Clodronate, Disodium Salt

sc-202547

Hazard Alert Code
Key:

EXTREME HIGH MODERATE LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME
Clodronate, Disodium Salt

STATEMENT OF HAZARDOUS NATURE

NFPA

Section 2 - HAZARDS IDENTIFICATION

CANADIAN WHMIS SYMBOLS

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

POTENTIAL HEALTH EFFECTS
ACUTE HEALTH EFFECTS
SWALLOWED

- Accidental ingestion of the material may be damaging 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 tetradsodium and pentasodium salt of ATMP were less acutely toxic with LD50 values of 6000 mg active acid/kg bw and 7120 mg active acid/kg bw, respectively. HEDP acid and its salts, respectively, HEDP acid and its salts were of low acute toxicity LD50s 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 occurs within days, months or years after starting. 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 may cause eye 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 observation period. The HEDP salts were less irritating to the rabbit eyes in studies with pure salts and formulations thereof tested without rinsing. The tetradsodium 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 have harmful health effects, however the material may still produce health damage following entry through wounds, lesions or abrasions.
- 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 tetradsodium 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.
- 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.
- 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 organ(s) or biochemical systems.
- Long term exposure to 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 aminomethylene(tetraphosphonic 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 fetotoxic effects were observed in the off-spring of 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.

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In a one-generation reproductive study the off-spring of rats, fed up to 3000 ppm DTPMPA (diethylenetriaminepentakis(methylene phosphonic acid)), showed no adverse effects although there was a slight decrease in birth weights.
Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

HAZARD RATINGS

<table>
<thead>
<tr>
<th></th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flammability:</td>
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</tr>
<tr>
<td>Toxicity:</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Body Contact:</td>
<td>2</td>
<td></td>
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<tr>
<td>Reactivity:</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Chronic:</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

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

NAME                  | CAS RN | %
---                   | ------ | ---
clodronic acid, sodium salt | 22560-50-5 | >98

Section 4 - FIRST AID MEASURES

SWALLOWED
- If swallowed do NOT induce vomiting.
- If vomiting occurs, lean patient forward or place on left side (head-down position, if possible) to maintain open airway and prevent aspiration.
- Observe the patient carefully.
- Never give liquid to a person showing signs of being sleepy or with reduced awareness; i.e. becoming unconscious.
- Give water to rinse out mouth, then provide liquid slowly and as much as casualty can comfortably drink.
- Seek medical advice.

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.
- 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.
- Transport to hospital, or doctor.

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 by 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

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<thead>
<tr>
<th>Property</th>
<th>Value</th>
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<tbody>
<tr>
<td>Vapour Pressure (mmHg)</td>
<td>Negligible</td>
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<tr>
<td>Upper Explosive Limit (%)</td>
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<tr>
<td>Specific Gravity (water=1)</td>
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</tr>
<tr>
<td>Lower Explosive Limit (%)</td>
<td>Not available</td>
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</tbody>
</table>

**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), hydrogen chloride, phosgene, 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 chloride etc. as ignition may result.

**PERSONAL PROTECTION**
- Glasses: Chemical goggles.
- Gloves: Particulate
- 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**

WARNING
MAY DECOMPOSE EXPLOSIVELY AT HIGH TEMPERATURES.

From IERG (Canada/Australia)
Isolation Distance
Downwind Protection Distance 10 meters

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.
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.
- Polyethylene or polypropylene container.
- Check all containers are clearly labelled and free from leaks.
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

<table>
<thead>
<tr>
<th>Source</th>
<th>Material</th>
<th>TWA ppm</th>
<th>TWA mg/m³</th>
<th>STEL ppm</th>
<th>STEL mg/m³</th>
<th>Peak ppm</th>
<th>Peak mg/m³</th>
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<tr>
<td>US - Oregon Permissible Exposure Limits (Z3)</td>
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<td>US OSHA Permissible Exposure Levels (PELs) - Table Z3</td>
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<td>US - Oregon Permissible Exposure Limits (Z3)</td>
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<td>US - Tennessee Occupational Exposure Limits - Limits For Air Contaminants</td>
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</table>

MATERIAL DATA

CLODRONIC ACID, SODIUM SALT:

■ It is the goal of the ACGIH (and other Agencies) to recommend TLVs (or their equivalent) for all substances for which there is evidence of health effects at airborne concentrations encountered in the workplace.

At this time no TLV has been established, even though this material may produce adverse health effects (as evidenced in animal experiments or clinical experience). Airborne concentrations must be maintained as low as is practically possible and occupational exposure must be kept to a minimum.

NOTE: The ACGIH occupational exposure standard for Particles Not Otherwise Specified (P.N.O.S) does NOT apply.

