

Bromhexine Hydrochloride

sc-204656

Material Safety Data Sheet



The Power to Question

Hazard Alert Code
Key:

EXTREME

HIGH

MODERATE

LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

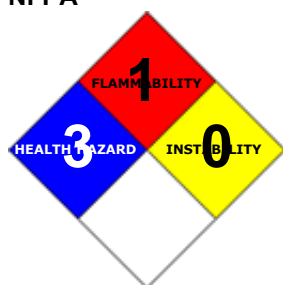
PRODUCT NAME

Bromhexine Hydrochloride

STATEMENT OF HAZARDOUS NATURE

CONSIDERED A HAZARDOUS SUBSTANCE ACCORDING TO OSHA 29 CFR 1910.1200.

NFPA



SUPPLIER

Company: Santa Cruz Biotechnology, Inc.

Address:

2145 Delaware Ave

Santa Cruz, CA 95060

Telephone: 800.457.3801 or 831.457.3800

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

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

PRODUCT USE

Expectorant. Reported to change the structure of bronchial secretions and to increase the volume and reduce the viscosity of sputum. Administered in bronchitis and other respiratory conditions. Normally given by mouth. Synthetic derivative of vasicine, the active principal of Adhatoda vasica.

SYNONYMS

C14-H20-Br2-N2.HCl, "2-amino-N-cyclohexyl-3, 5-dibromo-N-methylbenzylamine hydrochloride", "2-amino-N-cyclohexyl-3, 5-dibromo-N-methylbenzylamine hydrochloride", "benzenemethanamine, 2-amino-3, 5-dibromo-N-cyclohexyl-N-methyl-, ", "benzenemethanamine, 2-amino-3, 5-dibromo-N-cyclohexyl-N-methyl-, ", monohydrochloride, "benzylamine, 2-amino-N-cyclohexyl-3, 5-dibromo-N-methyl-, hydrochloride", "benzylamine, 2-amino-N-cyclohexyl-3, 5-dibromo-N-methyl-, hydrochloride", "bromhexin hydrochloride", "N-cyclohexyl-N-methyl-(2-amino-3, 5-dibromobenzyl) ammonium chloride", "N-cyclohexyl-N-methyl-(2-amino-3, 5-dibromobenzyl) ammonium chloride", Aletor, Bisolvomycin, Bisolvon, "Bisolvon Hydrochloride", Bromessina, Bromilate, Bronkocin, "Dakroy Biciron", Ophtosol, "quaternary ammonium expectorant"

Section 2 - HAZARDS IDENTIFICATION

CANADIAN WHMIS SYMBOLS



EMERGENCY OVERVIEW

RISK

Harmful if swallowed.

Irritating to skin.

Risk of serious damage to eyes.

Toxic to aquatic organisms.

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.
- Concentrated solutions of many cationics may cause corrosive damage to mucous membranes and the esophagus. Nausea and vomiting (sometimes bloody) may follow ingestion. Serious exposures may produce an immediate burning sensation of the mouth, throat and abdomen with profuse salivation, ulceration of mucous membranes, signs of circulatory shock (hypotension, labored breathing, and cyanosis) and a feeling of apprehension, restlessness, confusion and weakness. Weak convulsive movements may precede central nervous system depression. Erosion, ulceration, and petechial hemorrhage may occur through the small intestine with glottic, brain and pulmonary edema. Death may result from asphyxiation due to paralysis of the muscles of respiration or cardiovascular collapse. Fatal poisoning may arise even when the only pathological signs are visceral congestion, swallowing, mild pulmonary edema or varying signs of gastrointestinal irritation. Individuals who survive a period of severe hypertension may develop kidney failure. Cloudy swelling, patchy necrosis and fatty infiltration in such visceral organs as the heart, liver and kidneys shows at death.

EYE

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

SKIN

- This material can cause inflammation of the skin on contact in some persons.
- The material may accentuate any pre-existing dermatitis condition.
- 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 either adverse health effects or irritation of the respiratory tract following inhalation (as classified using animal models). Nevertheless, adverse effects have been produced following exposure of animals by at least one other route and good hygiene practice requires that exposure be kept to a minimum and that suitable control measures be used in an occupational setting.
- 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.

