 200 litres (55 US gallons) or less, such as a drum (jerrican or box with inner containers). Larger packages leaking less than 200 litres and compressed gas leaking from a small cylinder are also considered "small spills". LARGE SPILLS involve many small leaking packages or a leaking package of greater than 200 litres, such as a cargo tank, portable tank or a "one-tonne" compressed gas cylinder.

5 Guide 171 is taken from the US DOT emergency response guide book.

6 IERG information is derived from CANUTEC - Transport Canada.

ACUTE EXPOSURE GUIDELINE LEVELS (AEGL) (in ppm)

AEGL 1: The airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience notable discomfort, irritation, or certain asymptomatic nonsensory effects. However, the effects are not disabling and are transient and reversible upon cessation of exposure.

AEGL 2: The airborne concentration of a substance above which it is predicted

that the general population, including susceptible individuals, could experience irreversible or other serious, long-lasting adverse health effects or an impaired ability to escape.

AEGL 3: The airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience life-threatening health effects or death.

Section 7 - HANDLING AND STORAGE

PROCEDURE FOR HANDLING

-
- Avoid all personal contact, including inhalation.
- Wear protective clothing when risk of exposure occurs.
- Use in a well-ventilated area.
- Prevent concentration in hollows and sumps.
- DO NOT enter confined spaces until atmosphere has been checked.
- DO NOT allow material to contact humans, exposed food or food utensils.
- Avoid contact with incompatible materials.
- When handling, DO NOT eat, drink or smoke.
- Keep containers securely sealed when not in use.
- Avoid physical damage to containers.
- Always wash hands with soap and water after handling.
- Work clothes should be laundered separately.
- Launder contaminated clothing before re-use.
- Use good occupational work practice.
- Observe manufacturer's storing and handling recommendations.
- Atmosphere should be regularly checked against established exposure standards to ensure safe working conditions are maintained.

Empty containers may contain residual dust which has the potential to accumulate following settling. Such dusts may explode in the presence of an appropriate ignition source.

- Do NOT cut, drill, grind or weld such containers
- In addition ensure such activity is not performed near full, partially empty or empty containers without appropriate workplace safety authorisation or permit.

RECOMMENDED STORAGE METHODS

- Glass container.
- Packaging as recommended by manufacturer.
- Check that containers are clearly labelled.
- Tamper-proof containers.
- Polyethylene or polypropylene containers.
- Metal drum with sealed plastic liner.

STORAGE REQUIREMENTS

- Observe manufacturer's storing and handling recommendations.

SAFE STORAGE WITH OTHER CLASSIFIED CHEMICALS



X: Must not be stored together

O: May be stored together with specific preventions

+: May be stored together

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS

The following materials had no OELs on our records

- sodium alendronate: CAS:121268-17-5

MATERIAL DATA

SODIUM ALENDRONATE:

■ Airborne particulate or vapor must be kept to levels as low as is practicably achievable given access to modern engineering controls and monitoring hardware. Biologically active compounds may produce idiosyncratic effects which are entirely unpredictable on the basis of literature searches and prior clinical experience (both recent and past).

CEL TWA: 0.1 mg/m³ * Merck, Sharp and Dohme

Wipe test criteria: 1 mg/100 cm²

An acceptable daily intake (ADI) of 0.1 mg/day was derived using the no-effect level for effects on bone density that are considered clinically irrelevant. As absorption from the gastrointestinal tract is significantly less than 100% and is likely to be similar in the respiratory tract, no additional safety factor was thought to be necessary.

The exposure limit and wipe test criteria are based on the ADI

PERSONAL PROTECTION



Consult your EHS staff for recommendations

EYE

■ When handling very small quantities of the material eye protection may not be required.

