

Zoledronic acid hydrate

sc-202859



The Power to Question

Material Safety Data Sheet

Hazard Alert Code
Key:

EXTREME

HIGH

MODERATE

LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

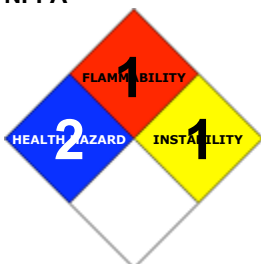
PRODUCT NAME

Zoledronic acid hydrate

STATEMENT OF HAZARDOUS NATURE

CONSIDERED A HAZARDOUS SUBSTANCE ACCORDING TO OSHA 29 CFR 1910.1200.

NFPA



SUPPLIER

Santa Cruz Biotechnology, Inc.
2145 Delaware Avenue
Santa Cruz, California 95060
800.457.3801 or 831.457.3800

EMERGENCY

ChemWatch
Within the US & Canada: 877-715-9305
Outside the US & Canada: +800 2436 2255
(1-800-CHEMCALL) or call +613 9573 3112

SYNONYMS

C5H10N2O7P2 • H2O

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS

| | Min | Max | |
|---------------|-----|-----|---|
| Flammability: | 1 | | |
| Toxicity: | 2 | | |
| Body Contact: | 3 | | |
| Reactivity: | 1 | | Min/Nil=0 Low=1 Moderate=2 High=3 Extreme=4 |
| Chronic: | 2 | | |

CANADIAN WHMIS SYMBOLS



EMERGENCY OVERVIEW

RISK

Possible risk of impaired fertility.

Possible risk of harm to the unborn child.

Harmful: danger of serious damage to health by prolonged exposure through inhalation.

Harmful: danger of serious damage to health by prolonged exposure if swallowed.

Harmful by inhalation, in contact with skin and if swallowed.

Irritating to eyes and skin.

Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

Cumulative effects may result following exposure*.

Eye contact may produce serious damage*.

* (limited evidence).

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 toxicity when swallowed.

Animal testing has shown ATMP acid to be of moderate toxicity, with an oral LD50 in rat of 2910 mg active acid/kg.

EYE

■ This material can cause eye irritation and damage in some persons.

■ The phosphonic acid compounds, ATMP, HEDP, DTPMP and their salts vary in their potential to irritate the eye, from virtually non-irritating to severely irritating with irreversible effects.

Animal testing showed that ATMP and its salts were at most moderate irritating, while HEDP acid was found to be severely irritating, its salts being less so.

■ If applied to the eyes, this material causes severe eye damage.

SKIN

■ Skin contact with the material may be harmful; systemic effects may result following absorption.

■ This material can cause inflammation of the skin on contact in some persons.

■ The material may accentuate any pre-existing dermatitis condition.

■ The acids and salts of ATMP, HEDP and DTPMP have a low level of acute skin toxicity.

ATMP acid and its salts, in testing, were found to be practically non-toxic.

■ 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.

INHALED

■ Inhalation of dusts, generated by the material, during the course of normal handling, may be harmful.

■ The material is not thought to produce respiratory irritation (as classified by EC Directives using animal models).

Nevertheless inhalation of dusts, or fumes, especially for prolonged periods, may produce respiratory discomfort and occasionally, distress.

■ 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.

If prior damage to the circulatory or nervous systems has occurred or if kidney damage has been sustained, proper screenings should be conducted on individuals who may be exposed to further risk if handling and use of the material result in excessive exposures.

CHRONIC HEALTH EFFECTS

■ Harmful: danger of serious damage to health by prolonged exposure if swallowed.

This material can cause serious damage if one is exposed to it for long periods. It can be assumed that it contains a substance which can produce severe defects. This has been demonstrated via both short- and long-term experimentation.

Ample evidence from experiments exists that there is a suspicion this material directly reduces fertility.

Based on experience with animal studies, exposure to the material may result in toxic effects to the development of the foetus, at levels which do not cause significant toxic effects to the mother.

