Etidronate Disodium

sc-205687

Material Safety Data Sheet

Hazard Alert Code Key:	EXTREME	HIGH	MODERATE	LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME
Etidronate Disodium

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
C2-H6-O7-P2.2Na, "phosphonic acid, (1-hydroxyethylidene)di-, disodium salt", "Didronel R", "disodium dihydrogen (1-hydroxyethylidene)diphosphonate", "disodium ethanol-1, 1-diphosphonate", "disodium ethydronate", "disodium 1-hydroxyethylidene phosphonate", "ethane-1-hydroxy-1, 1-diphosphonic acid, sodium salt", "(1-hydroxyethane-1, 1-diyl)diphosphonic acid, disodium salt", "(1-hydroxyethylidene)diphosphonic acid, disodium salt", "1-hydroxyethylidene-1, 1-diphosphonic acid disodium salt", "phosphonic acid, (1-hydroxyethane-1, 1-diyl)di-, disodium salt", "sodium ethidronate", "sodium ethydrate", "HEDP disodium"

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH 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

CANADIAN WHMIS SYMBOLS

EMERGENCY OVERVIEW

RISK

Harmful if swallowed.
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 osteodast 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.

EYE

■ There is some evidence to suggest that this material can causeeye irritation and damage in some persons.
■ 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 then tested salts and duration of exposure (i.e., as mimicked by rinsing/non-rinsing immediately after product installation) increased the observed symptoms.

SKIN

■ Skin contact is not thought to produce harmful health effects (as classified using animal models). Systemic harm, however, has been identified following exposure of animals by at least one other route and the material may still produce health damage following entry through wounds, lesions or abrasions.
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■ There is some evidence to suggest that this material can cause inflammation of the skin on contact in some persons.
■ 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 then 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.

INHALED

■ The material is not thought to produce respiratory irritation (as classified using animal models). Nevertheless inhalation of dusts, or fume, especially for prolonged periods, may produce respiratory discomfort and occasionally, distress.
■ Inhalation of dusts, generated by the material during the course of normal handling, may be damaging to the health of the individual.
■ Aliphatic, aromatic and substituted phosphonates exhibit moderate to high toxicity, and toxicity is increased when there are benzene rings and halogen or nitro group substitution.

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 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.
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.
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Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

NAME	CAS RN	%
disodium 1-hydroxyethylidene diphosphonate	7414-83-7	>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:

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.

SKIN

■ If skin contact occurs: · Immediately remove all contaminated clothing, including footwear · Flush skin and hair with running water (and soap if available).

INHALED

· If fumes or combustion products are inhaled remove from contaminated area. · Lay patient down. Keep warm and rested.

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.
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 reminder 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 is 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.

Section 5 - FIRE FIGHTING MEASURES

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

EXTINGUISHING MEDIA
· Water spray or fog.
· Foam.

FIRE FIGHTING
· Alert Emergency Responders and tell them location and nature of hazard.
· Wear breathing apparatus plus protective gloves.
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 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.
Combustion products include: carbon monoxide (CO), carbon dioxide (CO_2), phosphorus oxides (POx), 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
· Remove all ignition sources.
· Clean up all spills immediately.
· Avoid contact with skin and eyes.
· Control personal contact by using protective equipment.
· Use dry clean up procedures and avoid generating dust.
· Place in a suitable, labelled container for waste disposal.
Environmental hazard - contain spillage.
MAJOR SPILLS
■ Environmental hazard - contain spillage.
Moderate hazard.
· CAUTION: Advise personnel in area.
· Alert Emergency Responders and tell them location and nature of hazard.

Section 7 - HANDLING AND STORAGE

PROCEDURE FOR HANDLING
· Avoid all personal contact, including inhalation.

· Wear protective clothing when risk of exposure occurs.
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
· Polyethylene or polypropylene container.
· Check all containers are clearly labelled and free from leaks.

STORAGE REQUIREMENTS
■ Observe manufacturer's storing and handling recommendations.

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS

Source	Material	TWA ppm	TWA mg/m³	STEL ppm	STEL mg/m³	Peak ppm	Peak mg/m³	TWA F/CC	Notes
US - California Permissible Exposure Limits for Chemical Contaminants	disodium 1-hydroxyethylidene diphosphonate (Particulates not otherwise regulated Respirable fraction)		5						(n)
US - Tennessee Occupational Exposure Limits - Limits For Air Contaminants	disodium 1-hydroxyethylidene diphosphonate (Particulates not otherwise regulated Respirable fraction)		5						
US - Wyoming Toxic and Hazardous Substances Table Z1 Limits for Air Contaminants	disodium 1-hydroxyethylidene diphosphonate (Particulates not otherwise regulated (PNOR)(f)- Respirable fraction)		5						
US - Michigan Exposure Limits for Air Contaminants	disodium 1-hydroxyethylidene diphosphonate (Particulates not otherwise regulated, Respirable dust)		5						
Canada - Prince Edward Island Occupational Exposure Limits	disodium 1-hydroxyethylidene diphosphonate (Particles (Insoluble or Poorly Soluble) [NOS] Inhalable particles)		10						See Appendix B current TLV/BEI Book

ENDOELTABLE

PERSONAL PROTECTION




RESPIRATOR
Particulate
Consult your EHS staff for recommendations

EYE
· Safety glasses with side shields.
· Chemical goggles.