For laboratory, larger scale or bulk handling or where regular exposure in an occupational setting occurs:

- Chemical goggles
- Face shield. Full face shield may be required for supplementary but never for primary protection of eyes
- Contact lenses may pose a special hazard; soft contact lenses may absorb and concentrate irritants. A written policy document, describing the wearing of lens or restrictions on use, should be created for each workplace or task. This should include a review of lens absorption and adsorption for the class of chemicals in use and an account of injury experience. Medical and first-aid personnel should be trained in their removal and suitable equipment should be readily available. In the event of chemical exposure, begin eye irrigation immediately and remove contact lens as soon as practicable. Lens should be removed at the first signs of eye redness or irritation - lens should be removed in a clean environment only after workers have washed hands thoroughly. [CDC NIOSH Current Intelligence Bulletin 59]

HANDS/FEET

■ Suitability and durability of glove type is dependent on usage. Important factors in the selection of gloves include: such as:

- frequency and duration of contact,
- chemical resistance of glove material,
- glove thickness and
- dexterity

Select gloves tested to a relevant standard (e.g. Europe EN 374, US F739).

- When prolonged or frequently repeated contact may occur, a glove with a protection class of 5 or higher (breakthrough time greater than 240 minutes according to EN 374) is recommended.
- When only brief contact is expected, a glove with a protection class of 3 or higher (breakthrough time greater than 60 minutes according to EN 374) is recommended.
- Contaminated gloves should be replaced.

Gloves must only be worn on clean hands. After using gloves, hands should be washed and dried thoroughly. Application of a non-perfumed moisturiser is recommended.

- Rubber gloves (nitrile or low-protein, powder-free latex). Employees allergic to latex gloves should use nitrile gloves in preference.
- Double gloving should be considered.
- PVC gloves.
- Protective shoe covers.
- Head covering.

OTHER

-
- For quantities up to 500 grams a laboratory coat may be suitable.
- For quantities up to 1 kilogram a disposable laboratory coat or coverall of low permeability is recommended. Coveralls should be buttoned at collar and cuffs.
- For quantities over 1 kilogram and manufacturing operations, wear disposable coverall of low permeability and disposable shoe covers.
- For manufacturing operations, air-supplied full body suits may be required for the provision of advanced respiratory protection.
- Eye wash unit.
- Ensure there is ready access to an emergency shower.
- For Emergencies: Vinyl suit

RESPIRATOR

Protection Factor	Half-Face Respirator	Full-Face Respirator	Powered Air Respirator
10 x PEL	P1	-	PAPR-P1
	Air-line*	-	-
50 x PEL	Air-line**	P2	PAPR-P2
100 x PEL	-	P3	-
		Air-line*	-
100+ x PEL	-	Air-line**	PAPR-P3

* - Negative pressure demand ** - Continuous flow

Explanation of Respirator Codes:

Class 1 low to medium absorption capacity filters.

Class 2 medium absorption capacity filters.

Class 3 high absorption capacity filters.

PAPR Powered Air Purifying Respirator (positive pressure) cartridge.

Type A for use against certain organic gases and vapors.

Type AX for use against low boiling point organic compounds (less than 65°C).

Type B for use against certain inorganic gases and other acid gases and vapors.

Type E for use against sulfur dioxide and other acid gases and vapors.

Type K for use against ammonia and organic ammonia derivatives

Class P1 intended for use against mechanically generated particulates of sizes most commonly encountered in industry, e.g. asbestos, silica.

Class P2 intended for use against both mechanically and thermally generated particulates, e.g. metal fume.

Class P3 intended for use against all particulates containing highly toxic materials, e.g. beryllium.

The local concentration of material, quantity and conditions of use determine the type of personal protective equipment required.

Use appropriate NIOSH-certified respirator based on informed professional judgement. In conditions where no reasonable estimate of exposure can be made, assume the exposure is in a concentration IDLH and use NIOSH-certified full face pressure demand SCBA with a minimum service life of 30 minutes, or a combination full facepiece pressure demand SAR with auxiliary self-contained air supply. Respirators provided only for escape from IDLH atmospheres shall be NIOSH-certified for escape from the atmosphere in which they will be used.

ENGINEERING CONTROLS

■ Enclosed local exhaust ventilation is required at points of dust, fume or vapor generation.

HEPA terminated local exhaust ventilation should be considered at point of generation of dust, fumes or vapors.

Barrier protection or laminar flow cabinets should be considered for laboratory scale handling.

The need for respiratory protection should also be assessed where incidental or accidental exposure is anticipated: Dependent on levels of contamination, PAPR, full face air purifying devices with P2 or P3 filters or air supplied respirators should be evaluated.