Substance accumulation, in the human body, may occur and may cause some concern following repeated or long-term occupational exposure.

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.

Although the salt of the organophosphate has not been tested, animal testing on the free acid aminotris(methylenephosphonic) acid revealed loss in body weight and changes in the weight of the liver, spleen and kidney.

Imidazole is structurally related, and has been used to counteract the effects of histamine. Imidazoles have been reported to disrupt

male fertility, through disruption of the function of the testes.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

| NAME | CAS RN | % |
|-------------------------|-------------|-----|
| Zoledronic acid hydrate | 165800-06-6 | >98 |

Section 4 - FIRST AID MEASURES

SWALLOWED

- IF SWALLOWED, REFER FOR MEDICAL ATTENTION, WHERE POSSIBLE, WITHOUT DELAY.
- For advice, contact a Poisons Information Centre or a doctor.
- Urgent hospital treatment is likely to be needed.
- 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.

EYE

If this product comes in contact with the eyes:

- Immediately hold eyelids apart and flush the eye continuously with 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.
- Continue flushing until advised to stop by the Poisons Information Centre or a doctor, or for at least 15 minutes.
- Transport to hospital or doctor without delay.

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.
- Lay patient down. Keep warm and rested.
- Prostheses such as false teeth, which may block airway, should be removed, where possible, prior to initiating first aid procedures.
- Apply artificial respiration if not breathing, preferably with a demand valve resuscitator, bag-valve mask device, or pocket mask as trained. Perform CPR if necessary.

NOTES TO PHYSICIAN

- 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.

Clinical experience with acute overdosage of zoledronic acid is limited. Two patients received Zometa 32 mg over 5 minutes in clinical trials. Neither patient experienced any clinical or laboratory toxicity. Overdosage may cause clinically significant hypocalcemia, hypophosphatemia, and hypomagnesemia. Clinically relevant reductions in serum levels of calcium, phosphorus, and magnesium should be corrected by intravenous administration of calcium gluconate, potassium or sodium phosphate, and magnesium sulfate, respectively.

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

- Foam.
- Dry chemical powder.
- BCF (where regulations permit).
- Carbon dioxide.

FIRE FIGHTING

- Alert Fire Brigade 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 courses.
- Use water delivered as a fine spray to control fire and cool adjacent area.

When any large container (including road and rail tankers) is involved in a fire, consider evacuation by 100 metres in all directions.

GENERAL FIRE HAZARDS/HAZARDOUS COMBUSTIBLE PRODUCTS

- Combustible.
- Slight fire hazard when exposed to heat or flame.
- Acids may react with metals to produce hydrogen, a highly flammable and explosive gas.
- Heating may cause expansion or decomposition leading to violent rupture of containers.

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.

Isoperibolic decomposition (>8 h): 170 deg C (air open cup): Method Radex isoperibolic (long duration decomposition test open cup 16 h). Exothermal decomposition may occur with delay (autocatalysis)

Dynamic decomposition: 170 deg C (air open cup) 274 J/g Method: Radex dynamic decomposition test (temp. progr. 0.75 deg C/ min, examined up to 360 deg C). Reaction spontaneous exothermic

: 200 deg C (air open cup) Method: Grewer test method, air stream, as is (temp. progr. 1.2 deg / min, examined up to 350 deg C). Exothermic decomposition may occur with delay (autocatalysis)

: 220 deg C (air open cup) Method: Lutolf, open cup, as is (temp. progr. 2.5 deg C/ min, examined up to 350 deg C)

Combustibility (EC Method) Not highly flammable Method: 92/69/EC (L383) 10* flammability (solids)

Standard conditions: 2 = after ignition the fire dies out rapidly Method: Combustibility test safety laboratory

Dust Explosion Test: Positive: Min. dec. Energy >1 J Method: Modified Hartmann tube

Positive: Min de. Energy 1-2000 J: Method 20 lt ball at 10,000 Joule

Deflagration Test: No suspicion

Drop Weight Test: negative Method: Lutolf test method

FIRE INCOMPATIBILITY

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

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.

