

Physostigmine

sc-202764

Material Safety Data Sheet



The Power is Question

Hazard Alert Code Key:

EXTREME

HIGH

MODERATE

LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

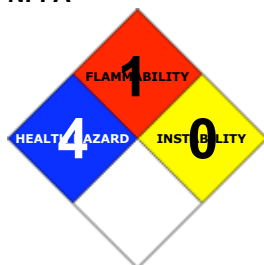
PRODUCT NAME

Physostigmine

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

SYNONYMS

C15-H21-N3-O2, "carbamic acid, methyl-, ester with eseroline", CS-58525, eserine, eserine, "eserolein, methylcarbamate (ester)", physostol, "(3aS, 8aR)-1, 2, 3, 3a, 8, 8a-hexahydro-1, 3a, 8-trimethylpyrrolo[2, 3-b]indol-5-ylmethylcarbamate, "miotic/parasympathomimetic/ anticholinesterase"

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS

		Min	Max
Flammability:	1		
Toxicity:	4		
Body Contact:	2		
Reactivity:	1		
Chronic:	2		

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



CANADIAN WHMIS SYMBOLS



EMERGENCY OVERVIEW

RISK

Very toxic by inhalation and if swallowed.

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED

- Severely toxic effects may result from the accidental ingestion of the material; animal experiments indicate that ingestion of less than 5 gram may be fatal or may produce serious damage to the health of the individual.
- Side effects of the parasympathomimetics are increased salivation, nausea, vomiting, abdominal cramps and diarrhea. Symptoms of overdose consist of excessive sweating, discharge of tears, increased bowel movements, loss of bowel and urine control, constriction of pupils, spasm of the eyelids, involuntary eye jerks, headache, slowing of heart beat and pulse, faintness low blood pressure, muscle cramps and twitches, weakness and paralysis. Respiratory effects include tight chest, wheezing and blockage of the airways. Central nervous system effects include inco-ordination confusion, slurred speech, agitation, fear and coma. Eventually respiratory failure or cardiac arrest can cause death.

EYE

- There is some evidence to suggest that this material can cause eye irritation and damage in some persons.
- Direct eye contact can produce tears, eyelid twitches, pupil contraction, loss of focus, and blurred or dimmed vision. Dilation of the pupils occasionally occurs.

SKIN

- The material is not thought to be a skin irritant (as classified using animal models). Abrasive damage however, may result from prolonged exposures. Good hygiene practice requires that exposure be kept to a minimum and that suitable gloves be used in an occupational setting.
- Skin contact with the material may damage the health of the individual; systemic effects may result following absorption.
- 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.
- There may be sweating and muscle twitches at site of contact. Reaction may be delayed by hours.

INHALED

- Inhalation of dusts, generated by the material, during the course of normal handling, may produce severely toxic effects; these may be fatal.
- 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.
- 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.
- Poisoning due to cholinesterase inhibitors causes symptoms such as increased blood flow to the nose, watery discharge, chest discomfort, shortness of breath and wheezing. Other symptoms include increased production of tears, nausea and vomiting, diarrhea, stomach pain, involuntary passing of urine and stools, chest pain, breathing difficulty, low blood pressure, irregular heartbeat, loss of reflexes, twitching, visual disturbances, altered pupil size, convulsions, lung congestion, coma and heart failure. Nervous system effects include inco-ordination, slurred speech, tremors of the tongue and eyelids, and paralysis of the limbs and muscles of breathing, which can cause death, although death is also seen due to cardiac arrest.
- Symptoms of carbamate poisoning are similar to that of organophosphate poisoning, however, recover from carbamate poisoning is quicker and generally less likely to be cause death.