Fume-hoods and other open-face containment devices are acceptable when face velocities of at least 1 m/s (200 feet/minute) are achieved. Partitions, barriers, and other partial containment technologies are required to prevent migration of the material to uncontrolled areas. For non-routine emergencies maximum local and general exhaust are necessary. Air contaminants generated in the workplace possess varying "escape" velocities which, in turn, determine the "capture velocities" of fresh circulating air required to effectively remove the contaminant.

Type of Contaminant:	Air Speed:
solvent, vapors, etc. evaporating from tank (in still air)	0.25-0.5 m/s (50-100 f/min.)
aerosols, fumes from pouring operations, intermittent container filling, low speed conveyor transfers (released at low velocity into zone of active generation)	0.5-1 m/s (100-200 f/min.)
direct spray, drum filling, conveyor loading, crusher dusts, gas discharge (active generation into zone of rapid air motion)	1-2.5 m/s (200-500 f/min.)

Within each range the appropriate value depends on:

Lower end of the range	Upper end of the range
1: Room air currents minimal or favourable to capture	1: Disturbing room air currents
2: Contaminants of low toxicity or of nuisance value only.	2: Contaminants of high toxicity
3: Intermittent, low production.	3: High production, heavy use
4: Large hood or large air mass in motion	4: Small hood-local control only

Simple theory shows that air velocity falls rapidly with distance away from the opening of a simple extraction pipe. Velocity generally decreases with the square of distance from the extraction point (in simple cases). Therefore the air speed at the extraction point should be adjusted, accordingly, after reference to distance from the contaminating source. The air velocity at the extraction fan, for example, should be a minimum of 1-2.5 m/s (200-500 f/min.) for extraction of gases discharged 2 meters distant from the extraction point. Other mechanical considerations, producing performance deficits within the extraction apparatus, make it essential that theoretical air velocities are multiplied by factors of 10 or more when extraction systems are installed or used.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES

Solid.

Mixes with water.

State	Divided solid	Molecular Weight	325.13
Melting Range (°F)	482- 536 (decomp)	Viscosity	Not Applicable
Boiling Range (°F)	Not available	Solubility in water (g/L)	Miscible
Flash Point (°F)	Not available	pH (1% solution)	4.3
Decomposition Temp (°F)	Not available.	pH (as supplied)	Not applicable
Autoignition Temp (°F)	Not available	Vapour Pressure (mmHG)	Negligible
Upper Explosive Limit (%)	Not available.	Specific Gravity (water=1)	Not available
Lower Explosive Limit (%)	Not available	Relative Vapor Density (air=1)	>1
Volatile Component (%vol)	Negligible	Evaporation Rate	Not applicable

APPEARANCE

White, free-flowing crystalline powder; mixes with water (40 g/l, 25 C).

Section 10 - CHEMICAL STABILITY

CONDITIONS CONTRIBUTING TO INSTABILITY

-
- Presence of incompatible materials.
- Product is considered stable.
- Hazardous polymerization will not occur.

STORAGE INCOMPATIBILITY

- Avoid reaction with oxidizing agents.

For incompatible materials - refer to Section 7 - Handling and Storage.

Section 11 - TOXICOLOGICAL INFORMATION

sodium alendronate

TOXICITY AND IRRITATION

■ unless otherwise specified data extracted from RTECS - Register of Toxic Effects of Chemical Substances.

TOXICITY	IRRITATION
Oral (rat) LD50: 552 mg/kg *	Eye (rabbit): SEVERE *
Oral (mouse) LD50: 978 mg/kg *	Skin (rabbit): SEVERE *

■ The material may produce severe irritation to the eye causing pronounced inflammation. Repeated or prolonged exposure to irritants may produce conjunctivitis.