CHRONIC HEALTH EFFECTS

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

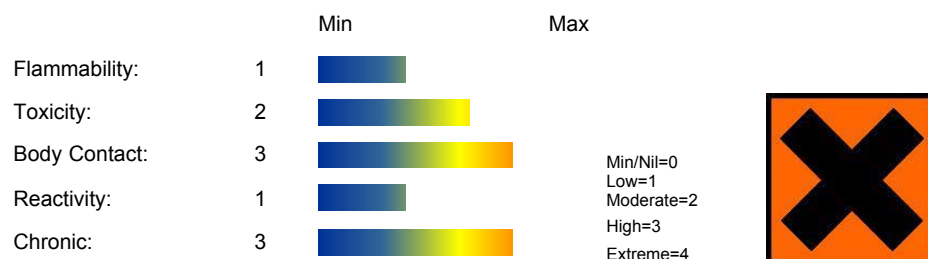
There is some evidence that human exposure to the material may result in developmental toxicity. This evidence is based on animal studies where effects have been observed in the absence of marked maternal toxicity, or at around the same dose levels as other toxic effects but which are not secondary non-specific consequences of the other toxic effects.

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.

Chronic intoxication with ionic bromides, historically, has resulted from medical use of bromides but not from environmental or occupational exposure; depression, hallucinosis, and schizophreniform psychosis can be seen in the absence of other signs of intoxication. Bromides may also induce sedation, irritability, agitation, delirium, memory loss, confusion, disorientation, forgetfulness (aphasias), dysarthria, weakness, fatigue, vertigo, stupor, coma, decreased appetite, nausea and vomiting, diarrhoea, hallucinations, an acne like rash on the face, legs and trunk, known as bromoderma (seen in 25-30% of case involving bromide ion), and a profuse discharge from the nostrils (coryza). Ataxia and generalised hyperreflexia have also been observed. Correlation of neurologic symptoms with blood levels of bromide is inexact. The use of substances such as brompheniramine, as antihistamines, largely reflect current day usage of bromides; ionic bromides have been largely withdrawn from therapeutic use due to their toxicity. Several cases of foetal abnormalities have been described in mothers who took large doses of bromides during pregnancy.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

HAZARD RATINGS



NAME	CAS RN	%
bromhexine hydrochloride	611-75-6	>98

Section 4 - FIRST AID MEASURES

SWALLOWED

- IF SWALLOWED, REFER FOR MEDICAL ATTENTION, WHERE POSSIBLE, WITHOUT DELAY.
- Where Medical attention is not immediately available or where the patient is more than 15 minutes from a hospital or unless instructed otherwise:
- For advice, contact a Poisons Information Center or a doctor.
- Urgent hospital treatment is likely to be needed.

- If conscious, give water to drink.
 - INDUCE vomiting with fingers down the back of the throat, ONLY IF CONSCIOUS. Lean patient forward or place on left side (head-down position, if possible) to maintain open airway and prevent aspiration.
- NOTE: Wear a protective glove when inducing vomiting by mechanical means.
- In the mean time, qualified first-aid personnel should treat the patient following observation and employing supportive measures as indicated by the patient's condition.
 - If the services of a medical officer or medical doctor are readily available, the patient should be placed in his/her care and a copy of the MSDS should be provided. Further action will be the responsibility of the medical specialist.
 - If medical attention is not available on the worksite or surroundings send the patient to a hospital together with a copy of the MSDS.

EYE

- If this product comes in contact with the eyes:
 - 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 Center or a doctor, or for at least 15 minutes.
 - Transport to hospital or doctor without delay.
 - 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 dust is inhaled, remove from contaminated area.
 - Encourage patient to blow nose to ensure clear passage of breathing.
 - If irritation or discomfort persists seek medical attention.

NOTES TO PHYSICIAN

- Treat symptomatically.