MAJOR SPILLS

Environmental hazard - contain spillage.

Moderate hazard.

- CAUTION: Advise personnel in area.
- Alert Emergency Services 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.

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.

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

- Lined metal can, lined metal pail/ can.
- Plastic pail.
- Polyliner drum.
- Packing as recommended by manufacturer.
- Glass container is suitable for laboratory quantities
- DO NOT use aluminium or galvanised containers

STORAGE REQUIREMENTS

- Store in original containers.
- Keep containers securely sealed.
- Store in a cool, dry area protected from environmental extremes.

- Store away from incompatible materials and foodstuff containers.

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS

The following materials had no OELs on our records

- zoledronic acid: CAS:118072-93-8 CAS:165800-06-6

PERSONAL PROTECTION



RESPIRATOR

- Particulate dust filter. (AS/NZS 1716 & 1715, EN 143:2000 & 149:2001, ANSI Z88 or national equivalent)

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], [AS/NZS 1336 or national equivalent]

HANDS/FEET

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

- frequency and duration of contact,
- chemical resistance of glove material,
- glove thickness and
- dexterity
- 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. [AS/NZS 2210]

Experience indicates that the following polymers are suitable as glove materials for protection against undissolved, dry solids, where abrasive particles are not present.

- polychloroprene
- nitrile rubber
- butyl rubber
- fluorocautchouc

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.

ENGINEERING CONTROLS

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

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

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

When handling quantities up to 500 gram in either a standard laboratory with general dilution ventilation (e.g. 6-12 air changes per hour) is preferred.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES

| | | | |
|---------------------------|-----------------|---------------------------------|-----------------|
| State | DIVIDED SOLID | Molecular Weight | 290.1 |
| Melting Range (°F) | 462(decomposes) | Viscosity | Not Applicable |
| Boiling Range (°F) | Not Applicable | Solubility in water (g/L) | Partly Miscible |
| Flash Point (°F) | Not Available | pH (1% solution) | 2 (0.7% sol) |
| Decomposition Temp (°F) | 462BAM | pH (as supplied) | Not Applicable |
| Autoignition Temp (°F) | 860 | Vapour Pressure (mmHG) | Negligible |
| Upper Explosive Limit (%) | Not Available | Specific Gravity (water=1) | Not Available |
| Lower Explosive Limit (%) | Not Available | Relative Vapour Density (air=1) | Not Applicable |
| Volatile Component (%vol) | Negligible | Evaporation Rate | Not Applicable |

APPEARANCE

Crystalline powder ; does not mix well with water (7 g/l). Zoledronic acid is highly soluble in 0.1N sodium hydroxide solution, sparingly soluble in water and 0.1N hydrochloric acid, and practically insoluble in organic solvents. Solubilities (g/l, 25 C): methanol 0.12, ethanol 0.13 The pH of a 0.7% solution of zoledronic acid in water is approximately 2.0.

Section 10 - CHEMICAL STABILITY

CONDITIONS CONTRIBUTING TO INSTABILITY

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

STORAGE INCOMPATIBILITY

- Reacts with mild steel, galvanised steel / zinc producing hydrogen gas which may form an explosive mixture with air.
- Avoid strong bases.
- Avoid reaction with oxidising agents

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

Section 11 - TOXICOLOGICAL INFORMATION

zoledronic acid

TOXICITY AND IRRITATION

■ Animal testing to date have not shown phosphonic acids or their salts to induce skin sensitisation. However, testing has been incomplete.

Animal testing have not shown that the acids or salts of ATMP, HEDP and DTPMP cause cancer. Overall, the data shows that ATMP and HEDP do not cause toxicity to the reproductive system. Data for DTPMP is less clear, but any effects were not considered to be of biological significance.

From a structural activity standpoint, none of the phosphonates possess structural components indicating the potential for genetic toxicity. In animal testing, there is no significant evidence that mutations are caused by phosphonates and their salts.