Asthma-like symptoms may continue for months or even years after exposure to the material ceases. This may be due to a non-allergic condition known as reactive airways dysfunction syndrome (RADS) which can occur following exposure to high levels of highly irritating compound. Key criteria for the diagnosis of RADS include the absence of preceding respiratory disease, in a non-atopic individual, with abrupt onset of persistent asthma-like symptoms within minutes to hours of a documented exposure to the irritant. A reversible airflow pattern, on spirometry, with the presence of moderate to severe bronchial hyperreactivity on methacholine challenge testing and the lack of minimal lymphocytic inflammation, without eosinophilia, have also been included in the criteria for diagnosis of RADS. RADS (or asthma) following an irritating inhalation is an infrequent disorder with rates related to the concentration of and duration of exposure to the irritating substance. Industrial bronchitis, on the other hand, is a disorder that occurs as result of exposure due to high concentrations of irritating substance (often particulate in nature) and is completely reversible after exposure ceases. The disorder is characterised by dyspnea, cough and mucus production.

The material may produce respiratory tract irritation, and result in damage to the lung including reduced lung function.

The material may cause severe skin irritation after prolonged or repeated exposure and may produce on contact skin redness, swelling, the production of vesicles, scaling and thickening of the skin. Repeated exposures may produce severe ulceration.

For phosphonic acid and its salts:

Phosphonic acids and their salts have not been shown to induce skin sensitisation in guinea pigs. None of the studies however follow OECD guidelines or were GLP compliant. However, only the investigation on the disodium salt of HEDP was recorded to a standard sufficient to support the robustness and reliability of the study design and conduct. Most studies were not reported in great detail, but they stated the adherence to well established protocol such as Buehler or Magnusson and Kligman. The information available provided, however, a coherent picture in that these compounds should not be considered skin sensitisers. The acids or salts of ATMP, HEDP and DTPMP did not show any carcinogenic activity when tested in rodents.

The effects of ATMP acid and its salts on the reproductive system can be evaluated on the basis of a well conducted 3-generation reproductive toxicity study. Although the study predated current guidelines (e.g., no evaluation of the oestrus cycle, sperm parameters and developmental milestones), the overall evidence suggests that ATMP acid and its salts are not selectively toxic to the male or female reproductive system. The absence of effects on the reproductive organs in well conducted subchronic and chronic toxicity studies with ATMP provides further support to this assessment. On the basis of a 3-generation reproductive toxicity study and also a well conducted FDA segment II study, there is further no evidence for foetotoxic or teratogenic effects of ATMP. In the absence of any guideline compliant reproductive toxicity studies, the reproductive toxicity of HEDP acid can be evaluated on the basis of subchronic oral feeding studies in rats and dogs which did not reveal any effects on the reproductive system at exposures up to 1500-1800 mg/kg bw/d. There were also no effects on fertility (i.e., indicated by the pregnancy rate) of the disodium salt of HEDP when fed at doses up to 447 mg/kg bw/d to rats in a 2-generation study. The reproductive toxicity of DTPMP acid and its salts can be evaluated on the basis of a well conducted 2-generation study in which Long Evan rats fed with DTPMP containing diet at levels up to 312 mg acid/kg bw/d. Although in this study, some alterations were observed with regard to a lower pregnancy rate in F2 (i.e., not statistically significant) and reduced pup body weight in F2a (i.e., statistically significant), these effects were not considered to be of biological significance as they were either not observed in F1 or could not be replicated in F2b. The absence of effects on the reproductive system could further be confirmed in an OECD guideline compliant subchronic toxicity study.

Generally, from a structure activity standpoint, none of the phosphonates possess structural elements that indicate the potential for genotoxicity.

Neither ATMP acid nor the salt induced gene mutations in bacterial systems. When testing ATMP acid in the acid form, it induced dose-dependent gene mutations in mouse lymphoma cells. However, this positive result was demonstrated to be an artefact of pH which was not observed when neutralized ATMP acid was tested in the in vitro mouse lymphoma assay up to the solubility limit. The pentasodium salt of ATMP did not induce chromosome damage either in vitro or in vivo.

The available data on in vivo and in vitro genotoxicity of HEDP and its salts indicate no potential of HEDP and its salts to cause mutagenicity in bacterial mutagenicity assays. Conflicting results were obtained in an in vitro mouse lymphoma assay. In this assay, a dose-dependent positive response was seen in the presence of metabolic activation which was, however, discounted because of high control values.