For exposures to quaternary ammonium compounds;

- For ingestion of concentrated solutions (10% or higher): Swallow promptly a large quantity of milk, egg whites / gelatin solution. If not readily available, a slurry of activated charcoal may be useful. Avoid alcohol. Because of probable mucosal damage omit gastric lavage and emetic drugs.
- For dilute solutions (2% or less): If little or no emesis appears spontaneously, administer syrup of Ipecac or perform gastric lavage.
- If hypotension becomes severe, institute measures against circulatory shock.
- If respiration laboured, administer oxygen and support breathing mechanically. Oropharyngeal airway may be inserted in absence of gag reflex. Epiglottic or laryngeal edema may necessitate a tracheotomy.
- Persistent convulsions may be controlled by cautious intravenous injection of diazepam or short-acting barbiturate drugs. [Gosselin et al, Clinical Toxicology of Commercial Products]

Absorbed from the gastrointestinal tract is excreted from the urine mainly as metabolites. Ambroxal is a metabolite.

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.
 - Water spray or fog - Large fires only.

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 bromide, hydrogen chloride, phosgene, nitrogen oxides (NO_x), other pyrolysis products typical of burning organic material.

May emit poisonous fumes.

May emit corrosive fumes.

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

■

- 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

- 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.

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

-
- Store in original containers.
- Keep containers securely sealed.
- Store in a cool, dry, well-ventilated area.
- Store away from incompatible materials and foodstuff containers.
- Protect containers against physical damage and check regularly for leaks.
- 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

Source	Material	TWA ppm	TWA mg/m ³	STEL ppm	STEL mg/m ³	Peak ppm	Peak mg/m ³	TWA F/CC	Notes
US - Oregon Permissible Exposure Limits (Z3)	bromhexine hydrochloride (Inert or Nuisance Dust: (d) Total dust)		10						*
US OSHA Permissible Exposure Levels (PELs) - Table Z3	bromhexine hydrochloride (Inert or Nuisance Dust: (d) Respirable fraction)		5						
US OSHA Permissible Exposure Levels (PELs) - Table Z3	bromhexine hydrochloride (Inert or Nuisance Dust: (d) Total dust)		15						
US - Hawaii Air Contaminant Limits	bromhexine hydrochloride (Particulates not other wise regulated - Total dust)		10						
US - Hawaii Air Contaminant Limits	bromhexine hydrochloride (Particulates not other wise regulated - Respirable fraction)		5						
US - Oregon Permissible Exposure Limits (Z3)	bromhexine hydrochloride (Inert or Nuisance Dust: (d) Respirable fraction)		5						*
US - Tennessee Occupational Exposure Limits - Limits For Air Contaminants	bromhexine hydrochloride (Particulates not otherwise regulated Respirable fraction)		5						
US - Wyoming Toxic and Hazardous Substances Table Z1 Limits for Air Contaminants	bromhexine hydrochloride (Particulates not otherwise regulated (PNOR)(f)- Respirable fraction)		5						
US - Michigan Exposure Limits for Air Contaminants	bromhexine hydrochloride (Particulates not otherwise regulated, Respirable dust)		5						

MATERIAL DATA

BROMHEXINE HYDROCHLORIDE:

- 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 lens or restrictions on use, should be created for each workplace or task. This should include a review of lens absorption and adsorption for the class of chemicals in use and an account of injury experience. Medical and first-aid personnel should be trained in their removal and suitable equipment should be readily available. In the event of chemical exposure, begin eye irrigation immediately and remove contact lens as soon as practicable. Lens should be removed at the first signs of eye redness or irritation - lens should be removed in a clean environment only after workers have washed hands thoroughly. [CDC NIOSH Current Intelligence Bulletin 59]

HANDS/FEET

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

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

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

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

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

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

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
- 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

Protection Factor	Half-Face Respirator	Full-Face Respirator	Powered Air Respirator
10 x PEL	P1	-	PAPR-P1
	Air-line*	-	-

50 x PEL	Air-line**	P2	PAPR-P2
100 x PEL	-	P3	-
		Air-line*	-
100+ x PEL	-	Air-line**	PAPR-P3

* - Negative pressure demand ** - Continuous flow

Explanation of Respirator Codes:

Class 1 low to medium absorption capacity filters.