Sensory irritants are chemicals that produce temporary and undesirable side-effects on the eyes, nose or throat. Historically occupational exposure standards for these irritants have been based on observation of workers’ responses to various airborne concentrations. Present day expectations require that nearly every individual should be protected against even minor sensory irritation and exposure standards are established using uncertainty factors or safety factors of 5 to 10 or more. On occasion animal no-observable-effect-levels (NOEL) are used to determine these limits where human results are unavailable. An additional approach, typically used by the TLV committee (USA) in determining respiratory standards for this group of chemicals, has been to assign ceiling values (TLV C) to rapidly acting irritants and to assign short-term exposure limits (TLV STELs) when the weight of evidence from irritation, bioaccumulation and other endpoints combine to warrant such a limit. In contrast the MAK Commission (Germany) uses a five-category system based on intensive odour, local irritation, and elimination half-life. However this system is being replaced to be consistent with the European Union (EU) Scientific Committee for Occupational Exposure Limits (SCOEL); this is more closely allied to that of the USA.

OSHA (USA) concluded that exposure to sensory irritants can:

- cause inflammation
- cause increased susceptibility to other irritants and infectious agents
- lead to permanent injury or dysfunction
- permit greater absorption of hazardous substances and
- acclimate the worker to the irritant warning properties of these substances thus increasing the risk of overexposure.

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).

**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 lenses 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.
  - 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
    - fluorocautouchouc
    - polyvinyl chloride
  - Gloves should be examined for wear and/ or degradation constantly.

**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
- Respirators may be necessary when engineering and administrative controls do not adequately prevent exposures.
  - The decision to use respiratory protection should be based on professional judgment that takes into account toxicity information, exposure measurement data, and frequency and likelihood of the worker's exposure - ensure users are not subject to high thermal loads which may result in heat stress or distress due to personal protective equipment (powered, positive flow, full face apparatus may be an option).
  - Published occupational exposure limits, where they exist, will assist in determining the adequacy of the selected respiratory. These may be government mandated or vendor recommended.
  - Certified respirators will be useful for protecting workers from inhalation of particulates when properly selected and fit tested as part of a complete respiratory protection program.
  - Use approved positive flow mask if significant quantities of dust becomes airborne.
  - Try to avoid creating dust conditions.

**RESPIRATOR**
-
Mixes with water.

**PHYSICAL PROPERTIES**

<table>
<thead>
<tr>
<th>Protection Factor</th>
<th>Half-Face Respirator</th>
<th>Full-Face Respirator</th>
<th>Powered Air Respirator</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 x PEL</td>
<td>Air-line*</td>
<td>-</td>
<td>PAPR-P1</td>
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<tr>
<td>50 x PEL</td>
<td>Air-line**</td>
<td>P2</td>
<td>PAPR-P2</td>
</tr>
<tr>
<td>100 x PEL</td>
<td>P3</td>
<td>Air-line*</td>
<td>-</td>
</tr>
<tr>
<td>100+ x PEL</td>
<td>-</td>
<td>-</td>
<td>PAPR-P3</td>
</tr>
</tbody>
</table>

* - Negative pressure demand  ** - Continuous flow

**Engineered 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.

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.

---

**PHYSICAL AND CHEMICAL PROPERTIES**

**Physical Properties**

- **State:** Solid.
- **Mixes with water:**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melting Range (°F)</td>
<td>Not available</td>
</tr>
<tr>
<td>Boiling Range (°F)</td>
<td>Not available</td>
</tr>
<tr>
<td>Flash Point (°F)</td>
<td>Not available</td>
</tr>
<tr>
<td>Autoignition Temp (°F)</td>
<td>Not available</td>
</tr>
<tr>
<td>Decomposition Temp (°F)</td>
<td>Not available</td>
</tr>
<tr>
<td>Solubility in water (g/L)</td>
<td>Miscible</td>
</tr>
<tr>
<td>pH (1% solution)</td>
<td>Not available</td>
</tr>
<tr>
<td>Vapour Pressure (mmHG)</td>
<td>Negligible</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular Weight</td>
<td>288.9</td>
</tr>
<tr>
<td>Viscosity</td>
<td>Not Applicable</td>
</tr>
<tr>
<td>Miscibility</td>
<td>Miscible</td>
</tr>
<tr>
<td>pH</td>
<td>Not available</td>
</tr>
<tr>
<td>Negligible</td>
<td>Negligible</td>
</tr>
</tbody>
</table>

---

**Chemical Properties**

- **Autoignition Temp:**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autoignition Temp (°F)</td>
<td>Not available</td>
</tr>
</tbody>
</table>

---

**Autoignition Temp (°F):**

- **Not available:**
- **Vapour Pressure (mmHG):** Negligible
- **pH (as supplied):** Not applicable

---

**Decomposition Temp (°F):**

- **Not available:**
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 pregnancy, there is limited information available to support this consideration.

Phosphonates

clodronic acid, sodium salt

TOXICITY AND IRRITATION

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

■ 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 that these compounds are not considered skin sensitisers.

■ For phosphonates: There are no mutagenic effects observed with phosphonates. Both, DTPMP acid and the salt were negative in well performed and guideline compliant bacterial mutagenicity assays. DTPMP acid could further be confirmed in an OECD guideline compliant subchronic toxicity study.