CHRONIC HEALTH EFFECTS

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

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

Repeated or prolonged exposures to cholinesterase inhibitors produce symptoms similar to acute effects. In addition workers exposed repeatedly to these substances may exhibit impaired memory and loss of concentration, severe depression and acute psychosis, irritability, confusion, apathy, emotional lability, speech difficulties, headache, spatial disorientation, delayed reaction times, sleepwalking, drowsiness or insomnia. An influenza-like condition with nausea, weakness, anorexia and malaise has been described. There is a growing body of evidence from epidemiological studies and from experimental laboratory studies that short-term exposure to some cholinesterase-inhibiting insecticides may produce behavioral or neuro-chemical changes lasting for days or months, presumably outlasting the cholinesterase inhibition. Although the number of adverse effects following humans poisonings subside, there are still effects in some workers months after cholinesterase activity returns to normal. These long-lasting effects include blurred vision, headache, weakness, and anorexia. The neurochemistry of animals exposed to chlorpyrifos or fenthion is reported to be altered permanently after a single exposure. These effects may be more severe in developing animals where both acetyl- and butyrylcholinesterase may play an integral part in the development of the nervous system. Padilla S., The Neurotoxicity of Cholinesterase-Inhibiting Insecticides: Past and Present Evidence Demonstrating Persistent Effects. Inhalation Toxicology 7:903-907, 1995.

NAME	CAS RN	%
physostigmine	57-47-6	>98
On exposure to heat, light, air, metals forms		
rubreserine	18455-27-1	

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 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, without delay.

NOTES TO PHYSICIAN

■ for neostigmine: If taken by mouth the stomach should be emptied by aspiration and lavage. Atropine sulfate, usually in doses of 1 to 2 mg may be given preferably intravenously, or else intramuscularly or subcutaneously to control muscurinic effects. This dose may be repeated as necessary. Nicotinic effects, including muscle weakness and paralysis are not antagonized by atropine; small doses of tubocurarine may be used to control muscle twitching. Supportive treatment should be given as required. MARTINDALE: The Extra Pharmacopoeia, Twenty-ninth Edition.

Section 5 - FIRE FIGHTING MEASURES

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

EXTINGUISHING MEDIA

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

- Carbon dioxide.

FIRE FIGHTING

-
- Alert Emergency Responders and tell them location and nature of hazard.
- Wear full body protective clothing with breathing apparatus.
- Prevent, by any means available, spillage from entering drains or water course.
- Use fire fighting procedures suitable for surrounding area.
- DO NOT approach containers suspected to be hot.
- Cool fire exposed containers with water spray from a protected location.
- If safe to do so, remove containers from path of fire.
- Equipment should be thoroughly decontaminated after use.

GENERAL FIRE HAZARDS/HAZARDOUS COMBUSTIBLE PRODUCTS

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

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

May emit poisonous 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:

Gloves:

Respirator:

Particulate

Section 6 - ACCIDENTAL RELEASE MEASURES

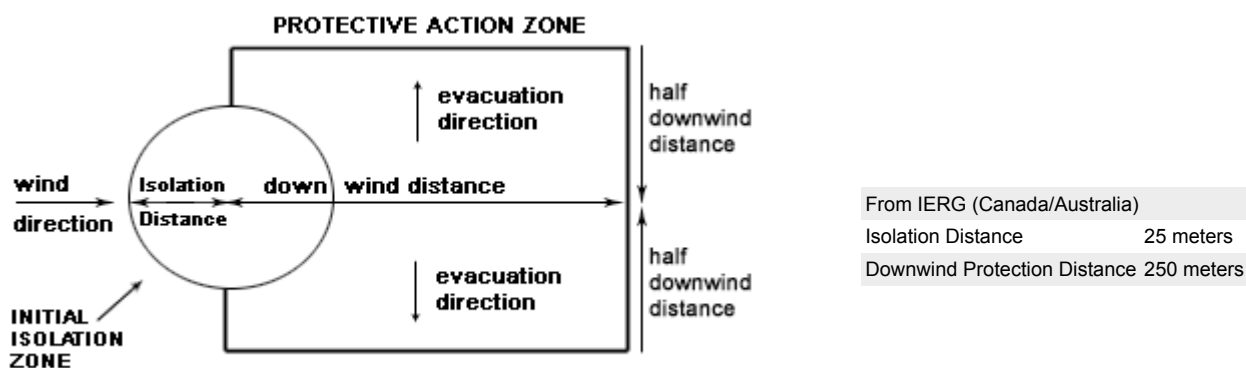
MINOR SPILLS

-
- 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

-
- Clear area of personnel and move upwind.
- Alert Emergency Responders and tell them location and nature of hazard.
- Wear full body protective clothing with breathing apparatus.
- Prevent, by any means available, spillage from entering drains or water course.
- Stop leak if safe to do so.
- Contain spill with sand, earth or vermiculite.
- Collect recoverable product into labeled containers for recycling.
- Neutralize/decontaminate residue.
- Collect solid residues and seal in labeled drums for disposal.
- Wash area and prevent runoff into drains.
- After clean up operations, decontaminate and launder all protective clothing and equipment before storing and re-using.
- If contamination of drains or waterways occurs, advise emergency services.

PROTECTIVE ACTIONS FOR SPILL



From US Emergency Response Guide 2000 Guide 151

FOOTNOTES

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

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

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

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

5 Guide 151 is taken from the US DOT emergency response guide book.

6 IERG information is derived from CANUTEC - Transport Canada.

ACUTE EXPOSURE GUIDELINE LEVELS (AEGL) (in ppm)

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

AEGL 2: The airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience irreversible or other serious, long-lasting adverse health effects or an impaired ability to escape.

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

Section 7 - HANDLING AND STORAGE

PROCEDURE FOR HANDLING

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

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

RECOMMENDED STORAGE METHODS

■ Glass container.

- Lined metal can, Lined metal pail/drum
- Plastic pail
- Polyliner drum
- Packing as recommended by manufacturer.
- Check all containers are clearly labeled and free from leaks.

For low viscosity materials

- Drums and jerricans must be of the non-removable head type.
- Where a can is to be used as an inner package, the can must have a screwed enclosure.

For materials with a viscosity of at least 2680 cSt. (23 deg. C) and solids (between 15 C deg. and 40 deg C.):

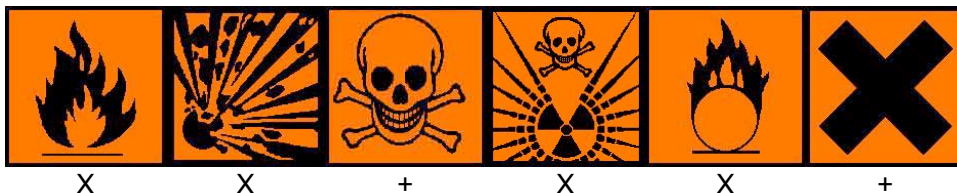
- Removable head packaging;
- Cans with friction closures and
- low pressure tubes and cartridges may be used.

- Where combination packages are used, and the inner packages are of glass, there must be sufficient inert cushioning material in contact with inner and outer packages *. - In addition, where inner packagings are glass and contain liquids of packing group I and II there must be sufficient inert absorbent to absorb any spillage *. - * unless the outer packaging is a close fitting molded plastic box and the substances are not incompatible with the plastic. All inner and sole packagings for substances that have been assigned to Packaging Groups I or II on the basis of inhalation toxicity criteria, must be hermetically sealed.

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 precautions

+: May be stored together

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS

The following materials had no OELs on our records

- physostigmine: CAS:57-47-6
- rubreserine: CAS:18455-27-1 CAS:24467-97-8

MATERIAL DATA

PHYSOSTIGMINE:

RUBRESERINE:

■ 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

-
- Chemical protective goggles with full seal
- Shielded mask (gas-type)
- Contact lenses may pose a special hazard; soft contact lenses may absorb and concentrate irritants. A written policy document, describing the wearing of lens or restrictions on use, should be created for each workplace or task. This should include a review of lens absorption and adsorption for the class of chemicals in use and an account of injury experience. Medical and first-aid personnel should be trained in their removal and suitable equipment should be readily available. In the event of chemical exposure, begin eye irrigation immediately and remove contact lens as soon as practicable. Lens should be removed at the first signs of eye redness or irritation - lens should be removed in a clean environment only after workers have washed hands thoroughly. [CDC NIOSH Current Intelligence Bulletin 59]

HANDS/FEET

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

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

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

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

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

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

OTHER

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

RESPIRATOR

-
- 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

■ For potent pharmacological agents:

Powders

To prevent contamination and overexposure, no open handling of powder should be allowed.

- Powder handling operations are to be done in a powders weighing hood, a glove box, or other equivalent ventilated containment system.
- In situations where these ventilated containment hoods have not been installed, a non-ventilated enclosed containment hood should be used.
- Pending changes resulting from additional air monitoring data, up to 300 mg can be handled outside of an enclosure provided that no grinding, crushing or other dust-generating process occurs.
- An air-purifying respirator should be worn by all personnel in the immediate area in cases where non-ventilated containment is used, where significant amounts of material (e.g., more than 2 grams) are used, or where the material may become airborne (as through grinding, etc.).
- Powder should be put into solution or a closed or covered container after handling.
- If using a ventilated enclosure that has not been validated, wear a half-mask respirator equipped with HEPA cartridges until the enclosure is validated for use.

Solutions Handling:

- Solutions can be handled outside a containment system or without local exhaust ventilation during procedures with no potential for aerosolisation. If the procedures have a potential for aerosolisation, an air-purifying respirator is to be worn by all personnel in the immediate area.
- Solutions used for procedures where aerosolisation may occur (e.g., vortexing, pumping) are to be handled within a containment system or with local exhaust ventilation.
- In situations where this is not feasible (may include animal dosing), an air-purifying respirator is to be worn by all personnel in the immediate area. If using a ventilated enclosure that has not been validated, wear a half-mask respirator equipped with HEPA cartridges until the enclosure is validated for use.
- Ensure gloves are protective against solvents in use.

Unless written procedures, specific to the workplace are available, the following is intended as a guide:

- For Laboratory-scale handling of Substances assessed to be toxic by inhalation. Quantities of up to 25 grams may be handled in Class II biological safety cabinets *; Quantities of 25 grams to 1 kilogram may be handled in Class II biological safety cabinets* or equivalent containment systems Quantities exceeding 1 kg may be handled either using specific containment, a hood or Class II biological safety cabinet*,
- HEPA terminated local exhaust ventilation should be considered at point of generation of dust, fumes or vapors.
- 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. When handling: Quantities of up to 25 grams, an approved respirator with HEPA filters or cartridges should be considered Quantities of 25 grams to 1 kilogram, a half-face negative pressure, full negative pressure, or powered helmet-type air purifying respirator should be considered. Quantities in excess of 1 kilogram, a full face negative pressure, helmet-type air purifying, or supplied air respirator should be considered.

Written procedures, specific to a particular work-place, may replace these recommendations

* For Class II Biological Safety Cabinets, Types B2 or B3 should be considered. Where only Class I, open fronted Cabinets are available, glove panels may be added, Laminar flow cabinets do not provide sufficient protection when handling these materials unless especially designed to do so.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES

Solid.

Mixes with water.

State	Divided solid	Molecular Weight	275.3
Melting Range (°F)	221- 224.6	Viscosity	Not Applicable
Boiling Range (°F)	Not applicable	Solubility in water (g/L)	Miscible
Flash Point (°F)	Not available	pH (1% solution)	Not available
Decomposition Temp (°F)	Not Available	pH (as supplied)	Not 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

APPEARANCE

Colourless or white, odourless, microcrystalline powder which becomes pink on exposure to heat, light, air or contact with traces of metal (owing to the formation of rubreserine); mixes with water (1:75), alcohol (1:10), chloroform (1:1), ether (1:30) and soft paraffin (1:180).