Both, DTPMP acid and the salt were negative in well performed and guideline compliant bacterial mutagenicity assays. DTPMP acid was further negative for gene mutations at the HPRT locus in CHO cells. Similarly to HEDP acid, the evidence for mutagenic potential is conflicting. While the salt of DTPMP was negative for mammalian gene mutations, DTPMP acid, even when neutralised, induced mutations at the thymidine kinase locus in mouse lymphoma L5178Y cells. Since pH effect has been excluded and increased osmolality is an unlikely cause (positive response was only seen in presence of S9 mix), it is possible that chelation of essential ions may have caused the positive response in the presence of S9. Iron chelation appears to play a role in contributing to positive responses in the mouse lymphoma assay.

HERA (Human and Environmental Risk Assessment on ingredients of European household cleaning products) - Phosphonates
Oral bisphosphonates (given in certain medical treatments) can give stomach upset and inflammation and erosions of the esophagus, which is the main problem of oral N-containing preparations. This can be prevented by remaining seated upright for 30 to 60 minutes after taking the medication. Intravenous bisphosphonates can give fever and flu-like symptoms after the first infusion, which is thought to occur because of their potential to activate human T cells. Notably, these symptoms do not recur with subsequent infusions. There is a slightly increased risk for electrolyte disturbances, but not enough to warrant regular monitoring. In chronic renal failure, the drugs are excreted much slower, and dose adjustment is required. Bisphosphonates have been associated with osteonecrosis of the jaw; with the mandible twice as frequently affected as the maxilla and most cases occurring following high-dose intravenous administration used for some cancer patients. Some 60% of cases are preceded by a dental surgical procedure and it has been suggested that bisphosphonate treatment should be postponed until after any dental work to eliminate potential sites of infection. A number of cases of severe bone, joint, or musculoskeletal pain have been reported, prompting labeling changes.

Bisphosphonates are incorporated into the bone matrix, from where they are gradually released over periods of weeks to years. The extent of bisphosphonate incorporation into adult bone, and hence, the amount available for release back into the systemic circulation, is directly related to the total dose and duration of bisphosphonate use. Although there are no data on foetal risk in humans, bisphosphonates do cause foetal harm in animals, and animal data suggest that uptake of bisphosphonates into foetal bone is greater than into maternal bone. Therefore, there is a theoretical risk of foetal harm (e.g., skeletal and other abnormalities) if a woman becomes pregnant after completing a course of bisphosphonate therapy. The impact of variables such as time between cessation of bisphosphonate therapy to conception, the particular bisphosphonate used, and the route of

administration (intravenous versus oral) on this risk has not been established.

The non-nitrogenous bisphosphonates (disphosphonates) are metabolised in the cell to compounds that compete with adenosine triphosphate (ATP) in the cellular energy metabolism. The osteoclast initiates apoptosis and dies, leading to an overall decrease in the breakdown of bone.

Nitrogenous bisphosphonates act on bone metabolism by binding and blocking the enzyme farnesyl diphosphate synthase (FPPS) in the HMG-CoA reductase pathway (also known as the mevalonate pathway). Disruption of the HMG CoA-reductase pathway at the level of FPPS prevents the formation of two metabolites (farnesol and geranylgeraniol) that are essential for connecting some small proteins to the cell membrane. This phenomenon is known as prenylation, and is important for proper sub-cellular protein trafficking.

ADI: 1 mg/day

Changes in structure/ function of oesophagus, gastrointestinal changes, ptosis, somnolence, stomach ulceration, ataxia, nausea, vomiting, body temperature increase, pigmented or nucleated red blood cells, changes in erythrocyte count, maternal effects, effects on newborn recorded.

* Merckle, Sharp and Dohme

Section 12 - ECOLOGICAL INFORMATION

Refer to data for ingredients, which follows:

SODIUM ALENDRONATE:

■ May cause long-term adverse effects in the aquatic environment.

■ Do NOT allow product to come in contact with surface waters or to intertidal areas below the mean high water mark. Do not contaminate water when cleaning equipment or disposing of equipment wash-waters.

Wastes resulting from use of the product must be disposed of on site or at approved waste sites.