Class 2 medium absorption capacity filters.

Class 3 high absorption capacity filters.

PAPR Powered Air Purifying Respirator (positive pressure) cartridge.

Type A for use against certain organic gases and vapors.

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

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

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

Type K for use against ammonia and organic ammonia derivatives

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

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

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

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

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

ENGINEERING CONTROLS

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

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

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

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

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

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

Within each range the appropriate value depends on:

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

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

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES

Solid.

Does not mix with water.

State	Divided solid	Molecular Weight	412.6
Melting Range (°F)	458.6- 460.4	Viscosity	Not Applicable
Boiling Range (°F)	Not available	Solubility in water (g/L)	Partly miscible
Flash Point (°F)	Not available	pH (1% solution)	Not applicable
Decomposition Temp (°F)	Not available.	pH (as supplied)	Not applicable
Autoignition Temp (°F)	Not available	Vapour Pressure (mmHG)	Negligible
Upper Explosive Limit (%)	Not available.	Specific Gravity (water=1)	Not available
Lower Explosive Limit (%)	Not available	Relative Vapor Density (air=1)	Not Applicable

Volatile Component (%vol)	Negligible	Evaporation Rate	Not applicable
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APPEARANCE

White, odourless, crystalline powder; does not mix well with water. Soluble in alcohol (1:100), methanol (1:50).

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

bromhexine hydrochloride

TOXICITY AND IRRITATION

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

TOXICITY	IRRITATION
Oral (rat) LD50: 6000 mg/kg	Nil Reported
Intraperitoneal (rat) LD50: 1680 mg/kg	
Subcutaneous (rat) LD50: >14000 mg/kg	
Oral (mouse) LD50: 3000 mg/kg	
Intraperitoneal (mouse) LD50: 2210 mg/kg	
Subcutaneous (mouse) LD50: >14000 mg/kg	
Intravenous (mouse) LD50: 44 mg/kg	
Oral (rabbit) LD50: 10000 mg/kg	

- Most undiluted cationic surfactants satisfy the criteria for classification as Harmful (Xn) with R22 and as Irritant (Xi) for skin and eyes with R38 and R41.

For quaternary ammonium compounds (QACs):

Quaternary ammonium compounds (QACs) are cationic surfactants. They are synthetic organically tetra-substituted ammonium compounds, where the R substituents are alkyl or heterocyclic radicals. A common characteristic of these synthetic compounds is that one of the R's is a long-chain hydrophobic aliphatic residue

The cationic surface active compounds are in general more toxic than the anionic and non-ionic surfactants. The positively-charged cationic portion is the functional part of the molecule and the local irritation effects of QACs appear to result from the quaternary ammonium cation.

Due to their relative ability to solubilise phospholipids and cholesterol in lipid membranes, QACs affect cell permeability which may lead to cell death. Further QACs denature proteins as cationic materials precipitate protein and are accompanied by generalised tissue irritation.

It has been suggested that the experimentally determined decrease in acute toxicity of QACs with chain lengths above C16 is due to decreased water solubility.

In general it appears that QACs with a single long-chain alkyl groups are more toxic and irritating than those with two such substitutions.

The straight chain aliphatic QACs have been shown to release histamine from minced guinea pig lung tissue. However, studies with benzalkonium chloride have shown that the effect on histamine release depends on the concentration of the solution. When cell suspensions (11% mast cells) from rats were exposed to low concentrations, a decrease in histamine release was seen. When exposed to high concentrations the opposite result was obtained.

In addition, QACs may show curare-like properties (specifically benzalkonium and cetylpyridinium derivatives, a muscular paralysis with no involvement of the central nervous system. This is most often associated with lethal doses. Parenteral injections in rats, rabbits and dogs have resulted in prompt but transient limb paralysis and sometimes fatal paresis of the respiratory muscles. This effect seems to be transient.