Asthma-like symptoms may continue for months or even years after exposure to the material ceases. This may be due to a non-allergenic condition known as reactive airways dysfunction syndrome (RADS) which can occur following exposure to high levels of highly irritating compound.

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

Section 12 - ECOLOGICAL INFORMATION

Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

This material and its container must be disposed of as hazardous waste.

Avoid release to the environment.

Refer to special instructions/ safety data sheets.

Ecotoxicity

| Ingredient | Persistence: Water/Soil | Persistence: Air | Bioaccumulation | Mobility |
|-----------------|----------------------------|-------------------|-----------------|----------|
| zoledronic acid | No Data Available | No Data Available | | |

Section 13 - DISPOSAL CONSIDERATIONS

Disposal Instructions

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

- Containers may still present a chemical hazard/ danger when empty.
- Return to supplier for reuse/ recycling if possible.

Otherwise:

- If container can not be cleaned sufficiently well to ensure that residuals do not remain or if the container cannot be used to store the same product, then puncture containers, to prevent re-use, and bury at an authorised landfill.
- Where possible retain label warnings and MSDS and observe all notices pertaining to the product.

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. In most instances the supplier of the material should be consulted.

- DO NOT allow wash water from cleaning or process equipment to enter drains.
- It may be necessary to collect all wash water for treatment before disposal.
- In all cases disposal to sewer may be subject to local laws and regulations and these should be considered first.
- Where in doubt contact the responsible authority.
- Recycle wherever possible.
- Consult manufacturer for recycling options or consult local or regional waste management authority for disposal if no suitable treatment or disposal facility can be identified.
- Dispose of by: burial in a land-fill specifically licenced to accept chemical and / or pharmaceutical wastes or Incineration in a licenced 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: | None |
| UN/ID Number: | 3077 | Packing Group: | III |
| Special provisions: | A97 | | |
| Cargo Only | | | |
| Packing Instructions: | 956 | Maximum Qty/Pack: | 400 kg |
| Passenger and Cargo | | Passenger and Cargo | |
| Packing Instructions: | 956 | Maximum Qty/Pack: | 400 kg |
| Passenger and Cargo Limited Quantity | | Passenger and Cargo Limited Quantity | |
| Packing Instructions: | Y956 | Maximum Qty/Pack: | 30 kg G |

Shipping name:ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S.(contains zoledronic acid)

Maritime Transport IMDG:

| | | | |
|---------------------|---------|---------------------|---------|
| IMDG Class: | 9 | IMDG Subrisk: | None |
| UN Number: | 3077 | Packing Group: | III |
| EMS Number: | F-A,S-F | Special provisions: | 274 335 |
| Limited Quantities: | 5 kg | Marine Pollutant: | Yes |

Shipping name:ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S.(contains zoledronic acid)

Section 15 - REGULATORY INFORMATION



zoledronic acid (CAS: 118072-93-8, 165800-06-6) is found on the following regulatory lists;

"Canada Substances in Products Regulated Under the Food and Drugs Act (F&DA) That Were In Commerce between January 1, 1987 and September 13, 2001 (English)", "US Postal Service (USPS) Numerical Listing of Proper Shipping Names by Identification (ID) Number"

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE

■ Cumulative effects may result following exposure*.

■ Eye contact may produce serious damage*.

* (limited evidence).

Ingredients with multiple CAS Nos

| Ingredient Name | CAS |
|-----------------|--------------------------|
| zoledronic acid | 118072-93-8, 165800-06-6 |

■ Classification of the preparation 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.

■ For detailed advice on Personal Protective Equipment, refer to the following U.S. Regulations and Standards:

OSHA Standards - 29 CFR:

1910.132 - Personal Protective Equipment - General requirements

1910.133 - Eye and face protection

1910.134 - Respiratory Protection

1910.136 - Occupational foot protection

1910.138 - Hand Protection

Eye and face protection - ANSI Z87.1

Foot protection - ANSI Z41
Respirators must be NIOSH approved.

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