■ The principal problems of phosphate contamination of the environment relates to eutrophication processes in lakes and ponds. Phosphorus is an essential plant nutrient and is usually the limiting nutrient for blue-green algae. A lake undergoing eutrophication shows a rapid growth of algae in surface waters. Planktonic algae cause turbidity and flotation films. Shore algae cause ugly muddying, films and damage to reeds. Decay of these algae causes oxygen depletion in the deep water and shallow water near the shore. The process is self-perpetuating because anoxic conditions at the sediment/ water interface causes the release of more adsorbed phosphates from the sediment. The growth of algae produces undesirable effects on the treatment of water for drinking purposes, on fisheries, and on the use of lakes for recreational purposes.

■ For phosphonates:

The physico-chemical characteristics determining the health and environmental behaviour of phosphonates are: high water solubility, non-volatility, very low octanol-water partition coefficients, moderate to high sorption coefficients, multi-protic acidity and strong (transition) metal complexation

Environmental fate:

Biodegradation: Orthophosphate has been found to suppress phosphonate utilisation in many microorganisms. Thus organisms preferentially use inorganic phosphate, which may explain the low biodegradability of phosphonates in synthetic test media and natural sewage systems. The classical tests, such as the OECD screening test, BOD20 test or the closed bottle test show only a low degree of ultimate biodegradation of phosphonate derivatives. For ATMP and HEDP a DOC (Dissolved Organic Carbon) removal of 23 - 33 % was observed in an inherent biodegradability test (Zahn-Wellens test), but mineralisation was very low even after long-term incubation. However, several studies have shown that phosphonate degrading bacteria can be found in almost any environment whether soil, activated sludge or river water. At low ortho-phosphate concentration, i.e. if phosphate is the growth-limiting factor, phosphonate degradation occurs with almost complete breakdown of HEDP (94 %). DTPMP showed 60 % degradation under similar conditions. No quantitative study was done for ATMP. These phosphate-limited conditions are not likely to occur in most environments. Inherent biodegradation tests (Zahn-Wellens, SCAS testing) also indicate a low degree of biodegradation under the standard test conditions. For example, biodegradation of radiolabelled ATMP, HEDP and DTPMP resulted in SCAS tests in 0.5 to 10.2 % release of $^{14}\text{CO}_2$ over a 210 day period. As a consequence, it is assumed that biodegradation does not occur in sewage treatment plants.

Degradation does occur in the presence of river sediment; however studies indicate that phosphonates become tightly bound onto the sediment, for a significant part irreversibly. This leads to the conclusion that the major part of the (bio)degradation may occur in the sediment but not in the water phase. Half-lives for this degradation were calculated, assuming an exponential decay, from the average measured values, i.e. for ATMP 8.8% in 50 days, for HEDP 7.1 % in 50 days and for DTPMP 15.9% in 50 days and 29.6 % in 38 days. The corresponding half-lives are 376 days for ATMP, 471 days for HEDP and 200 days and 75 days for DTPMP. For the latter a half-life of 137.5 days was used in the assessment.

Anaerobic degradation has not been studied extensively. It has been reported only minor conversion of ATMP and HEDP occurs in model digestors. No inhibitory effect was observed neither for ATMP up to 100 mg/liter and for HEDP up to 5 mg/g dry sludge.

In soils, biodegradation of DTPMP has been shown. ATMP and HEDP also show degradation, but slower than DTPMP. When sludges or sediments are disposed of at land, this will ensure mineralisation and removal from the environment.

Hydrolysis: Phosphonates are quite stable in water as evidenced by the dark controls in the photolysis studies. However it was found that ATMP would hydrolyse fairly easily at low concentrations (70 ppb) with complete primary degradation in a few days. Another study reported 37 % degradation of HEDP in the presence of copper ions. Yet another study on the hydrolysis of phosphonates came to the conclusion that metal ions, aerobic conditions and light were favourable conditions of the hydrolysis/degradation of these substances. Although hydrolytic degradation mechanisms have been identified, they appear to be strongly dependent on the specific environmental conditions, and in particular on the presences of certain metal ions and light. Hydrolysis half-lives in the range of 50 -200 days at 15 ? 25 °C have been calculated. In colder environments the half-life for hydrolysis might be of the same order as biodegradation.

