1-Adamantylamine

sc-251475

Material Safety Data Sheet

Hazard Alert Code Key:	EXTREME	HIGH	MODERATE	LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME
1-Adamantylamine

STATEMENT OF HAZARDOUS NATURE
CONSIDERED A HAZARDOUS SUBSTANCE ACCORDING TO OSHA 29 CFR 1910.1200.

NFPA

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

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

SYNONYMS
C10-H17-N, "tricylo[3.3.1.1(sup3, 7)]decan-1-amine", 1-adamantamine, 1-adamantanamine, 1-amino-adamantane, 1-aminoadamatane, 1-aminodiamantane, 1-aminotricyclo[3.3.1.1(sup3.7)]decane, Exp-105-1, PK-Merz, Symmetrel, "NMDA antagonist"

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS

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

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

CANADIAN WHMIS SYMBOLS

EMERGENCY OVERVIEW

RISK

Harmful if swallowed.
Possible risk of impaired fertility.
Possible risk of harm to the unborn child.
Irritating to eyes, respiratory system and skin.

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.
■ Dopamine receptor antagonists block dopamine receptors.
There are five types of dopamine receptor in the human body; these are found in the brain, peripheral nervous system, blood vessels and the kidney.

EYE

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

SKIN

■ This material can cause inflammation of the skin oncontact 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 can cause respiratory irritation in some persons.
The body's response to such irritation can cause further lung damage.
■ 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

■ Long-term exposure to respiratory irritants may result in disease of the airways involving difficult breathing and related systemic problems.
Ample evidence from experiments exists that there is a suspicionthis material directly reduces fertility.
Results in experiments suggest that this material may cause disorders in the development of the embryo or fetus, even when no signs of poisoning show in the mother.
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.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

NAME	CAS RN	%
amantadine	768-94-5	>98

Section 4 - FIRST AID MEASURES

SWALLOWED

· IF SWALLOWED, REFER FOR MEDICAL ATTENTION, WHERE POSSIBLE, WITHOUT DELAY. · Where Medical attention is not immediately available or where the patient is more than 15 minutes from a hospital or unless instructed otherwise:

EYE

■ If this product comes in contact with the eyes: · Wash out immediately with fresh running water. · Ensure complete irrigation of the eye by keeping eyelids apart and away from eye and moving the eyelids by occasionally lifting the upper and lower lids.

SKIN

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

INHALED

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

NOTES TO PHYSICIAN

■ For amantadine intoxication:
· If overdose occurs the stomach should be emptied by aspiration and lavage.
· In particular, symptoms of excessive central stimulation with convulsions and psychosis should be treated appropriately.
· Anti-arrhythmic agents may be required.
· Bladder catherisation may be required.
· Elimination of amantadine has been reported to be increased in acid urine
MARTINDALE: The Extra Pharmacopoeia, 27th Ed.
· There is no specific antidote for an overdose of However, slowly administered intravenous physostigmine in 1 and 2 mg doses in an adult at 1- to 2-hour intervals and 0.5 mg doses in a child at 5- to 10-minute intervals up to a maximum of 2 mg/hour have been reported to be

effective in the control of central nervous system toxicity caused by amantadine hydrochloride.
· For acute overdosing, general supportive measures should be employed along with immediate gastric lavage or induction of emesis. Fluids should be forced, and if necessary, given intravenously.
· The pH of the urine has been reported to influence the excretion rate of the drug. Since the excretion rate of the drug increases rapidly when the urine is acidic, the administration of urine acidifying drugs may increase the elimination of the drug from the body.
· The blood pressure, pulse, respiration and temperature should be monitored.
· The patient should be observed for hyperactivity and convulsions; if required, sedation, and anticonvulsant therapy should be administered. The patient should be observed for the possible development of arrhythmias and hypotension; if required, appropriate antiarrhythmic and antihypotensive therapy should be given.
· Electrocardiographic monitoring may be required after ingestion, since malignant tachyarrhythmias can appear after overdose.
· Care should be exercised when administering adrenergic agents, such as isoproterenol, to patients with a drug overdose, since the dopaminergic activity of the drug has been reported to induce malignant arrhythmias.
· The blood electrolytes, urine pH and urinary output should be monitored. If there is no record of recent voiding, catheterisation should be done
RxList for Symmetrel.

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.