From human testing of different QACs the generalised conclusion is obtained that all the compounds investigated to date exhibit similar toxicological properties.

Acute toxicity: Studies in rats have indicated poor intestinal absorption of QACs. Acute toxicity of QACs varies with the compound and, especially, the route of administration. For some substances the LD50 value is several hundreds times lower by the i.p. or i.v. than the oral route, whereas toxicities between the congeners only differ in the range of two to five times.

At least some QACs are significantly more toxic in 50% dimethyl sulfoxide than in plain water when given orally. Probably all common QAC derivatives produce similar toxic reactions, but as tested in laboratory animals the oral mean lethal dose varies with the compound.

Oral toxicity: LD50 values for QACs have been reported within the range of 250-1000 mg/kg for rats, 150-1000 mg/kg for mice, 150-300 mg/kg for guinea pigs and about 500 mg/kg b.w. for rabbits and dogs. The ranges observed reflect differences in the study designs of these rather old experiments as well as differences between the various QACs.

The oral route of administration was characterised by delayed deaths, gastrointestinal lesions and respiratory and central nervous system depression. It was also found that given into a full stomach, the QACs lead to lower mortality and fewer gastrointestinal symptoms. This supports the suggestion of an irritating effect.

Dermal toxicity: It has been concluded that the maximum concentration that did not produce irritating effect on intact skin is 0.1%. Irritation became manifest in the 1-10% range. Concentrations below 0.1% have caused irritation in persons with contact dermatitis or broken skin.

Although the absorption of QACs through normal skin probably is of less importance than by other routes, studies with excised guinea pig skin have shown that the permeability constants strongly depend on the exposure time and type of skin.

Sensitisation: Topical mucosal application of QACs may produce sensitisation. Reports on case stories and patch test have

shown that compounds such as benzalkonium chloride, cetalkonium chloride and cetrimide may possibly act as sensitisers. However, in general it is suggested that QACs have a low potential for sensitising man. It is difficult to distinguish between an allergic and an irritative skin reaction due to the inherent skin irritating effect of QACs.

Long term/repeated exposure:

Inhalation: A group of 196 farmers (with or without respiratory symptoms) were evaluated for the relationship between exposure to QACs (unspecified, exposure levels not given) and respiratory disorders by testing for lung function and bronchial responsiveness to histamine. After histamine provocation statistically significant associations were found between the prevalence of mild bronchial responsiveness (including asthma-like symptoms) and the use of QACs as disinfectant. The association seems even stronger in people without respiratory symptoms.

Genetic toxicity: QACs have been investigated for mutagenicity in microbial test systems. In Ames tests using *Salmonella typhimurium* with and without metabolic activation no signs of mutagenicity have been observed. Negative results were also obtained in *E. coli* reversion and *B. subtilis* rec assays. However, for benzalkonium chloride also positive and equivocal results were seen in the *B. subtilis* rec assays.

Lachrymation, tremor, ataxia recorded.

CARCINOGEN

BROMINE COMPOUNDS (ORGANIC OR INORGANIC)

US Environmental Defense Scorecard Suspected Carcinogens

Reference(s) P65-MC

Section 12 - ECOLOGICAL INFORMATION

Refer to data for ingredients, which follows:

BROMHEXINE HYDROCHLORIDE:

■ Toxic to aquatic organisms.

■ 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.

■ For quaternary ammonium compounds (QACs):

QACs are white, crystalline powders. Low molecular weight QACs are very soluble in water, but slightly or not at all soluble in solvents such as ether, petrol and benzene. As the molecular weight and chain lengths increase, the solubility in polar solvents (e.g. water) decreases and the solubility in non-polar solvents increases.

Environmental fate

A major part of the QACs is discharged into wastewater and removed in the biological processes of sewage treatment plant. A 90% reduction of the QACs in the water phase of sludge has been reported and alkyl di-/trimethyl ammonium and alkyl dimethyl benzyl ammonium compounds seem almost completely degraded in sewage sludge.