Photodegradation: Photodegradation is another important route of the environmental removal of phosphonates. It is catalysed by transition metal ions and is pH dependent. It is especially pronounced in the presence of iron ions when 40 to 90 % degradation of the phosphonate-residues to ortho-phosphate occurs in 17 days. Other transition metals also stimulate photodegradation, in particular for HEDP. Further studies on HEDP confirmed these findings. HEDP was found to be degradable in river waters at neutral pH simulating day-light conditions. The rate of degradation was concentration dependent. At 3 mg/l, 70% was degraded in 8 days, at 10 mg/l, only 12.5 % was degraded. The half life was estimated at about. 100 hrs at 3 mg/l.

Bioaccumulation: As expected for highly water-soluble substances, the log Kow values for phosphonates are low (ATMP: -3.53; HEDP: -3.49; EDTMP: -4.10; HDTMP: -4.43; DTMPP: -3.40). The potential for bioaccumulation of phosphonates in aquatic organisms is therefore expected to be low as well. Experimental bioconcentration studies with zebra fish have been conducted with radiolabelled ATMP and HEDP. For both substances, the BCF values determined after 4-6 weeks of exposure were less than 24.

Metal remobilisation: Metal remobilisation is the re-dissolution of metals such as zinc, copper, chromium, cadmium, mercury etc., which are precipitated in river and lake sediments. This could lead to several problems: increased exposure of water life to these metals at toxic levels, and passing through of the metal to drinking water abstracted from surface water. It has been suggested that the increased metal concentrations may stimulate algal growth, leading to algae blooms in summer.

Studies have shown that phosphonates only remobilise metals at concentrations of at least 100 to 300 ppb. This is well above the predicted environmental concentration of less than 1 ppb. Even at concentrations estimated for a worst case situation of 10 to 30 ppb, no metal remobilisation is expected.

Ecotoxicity

Chelating agents can inhibit algae growth, due to complexation of essential nutrients. The 96 hours EC50 values for the species *Selenastrum* range from 0.45 mg/L for DTPMP up to 12 mg/L for ATMP. Very large differences have been observed between species. In an 8-day study the effect concentration (EC50) for *Chlorella* was well above 10 mg/l for all phosphonates. With many chelating agents, algal growth inhibition results may be strongly affected by chelation of trace metal nutrients. This is often interpreted incorrectly as a toxic effect on algae, whereas the real cause is nutrient limitation. It may also induce a high degree of variability between test labs and individual tests, due to variations in the organisms tested and small variations in the test medium composition.

Tests on invertebrates (*Chironomus*, *Daphnia*, Grass shrimp) show low toxicity. The most sensitive species is *Daphnia magna* with 24 and 48 hours LC50 values of 165 to 242 mg/l.

Phosphonates were tested on a number of fish species and demonstrated a low toxicity to fish; the 96 hours LC50 values range from 125 (48 hours) to > 2400 mg/l for freshwater fish (Bluegill Sunfish, Channel Catfish and Rainbow Trout), and from > 1000 up to 8132 mg/l for marine fish (Sheepshead minnow). All phosphonates were tested for 14 days on rainbow trout LC50 values ranged from 150 to >262 mg/l. NOEC's based on mortality and behaviour ranged from 47 mg/l (ATMP) to 139 mg/l (DTPMP).

Because of their chelating properties, a small effect is observed on oysters (Eastern oyster) due to interference with the shell building metabolism. The 96 hours EC50 ranges from 67 to 200 mg/L, with NOEC's of 55 to 95 mg/l.

The acute toxicity of ATMP and HEDP towards microorganisms relevant for sewage treatment plants was investigated in a bacterial respiration inhibition test with *Pseudomonas putida* showing EC0 values of >500 mg/l. The toxicity to microorganisms using a photoluminescence test. The EC50 was above 2500 mg/l for ATMP and DTPMP and above 250 mg/l for HEDP.

Test data on earthworm (*Eisenia foetida*) show low toxicity of ATMP and HEDP with 14 day NOEC of 1000 mg/kg soil dw and > 1000 mg/kg soil dw.

HERA (Human and Environmental Risk Assessment on ingredients of European household cleaning products) - Phosphonates.

■ DO NOT discharge into sewer or waterways.