FIRE FIGHTING
· Alert Emergency Responders and tell them location and nature of hazard.
· Wear breathing apparatus plus protective gloves.

GENERAL FIRE HAZARDS/HAZARDOUS COMBUSTIBLE PRODUCTS
· Combustible solid which burns but propagates flame with difficulty.
· Avoid generating dust, particularly clouds of dust in a confined or unventilated space as dusts may form an explosive mixture with air, and any source of ignition, i.e. flame or spark, will cause fire or explosion. Dust clouds generated by the fine grinding of the solid are a particular hazard; accumulations of fine dust may burn rapidly and fiercely if ignited.
Combustion products include: carbon monoxide (CO), carbon dioxide (CO_2), nitrogen oxides (NOx), 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.

Section 7 - HANDLING AND STORAGE

PROCEDURE FOR HANDLING
· Avoid all personal contact, including inhalation.
· Wear protective clothing when risk of exposure occurs.

Empty containers may contain residual dust which has the potential to accumulate following settling. Such dusts may explode in the presence of an appropriate ignition source.
· Do NOT cut, drill, grind or weld such containers.
· In addition ensure such activity is not performed near full, partially empty or empty containers without appropriate workplace safety authorisation or permit.

RECOMMENDED STORAGE METHODS

■ 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.

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

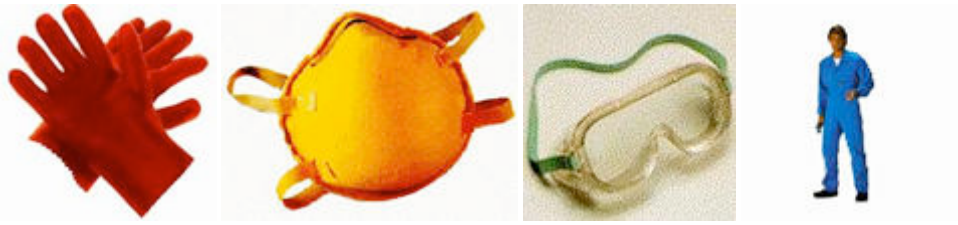
EXPOSURE CONTROLS

Source	Material	TWA ppm	TWA mg/m³	STEL ppm	STEL mg/m³	Peak ppm	Peak mg/m³	TWA F/CC	Notes
Canada - British Columbia Occupational Exposure Limits	amantadine (Particles (Insoluble or Poorly Soluble) Not Otherwise Classified (PNOC))		10 (N)						
US - Wyoming Toxic and Hazardous Substances Table Z1 Limits for Air Contaminants	amantadine (Particulates not otherwise regulated (PNOR)(f)-Respirable fraction)		5						
US - Tennessee Occupational Exposure Limits - Limits For Air Contaminants	amantadine (Particulates not otherwise regulated Respirable fraction)		5						
US - California Permissible Exposure Limits for Chemical Contaminants	amantadine (Particulates not otherwise regulated Respirable fraction)		5						(n)
US - Oregon Permissible Exposure Limits (Z-1)	amantadine (Particulates not otherwise regulated (PNOR) (f) Total Dust)	-	10						Bold print identifies substances for which the Oregon Permissible Exposure Limits (PELs) are different than the federal Limits. PNOR means “particles not otherwise regulated.”
US - Michigan Exposure Limits for Air Contaminants	amantadine (Particulates not otherwise regulated, Respirable dust)		5						

Canada - Prince Edward Island Occupational Exposure Limits	amantadine (Particles (Insoluble or Poorly Soluble) [NOS] Inhalable particles)		10		See Appendix B current TLV/BEI Book
US - Oregon Permissible Exposure Limits (Z-1)	amantadine (Particulates not otherwise regulated (PNOR) (f) Respirable Fraction)	-	5		Bold print identifies substances for which the Oregon Permissible Exposure Limits (PELs) are different than the federal Limits. PNOR means “particles not otherwise regulated.”

ENDOELTABLE

PERSONAL PROTECTION



RESPIRATOR

• particulate.

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

· fluorocaoutchouc

· 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.

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.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES

Solid.
Does not mix with water.

State	Divided solid	Molecular Weight	151.25
Melting Range (°F)	403- 406	Viscosity	Not Applicable
Boiling Range (°F)	Not available	Solubility in water (g/L)	Immiscible
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

APPEARANCE

Off-white to yellow powder; does not mix with water.