However, the aerobic and anaerobic biodegradability of QACs is not well investigated. Only sparse data are available concerning stability, solubility and biodegradability. In general, it seems that the biodegradability decreases with increasing numbers of alkyl chains: $R(CH_3)_3N^+ > R_2(CH_3)_2N^+ > R_3(CH_3)N^+$. Within each category the biodegradability seems inversely proportional to the alkyl chain length. Heterocyclic QACs are less degradable than the non-cyclic.

Investigations have shown that bioaccumulation of considerable dimensions will probably not take place.

Ecotoxicity:

Quaternary ammonium compounds and their polymers may be highly toxic to fish and other aquatic organisms. The toxicity of the quaternary ammoniums is known to be greatly reduced in the environment because of preferential binding to dissolved organics in surface water.

■ Although inorganic chloride ions are not normally considered toxic they can exist in effluents at acutely toxic levels (chloride >3000 mg/l). the resulting salinity can exceed the tolerances of most freshwater organisms.

Inorganic chlorine eventually finds its way into the aqueous compartment and as such is bioavailable. Incidental exposure to inorganic chloride may occur in occupational settings where chemicals management policies are improperly applied. The toxicity of chloride salts depends on the counter-ion (cation) present; that of chloride itself is unknown. Chloride toxicity has not been observed in humans except in the special case of impaired sodium chloride metabolism, e.g. in congestive heart failure. Healthy individuals can tolerate the intake of large quantities of chloride provided that there is a concomitant intake of fresh water.

Although excessive intake of drinking-water containing sodium chloride at concentrations.

above 2.5 g/litre has been reported to produce hypertension, this effect is believed to be related to the sodium ion concentration.

Chloride concentrations in excess of about 250 mg/litre can give rise to detectable taste in water, but the threshold depends upon the associated cations. Consumers can, however, become accustomed to concentrations in excess of 250 mg/litre. No health-based guideline value is proposed for chloride in drinking-water.

In humans, 88% of chloride is extracellular and contributes to the osmotic activity of body fluids. The electrolyte balance in the body is maintained by adjusting total dietary intake and by excretion via the kidneys and gastrointestinal tract. Chloride is almost completely absorbed in normal individuals, mostly from the proximal half of the small intestine. Normal fluid loss amounts to about 1.5-2 liters/day, together with about 4 g of chloride per day. Most (90 - 95%) is excreted in the urine, with minor amounts in faeces (4- %) and sweat (2%).

Chloride increases the electrical conductivity of water and thus increases its corrosivity. In metal pipes, chloride reacts with metal ions to form soluble salts thus increasing levels of metals in drinking-water. In lead pipes, a protective oxide layer is built up, but chloride enhances galvanic corrosion. It can also increase the rate of pitting corrosion of metal pipes.

■ Bromide ion may be introduced to the environment after the dissociation of various salts and complexes or the degradation of organobromide compounds.

Although not a significant toxin in mammalian or avian systems it is highly toxic to rainbow trout and *Daphnia magna*. Bromides may also affect the growth of micro-organisms and have been used for this purpose in industry.

Bromides in drinking water are occasionally subject to disinfection processes involving ozone of chlorine. Bromide may be oxidised to produce hypobromous acid which in turn may react with natural organic matter to form brominated compounds. The formation of bromoform has been well documented, as has the formation of bromoacetic acids, bromopicrin, cyanogen bromide, and bromoacetone. Bromates may also be formed following ozonation or chlorination if pH is relatively high. Bromates may be animal carcinogens.

■ 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.

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

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

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

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

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

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

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

Section 14 - TRANSPORTATION INFORMATION

NOT REGULATED FOR TRANSPORT OF DANGEROUS GOODS: DOT, IATA, IMDG

Section 15 - REGULATORY INFORMATION

bromhexine hydrochloride (CAS: 611-75-6) is found on the following regulatory lists;

"OECD Representative List of High Production Volume (HPV) Chemicals"

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE

- Cumulative effects may result following exposure*.
- May be harmful to the fetus/ embryo*.

* (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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