Section 10 - CHEMICAL STABILITY

CONDITIONS CONTRIBUTING TO INSTABILITY

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

STORAGE INCOMPATIBILITY

-
- Carbamates are incompatible with strong acids and bases, and especially incompatible with strong reducing agents such as hydrides.
- Flammable gaseous hydrogen is produced by the combination of active metals or nitrides with carbamates.
- Strongly oxidizing acids, peroxides, and hydroperoxides are incompatible with carbamates.

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

Section 11 - TOXICOLOGICAL INFORMATION

PHYSOSTIGMINE

TOXICITY AND IRRITATION

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

TOXICITY	IRRITATION
Unreported (man) LDLo: 0.882 mg/kg	Nil Reported
Intraperitoneal (rat) LD50: 2 mg/kg	
Oral (mouse) LD50: 3 mg/kg	
Intraperitoneal (mouse) LD50: 0.644 mg/kg	
Subcutaneous (mouse) LD50: 0.74 mg/kg	
Oral (rabbit) LD50: 11.2 mg/kg	
Subcutaneous (rabbit) LD50: 3 mg/kg	
Intramuscular (rabbit) LD50: 2.2 mg/kg	

■ for carbamates:

Carbamates are effective insecticides by virtue of their ability to inhibit acetylcholinesterase (AChE) (EC 3.1.1.7) in the nervous system. They can also inhibit other esterases. The carbamylation of the enzyme is unstable, and the regeneration of AChE is relatively rapid compared with that from a phosphorylated enzyme. Thus, carbamate pesticides are less dangerous with regard to human exposure than organophosphorus pesticides. The ratio between the dose required to produce death and the dose required to produce minimum symptoms of poisoning is substantially larger for carbamate compounds than for organophosphorus compounds. A dose-effect relationship exists between the dose, the severity of symptoms, and the degree of cholinesterase (ChE) inhibition. Because most carbamates have a low volatility, inhalation studies are mainly carried out using a dust or mist. In these studies, the toxicity is highly dependent on the size of the particles or droplets and, therefore, difficult to evaluate. The acute dermal toxicity of carbamates is generally low to moderate.

From controlled human studies, it is clear that poisoning symptoms can be seen a few minutes after exposure, and can last for a few hours. Thereafter, recovery starts and within hours, the symptoms disappear, and the ChE activity in erythrocytes and plasma returns to normal, because the carbamate is rather rapidly metabolised and the metabolites excreted. The appearance of these metabolites in the urine may be used for biological monitoring. Apart from the symptoms indicative of ChE poisoning, other signs and symptoms induced by certain carbamates have been described, such as skin and eye irritation, hyperpigmentation, and influence on the function of testes (slight increase of sperm abnormalities). These signs and symptoms were found in a few studies and should be confirmed before it can be stated that they were induced by carbamates. Epidemiological studies with persons primarily exposed to carbamates are not available.

Carbamates produce slight to moderate skin and eye irritation, depending on the vehicle used, duration of contact, and on whether the substance is applied to the abraded or intact skin. From the available data, it cannot be excluded that some of the carbamates will have a slight to moderate sensitization potential. Short- and long-term toxicity studies have been carried out. Some carbamates are very toxic and others are less toxic in long- term studies. From these studies, it is evident that, apart from the anticholinesterase activity, the following changes can be found: an influence on the haemopoietic system, an influence on the functioning of, and, at higher dosages, degeneration of, the liver and kidneys, and degeneration of testes. These abnormalities in the different organ systems depend on the animal strain and on the chemical structure of the carbamate. A clear influence on the nervous system, functional as well as histological, was found, particularly in non-laboratory animals such as pigs.