Section 10 - CHEMICAL STABILITY

CONDITIONS CONTRIBUTING TO INSTABILITY

· Presence of incompatible materials.
· Product is considered stable.

STORAGE INCOMPATIBILITY

■ Avoid reaction with oxidizing agents.

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

Section 11 - TOXICOLOGICAL INFORMATION

amantadine

TOXICITY AND IRRITATION

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

TOXICITY	IRRITATION
Oral (rat) LD50: 900 mg/kg	Nil Reported
Oral (mouse) LD50: 900 mg/kg	
Intraperitoneal (mouse) LD50: 245 mg/kg	

■ Asthma-like symptoms may continue for months or even years after exposure to the material ceases. This may be due to a non-allergenic condition known as reactive airways dysfunction syndrome (RADS) which can occur following exposure to high levels of highly irritating compound. Key criteria for the diagnosis of RADS include the absence of preceding respiratory disease, in a non-atopic individual, with abrupt onset of persistent asthma-like symptoms within minutes to hours of a documented exposure to the irritant. A reversible airflow pattern, on spirometry, with the presence of moderate to severe bronchial hyperreactivity on methacholine challenge testing and the lack of minimal lymphocytic inflammation, without eosinophilia, have also been included in the criteria for diagnosis of RADS. RADS (or asthma) following an irritating inhalation is an infrequent disorder with rates related to the concentration of and duration of exposure to the irritating substance. Industrial bronchitis, on the other hand, is a disorder that occurs as result of exposure due to high concentrations of irritating substance (often particulate in nature) and is completely reversible after exposure ceases. The disorder is characterised by dyspnea, cough and mucus production.

Amantadine (an adamantane or amantane) has been associated with several central nervous system side effects, likely due to amantadine's dopaminergic and adrenergic activity, and to a lesser extent, its activity as an anticholinergic.
Common side-effects associated with amantadine therapy include ankle oedema, nervous excitement, confusion, difficulty in concentration, dizziness, light-headedness, orthostatic hypotension, urinary retention, slurred speech, ataxia, depression, insomnia, lethargy, nausea, anorexia, vomiting, dry mouth, constipation, skin rash, discoloured spots or skin patches (livedo reticularis) and visual disturbances. More serious side-effects may include congestive heart-failure, psychosis and leucopenia. Dose-related responses include hallucination, feelings of detachment and convulsions.
Deaths have been reported from overdose with amantadine. The lowest reported acute lethal dose was 1 gram. Acute toxicity may be attributable to the anticholinergic effects of amantadine. Drug overdose has resulted in cardiac, respiratory, renal or central nervous system toxicity. Cardiac dysfunction includes arrhythmia, tachycardia and hypertension
Suicide attempts, some of which have been fatal, have been reported in patients treated with amantadine many of whom received short courses for influenza treatment or prophylaxis. The incidence of suicide attempts is not known and the pathophysiologic mechanism is not understood. Suicide attempts and suicidal ideation have been reported in patients with and without prior history of psychiatric illness.
Sporadic cases of possible Neuroleptic Malignant Syndrome (NMS) have been reported in association with dose reduction or withdrawal of the drug. NMS is an uncommon but life-threatening syndrome characterised by fever or hyperthermia; neurologic findings including muscle rigidity, involuntary movements, altered consciousness; mental status changes; other disturbances such as autonomic dysfunction, tachycardia, tachypnea, hyper- or hypotension; laboratory findings such as creatine phosphokinase elevation, leukocytosis, myoglobinuria, and increased serum myoglobin.
Carcinogenicity and mutagenicity: Long-term in vivo animal studies designed to evaluate the carcinogenic potential of amantadine have not been performed. In several in vitro assays for gene mutation, the drug did not increase the number of spontaneously observed mutations in four strains of Salmonella typhimurium (Ames Test) or in a mammalian cell line (Chinese Hamster Ovary cells) when incubations were performed either with or without a liver metabolic activation extract. Further, there was no evidence of chromosome damage observed in an in vitro test using freshly derived and stimulated human peripheral blood lymphocytes (with and without metabolic activation) or in an in vivo mouse bone marrow micronucleus test (140-550 mg/kg; estimated human equivalent doses of 11.7-45.8 mg/kg based on body surface area conversion).
Reproductive toxicity: In a three litter, non-GLP, reproduction study in rats, amantadine at a dose of 32 mg/kg/day (equal to the maximum recommended human dose on a mg/m2 basis) administered to both males and females slightly impaired fertility. There were no effects on fertility at a dose level of 10 mg/kg/day (or 0.3 times the maximum recommended human dose on a mg/m2 basis); intermediate doses were not tested.
Failed fertility has been reported during human in vitro fertilization (IVF) when the sperm donor ingested amantadine 2 weeks prior to, and during the IVF cycle.
Developmental toxicity: The hydrochloride is embryotoxic and teratogenic in rats at 50 mg/kg/day (about 12 times a recommended human dose). These effects do not occur at 37 mg/kg/day nor do they occur in rabbits.
In two non-GLP studies in rats in which females were dosed from 5 days prior to mating to Day 6 of gestation or on Days 7-14 of gestation, amantadine produced increases in embryonic death at an oral dose of 100 mg/kg (or 3 times the maximum recommended human dose on a mg/m2 basis). In the non-GLP rat study in which females were dosed on Days 7-14 of gestation, there was a marked increase in severe visceral and skeletal malformations at oral doses of 50 and 100 mg/kg (or 1.5 and 3 times, respectively, the maximum recommended human dose on a mg/m2 basis). The no-effect dose for teratogenicity was 37 mg/kg (equal to the maximum recommended human dose on a mg/m2 basis).
Cardiovascular maldevelopment (single ventricle with pulmonary atresia) has been associated with maternal exposure to amantadine (100 mg/d) administered during the first 2 weeks of pregnancy.
Tremors, convulsions, ataxia recorded.