■ For clodronic acid, sodium salt: clodronic acid is directly related to the total dose and duration of bisphosphonate use. Although there are no data on foetal risk in pregnancy, there is limited information available to support this consideration.

APPEARANCE

Solid; mixes with water.

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

DESCRIPTION

clodronic acid, sodium salt

Clodronic acid is a bisphosphonate that is used in the treatment of bone diseases such as osteoporosis and Paget's disease. It is known for its ability to inhibit bone resorption and promote bone formation.

PHYSICAL DATA

APPEARANCE

Solid; mixes with water.

PHYSICAL AND CHEMICAL PROPERTIES

■ Upper Explosive Limit (%): Not available.
■ Lower Explosive Limit (%): Not available.
■ Volatile Component (%vol): Negligible.
■ Specific Gravity (water=1): Not available.
■ Relative Vapor Density (air=1): >1.
■ Evaporation Rate: Not Applicable.

ENVIRONMENTAL INFORMATION

■ Biological Oxidation: Not available.
■ Biodegradability: Not available.
■ Toxicity: Not available.
■ Persistence: Not available.
■ Bioaccumulation: Not available.

ACUTE TOXICITY

■ Oral LD50 in rats: 1628 mg/kg bw.
■ Inhalation LD50 in rats: Not available.
■ Skin LD50 in rabbits: 210 mg/kg bw.

CHRONIC TOXICITY

■ Oral LD50 in rats: 1628 mg/kg bw.
■ Inhalation LD50 in rats: Not available.
■ Skin LD50 in rabbits: 210 mg/kg bw.

ECOTOXICITY

■ Acute aquatic toxicity: Not available.
■ Chronic aquatic toxicity: Not available.

STABILITY

■ Stable at room temperature.
■ Stable under refrigeration.
■ Stable under freezing.

INCOMPATIBILITIES

■ Incompatible with strong oxidising agents.
■ Incompatible with strong alkalis.

HAZARDS IN HANDLING

■ Irritating to the skin and eyes.
■ May cause sensitisation.

HAZARDS IN STORAGE

■ Keep out of reach of children.
■ Store in a cool, dry place.

HAZARDS IN DISPOSAL

■ Dispose of according to local regulations.
■ Avoid release of waste products into the environment.

REFERENCES

■ 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. Confirming 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 slight increase in 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 pregnancy, there is limited information available to support this consideration.
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 farnesyldiphosphate synthase (FPPS) in the HMG-CoA reduction 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. No significant acute toxicological data identified in literature search.

Section 12 - ECOLOGICAL INFORMATION

Refer to data for ingredients, which follows:

■ CLODRONIC ACID, SODIUM SALT:
  ▪ 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 when phosphate contamination of the environment relates to eutrophication processes in lakes and ponds. Phosphorus is an essential nutrient for blue-green algae. A lake undergoing eutrophication shows a rapid growth of algae in surface waters. Planktonic algae cause turbidity and fluctuation 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 cause 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-prolic 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 phosphate 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 phosphate degrading bacteria can be found in almost all environments whether sediment 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 14CO2 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.

Anoxic degradation has not been studied extensively. It has been reported only minor conversion of ATMP and HEDP occurs in model digesters. No inhibitory effect was observed neither for ATMP up to 100 mg/liter and for HEDP up to 5 mg/l 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 presence of certain metal ions and light. Hydrolysis half-lives in the range of 50 -200 days at 15 °C and 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; HDMTP: -4.43; DTPMP: -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 studied 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 fetida) 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.

Section 13 - DISPOSAL CONSIDERATIONS

Disposal Instructions
All waste must be handled in accordance with local, state and federal regulations. 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: | No limit |
| Passenger aircraft/rail: | No limit |
| Quantity Limitations: Cargo aircraft only: | No limit |
| Vessel stowage: | A |
| Vessel stowage: Other: | None |
| Hazardous materials descriptions and proper shipping names: | None |
| Environmentally hazardous substance, solid, n.o.s | |
| Air Transport IATA: | 9 |
| ICAO/IATA Subrisk: | 9 |

ICAO/IATA Class: 9
ICAO/IATA Subrisk: 9

Hazardous materials descriptions and proper shipping names:
Environmentally hazardous substance, solid, n.o.s
Air Transport IATA:
UN/ID Number: 3077  |  Packing Group: III
Special provisions: A97

Shipping Name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. *(CONTAINS CLODRONIC ACID, SODIUM SALT)

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 clodronic acid, sodium salt)

Section 15 - REGULATORY INFORMATION

clodronic acid, sodium salt (CAS: 22560-50-5) is found on the following regulatory lists;
"US - Hawaii Air Contaminant Limits","US - Oregon Permissible Exposure Limits (Z3)","US OSHA Permissible Exposure Levels (PELs) - Table Z3"

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE

■ Inhalation and/or ingestion may produce health damage*.
■ Cumulative effects may result following exposure*.
■ May produce discomfort of the eyes and skin*.
* (limited evidence).

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■ 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-22-2009
Print Date:Apr-22-2010