HANDS/FEET
■ Wear chemical protective gloves, eg. PVC.
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.

OTHER
· Overalls.
· P.V.C. apron.
· Barrier cream.
· Skin cleansing cream.
· Eye wash unit.

ENGINEERING CONTROLS
· Local exhaust ventilation is required where solids are handled as powders or crystals; even when particulates are relatively large, a certain proportion will be powdered by mutual friction.
· Exhaust ventilation should be designed to prevent accumulation and recirculation of particulates in the workplace.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES
Solid.
Mixes with water.

State	Divided solid	Molecular Weight	250.0 as disod.
Melting Range (°F)	Not available	Viscosity	Not Applicable
Boiling Range (°F)	Not applicable	Solubility in water (g/L)	Miscible
Flash Point (°F)	Not Available	pH (1% solution)	Not available
Decomposition Temp (°F)	Not available	pH (as supplied)	Not available
Autoignition Temp (°F)	Not available	Vapour Pressure (mmHG)	Not available
Upper Explosive Limit (%)	Not available	Specific Gravity (water=1)	Not available
Lower Explosive Limit (%)	Not available	Relative Vapor Density (air=1)	Not Applicable
Volatile Component (%vol)	Nil	Evaporation Rate	Non Volatile

APPEARANCE
White powder. Very soluble in water. Commercial material may be a mixture containing disodium 1-hydroxyethylidene diphosphonate CAS RN 7414-83-7 tetrasodium 1-hydroxyethylidene diphosphonate CAS RN 3794-83-0 sodium 1-hydroxyethylidene diphosphonate CAS RN 29329-71-3

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; DTMP: -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.

Material	Value

Section 10 - CHEMICAL STABILITY

CONDITIONS CONTRIBUTING TO INSTABILITY
· Presence of incompatible materials.
· Product is considered stable.

STORAGE INCOMPATIBILITY

■ Avoid reaction with oxidizing agents.

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

Section 11 - TOXICOLOGICAL INFORMATION

DISODIUM 1-HYDROXYETHYLIDENE DIPHOSPHONATE

TOXICITY AND IRRITATION

DISODIUM 1-HYDROXYETHYLIDENE DIPHOSPHONATE:

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

TOXICITY	IRRITATION
Oral (rat) LD50: 1340 mg/kg	Nil Reported

▪ 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.
as CAS RN 7414-883-7
Reproductive effector in rats

Section 12 - ECOLOGICAL INFORMATION

May cause long-term adverse effects in the aquatic environment.
This material and its container must be disposed of as hazardous waste.

Ecotoxicity

Ingredient	Persistence: Water/Soil	Persistence: Air	Bioaccumulation	Mobility
disodium 1-hydroxyethylidene diphosphonate			LOW	

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.

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: No limit
Passenger aircraft/rail:
Quantity Limitations: Cargo No limit Vessel stowage: Location: A

aircraft only:
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: 911 Maximum Qty/Pack: 400 kg
Passenger and Cargo Passenger and Cargo
Packing Instructions: 911 Maximum Qty/Pack: 400 kg
Passenger and Cargo Limited Quantity Passenger and Cargo Limited Quantity
Packing Instructions: Y911 Maximum Qty/Pack: 30 kg G
Shipping Name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. *(CONTAINS DISODIUM 1-HYDROXYETHYLIDENE DIPHOSPHONATE)

Maritime Transport IMDG:
IMDG Class: 9 IMDG Subrisk: None
UN Number: 3077 Packing Group: III
EMS Number: F-A , S-F Special provisions: 179 274 335 909
Limited Quantities: 5 kg Marine Pollutant: Yes
Shipping Name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S.

Section 15 - REGULATORY INFORMATION

disodium 1-hydroxyethylidene diphosphonate (CAS: 7414-83-7,29329-71-3) is found on the following regulatory lists;
"Canada Non-Domestic Substances List (NDSL)","International Council of Chemical Associations (ICCA) - High Production Volume List","OECD Representative List of High Production Volume (HPV) Chemicals","US EPA High Production Volume Chemicals Additional List","US Toxic Substances Control Act (TSCA) - Inventory"

Section 16 - OTHER INFORMATION

ND
Substance CAS Suggested codes disodium 1- hydroxyethylidene 7414- 83- 7 diphosphonate disodium 1- hydroxyethylidene 29329- 71- 3 diphosphonate

Ingredients with multiple CAS Nos
Ingredient Name CAS disodium 1-hydroxyethylidene diphosphonate 7414-83-7, 29329-71-3

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■ 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. 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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