A considerable number of reproduction and teratogenicity studies have been carried out with different carbamates and various animal species. Different types of abnormalities were found, i.e., increase in mortality, disturbance of the endocrine system, and effects on the hypophysis and its gonadotrophic function. These effects were mainly seen at high dose levels. Generally, the fetal effects included an increase in mortality, decreased weight gain in the first weeks after birth, and induction of early embryonic death. All these effects can be

summarized as embryotoxic effects. Certain carbamates also induce teratogenic effects, mainly at high dose levels applied by stomach tube. When the same dose level was administered with the diet, no effects were seen.

Some carbamates induce mutagenic effects, others are negative. In general, the methyl carbamates are negative in mammalian tests, while compounds such as carbendazim, benomyl, and the 2 thiophanate derivatives showed a positive effect with very high dose levels in certain systems. The benzimidazole moiety may act as a base analogue for DNA and as a spindle poison. They are antimitotic agents and cause mitotic arrest, mitotic delay, and a low incidence of chromosome damage. Sometimes, the results are contradictory or cannot be reproduced, but positive results for point mutation and chromosome aberrations are well documented. These benzimidazole derivatives can be considered as weak mutagenic compounds.

Carcinogenicity studies with benzimidazole derivatives showed either positive or equivocal results. Added to the fact that certain mutagenicity studies also give positive results, it cannot be excluded that these compounds may have carcinogenic or promotor properties. Carbamate pesticides may be converted to N -nitroso compounds. This was demonstrated in a great number of in vivo nitrosation studies in which high levels of the carbamates were administered to animals in combination with high levels of nitrite. These N - nitroso compounds have to be considered as mutagenic and carcinogenic. However, the amount of nitroso compounds that can be expected to result from dietary intake of carbamate pesticide residues is negligible in comparison with nitroso-precursors that occur naturally in food and drinking-water.

The metabolic fate of carbamates is basically the same in plants, insects, and mammals. Carbamates are usually easily absorbed through the skin, mucous membranes, and respiratory and gastrointestinal tracts, but there are exceptions. Generally, the metabolites are less toxic than the parent compounds. However, in certain cases, the metabolites are just as toxic or even more toxic than the parent carbamate. In most mammals, the metabolites are mainly excreted rather rapidly in the urine. The dog seems to be different in this respect. Accumulation takes place in certain cases, but is of minor importance because of the rapid metabolism. The first step in the metabolism of carbamates is hydrolysis to carbamic acid, which decomposes to carbon dioxide (CO₂) and the corresponding amine. The rate of hydrolysis by esterases is faster in mammals than in plants and insects.

The organs in which residues have been reported are the liver, kidneys, brain, fat, and muscle. The half-life in the rat is of the order of 3 - 8 h. From the limited data available, it seems that the excretion of carbamates via urine is also rapid in man, and that the metabolic pathways in man are the same as those in the rat.

Intraperitoneal (rabbit): 2.47 mg/kg

Section 12 - ECOLOGICAL INFORMATION

Refer to data for ingredients, which follows:

RUBRESERINE:

PHYSOSTIGMINE:

■ DO NOT discharge into sewer or waterways.

PHYSOSTIGMINE:

■ Carbamate pesticides are relatively non-persistent in the environment with half-lives ranging from hours to several weeks or months. Only rarely are they found in crops beyond the growing season during which they are applied. Chemical or photochemical mechanisms may produce a leaving group which is easily degraded. As a rule these compounds do not represent a serious problem as contaminants of soil and water. Breakdown products are usually non-toxic being composed of low-molecular weight, volatile molecules that are easily degraded and utilized by micro-organisms. Being esters they are also susceptible to hydrolysis. Most carbamate pesticides are stable to acid pHs but under alkaline conditions hydrolysis is rapid with the breakdown rate increasing 10-fold for each pH unit above 7. An increase of 10 deg. C of temperature will increase the hydrolysis rate approximately 4-fold. When these compounds are present in the soil their disappearance is affected by their interaction with the physical characteristics and water content of the soil, and the microflora present. In certain types of soil strong binding may make them unavailable for biological decomposition. In such soils even running water produces little movement and thus minimal contamination of water supplies. Less tightly bound substances are similarly unlikely to produce substantial contamination because of rapid breakdown. In general only minute amounts of pesticide residue and their breakdown products are found in natural water systems. In soil however there is a greater likelihood of the presence and buildup of toxic residues.