Ecotoxicology:

Fish LC50 (96 h): rainbow trout 1000 mg/l (practically non-toxic)

(48 h): fathead minnow 1450 mg/l (practically non-toxic)

Daphnia magna (48 h) 21.7 mg/l (slightly toxic to marine organisms)

Environmental fate:

The material is freely soluble in water and has a low potential for bioaccumulation. It is stable in the aquatic environment and under natural light in aquatic media. Test studies indicate that alendronate sodium is not readily biodegradable and no biological inhibition of activated sludge

was seen at concentrations of less than or equal to 4320 g/l.

Section 13 - DISPOSAL CONSIDERATIONS

Disposal Instructions

All waste must be handled in accordance with local, state and federal regulations.

! Puncture containers to prevent re-use and bury at an authorized landfill.

Legislation addressing waste disposal requirements may differ by country, state and/ or territory. Each user must refer to laws operating in their area. In some areas, certain wastes must be tracked.

A Hierarchy of Controls seems to be common - the user should investigate:

- Reduction
- Reuse
- Recycling
- Disposal (if all else fails)

This material may be recycled if unused, or if it has not been contaminated so as to make it unsuitable for its intended use. Shelf life considerations should also be applied in making decisions of this type. Note that properties of a material may change in use, and recycling or reuse may not always be appropriate.

DO NOT allow wash water from cleaning equipment to enter drains. Collect all wash water for treatment before disposal.

- Recycle wherever possible.
- Consult manufacturer for recycling options or consult Waste Management Authority for disposal if no suitable treatment or disposal facility can be identified.
- Dispose of by: Burial in a licensed land-fill or Incineration in a licensed apparatus (after admixture with suitable combustible material)
- Decontaminate empty containers. Observe all label safeguards until containers are cleaned and destroyed.

Section 14 - TRANSPORTATION INFORMATION



DOT:

Symbols:	G	Hazard class or Division:	9
Identification Numbers:	UN3077	PG:	III
Label Codes:	9	Special provisions:	8, 146, 335, B54, IB8, IP3, N20, T1, TP33
Packaging: Exceptions:	155	Packaging: Non-bulk:	213
Packaging: Exceptions:	155	Quantity limitations: Passenger aircraft/rail:	No limit

Quantity Limitations: Cargo aircraft only:	No limit	Vessel stowage: Location:	A
Vessel stowage: Other:	None		
Hazardous materials descriptions and proper shipping names: Environmentally hazardous substance, solid, n.o.s			
Air Transport IATA:			
ICAO/IATA Class:	9	ICAO/IATA Subrisk:	III
UN/ID Number:	3077	Packing Group:	III
Special provisions:	A97		
Shipping Name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. *(CONTAINS SODIUM ALENDRONATE)			
Maritime Transport IMDG:			
IMDG Class:	9	IMDG Subrisk:	None
UN Number:	3077	Packing Group:	III
EMS Number:	F-A,S-F	Special provisions:	274 909 944
Limited Quantities:	5 kg		
Shipping Name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S.(contains sodium alendronate)			

Section 15 - REGULATORY INFORMATION

sodium alendronate (CAS: 121268-17-5) is found on the following regulatory lists;

"US - California Air Toxics ""Hot Spots"" List (Assembly Bill 2588) Substances for which emissions must be quantified"

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE

- Cumulative effects may result following exposure*.
 - May produce discomfort of the respiratory system*.
- * (limited evidence).

Reasonable care has been taken in the preparation of this information, but the author makes no warranty of merchantability or any other warranty, expressed or implied, with respect to this information. The author makes no representations and assumes no liability for any direct, incidental or consequential damages resulting from its use. For additional technical information please call our toxicology department on +800 CHEMCALL.

- Classification of the mixture and its individual components has drawn on official and authoritative sources as well as independent review by the Chemwatch Classification committee using available literature references.

A list of reference resources used to assist the committee may be found at:
www.chemwatch.net/references.

- The (M)SDS is a Hazard Communication tool and should be used to assist in the Risk Assessment. Many factors determine whether the reported Hazards are Risks in the workplace or other settings. Risks may be determined by reference to Exposures Scenarios. Scale of use, frequency of use and current or available engineering controls must be considered.

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Issue Date: Jan-8-2008

Print Date: Apr-21-2010