Section 12 - ECOLOGICAL INFORMATION

No data

Ecotoxicity

Ingredient	Persistence: Water/Soil	Persistence: Air	Bioaccumulation	Mobility
amantadine	HIGH	No Data Available	LOW	MED

Section 13 - DISPOSAL CONSIDERATIONS

Disposal Instructions

All waste must be handled in accordance with local, state and federal regulations.
¦ Puncture containers to prevent re-use and bury at an authorized landfill.
Legislation addressing waste disposal requirements may differ by country, state and/ or territory. Each user must refer to laws operating in their area. In some areas, certain wastes must be tracked.
A Hierarchy of Controls seems to be common - the user should investigate:
· Reduction
· Reuse
· Recycling
· Disposal (if all else fails)
This material may be recycled if unused, or if it has not been contaminated so as to make it unsuitable for its intended use. Shelf life considerations should also be applied in making decisions of this type. Note that properties of a material may change in use, and recycling or reuse may not always be appropriate.
DO NOT allow wash water from cleaning equipment to enter drains. Collect all wash water for treatment before disposal.
· Recycle wherever possible.
· Consult manufacturer for recycling options or consult Waste Management Authority for disposal if no suitable treatment or disposal facility can be identified.

Section 14 - TRANSPORTATION INFORMATION

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

Section 15 - REGULATORY INFORMATION

amantadine (CAS: 768-94-5) is found on the following regulatory lists;
"Canada Non-Domestic Substances List (NDSL)","Canada Toxicological Index Service - Workplace Hazardous Materials Information System - WHMIS (English)","US Toxic Substances Control Act (TSCA) - Inventory"

Section 16 - OTHER INFORMATION

ND
Substance CAS Suggested codes amantadine 768- 94- 5 Xn; R22

Reasonable care has been taken in the preparation of this information, but the author makes no warranty of merchantability or any other warranty, expressed or implied, with respect to this information. The author makes no representations and assumes no liability for any direct, incidental or consequential damages resulting from its use. For additional technical information please call our toxicology department on +800 CHEMCALL.

■ Classification of the preparation and its individual components has drawn on official and authoritative sources as well as independent review by the Chemwatch Classification committee using available literature references.
A list of reference resources used to assist the committee may be found at:
www.chemwatch.net/references.

■ The (M)SDS is a Hazard Communication tool and should be used to assist in the Risk Assessment. Many factors determine whether the reported Hazards are Risks in the workplace or other settings. Risks may be determined by reference to Exposures Scenarios. Scale of use, frequency of use and current or available engineering controls must be considered.

Issue Date: Oct-18-2009

Print Date:Apr-13-2011