RUBRESERINE:

Ecotoxicity

Ingredient	Persistence: Water/Soil	Persistence: Air	Bioaccumulation	Mobility
physostigmine	HIGH		LOW	MED

Section 13 - DISPOSAL CONSIDERATIONS

US EPA Waste Number & Descriptions

B. Component Waste Numbers

When physostigmine is present as a solid waste as a discarded commercial chemical product, off-specification species, as a container residue, or a spill residue, use EPA waste number P204 (waste code T).

Disposal Instructions

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

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

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

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

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

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

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

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

Section 14 - TRANSPORTATION INFORMATION



DOT:

Symbols:	G	Hazard class or Division:	6.1
Identification Numbers:	UN1544	PG:	I
Label Codes:	6.1	Special provisions:	IB7, IP1, T6, TP33
Packaging: Exceptions:	None	Packaging: Non-bulk:	211
Packaging: Exceptions:	None	Quantity limitations: Passenger aircraft/rail:	5 kg
Quantity Limitations: Cargo aircraft only:	50 kg	Vessel stowage: Location:	A
Vessel stowage: Other:	None		

Hazardous materials descriptions and proper shipping names:

Alkaloids, solid, n.o.s. or Alkaloid salts, solid, n.o.s. poisonous

Air Transport IATA:

ICAO/IATA Class:	6.1	ICAO/IATA Subrisk:	None
UN/ID Number:	1544	Packing Group:	I
Special provisions:	A3		

Shipping Name: ALKALOID SALTS, SOLID, N.O.S. *(CONTAINS PHYSOSTIGMINE)

Maritime Transport IMDG:

IMDG Class:	6.1	IMDG Subrisk:	None
UN Number:	1544	Packing Group:	I
EMS Number:	F-A, S-A	Special provisions:	43 274
Limited Quantities:	0		

Shipping Name: ALKALOIDS, SOLID, N.O.S. or ALKALOIDS SALTS, SOLID, N.O.S.(contains physostigmine)

Section 15 - REGULATORY INFORMATION



REGULATIONS

physostigmine (CAS: 57-47-6) is found on the following regulatory lists;

"Canada Non-Domestic Substances List (NDSL)", "US - Massachusetts Oil & Hazardous Material List", "US - Pennsylvania - Hazardous Substance List", "US - Vermont Hazardous Constituents", "US - Vermont Hazardous Waste - Acutely Hazardous Wastes", "US - Washington Dangerous waste constituents list", "US - Washington Discarded Chemical Products List - ""P"" Chemical Products", "US Department of Transportation (DOT) List of Hazardous Substances and Reportable Quantities - Hazardous Substances Other Than Radionuclides", "US DOE Temporary Emergency Exposure Limits (TEELs)", "US List of Lists - Consolidated List of Chemicals Subject to the Emergency Planning and Community Right-to-Know Act (EPCRA) and Section 112(r) of the Clean Air Act", "US RCRA (Resource Conservation & Recovery Act) - Hazardous Constituents - Appendix VIII to 40 CFR 261", "US RCRA (Resource Conservation & Recovery Act) - List of Hazardous Wastes", "US RCRA (Resource Conservation & Recovery Act) - Phase 4 LDR Rule - Universal Treatment Standards", "US SARA Section 302 Extremely Hazardous Substances", "US Toxic Substances Control Act (TSCA) - Inventory"

Regulations for ingredients

No data for rubreserine (CAS: , 18455-27-1, 24467-97-8)

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE

- Skin contact may produce health damage*.
- Cumulative effects may result following exposure*.
- May produce discomfort of the eyes*.

* (limited evidence).

Ingredients with multiple CAS Nos

Ingredient Name	CAS
rubreserine	18455-27-1, 24467-97-8

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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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