Toremifene citrate

sc-253712

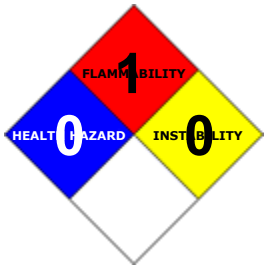
Material Safety Data Sheet

Hazard Alert Code Key:	EXTREME	HIGH	MODERATE	LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME
Toremifene citrate

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
C26-H28-Cl-N-O.C6-H8-O7, "(Z)-2-[4-(4-chloro-1, 2-diphenyl-1-butenyl)phenoxy]-N, N-", "dimethylethanamine, ", "2-hydroxy-1, 2, 3-propanetricarboxylate (1:1)", "citrate of:", "ethanamine, 2-[4-(4-chloro-1, 2-diphenyl-1-butenyl)phenoxy]-N, N-", "dimethyl-, ", (Z)-, "(Z)-2-[4-(4-chloro-1, 2-diphenyl-1-butenyl)phenoxy]-N, N-", dimethylethanamine, "2-[para-((Z)-4-chloro-1, 2-diphenyl-1butenyl)phenoxy]-N, N-", dimethylethylamine, "(Z)-4-chloro-1, 2-diphenyl-1-[4-(2-(N, N-dimethylamino)ethoxy)phenyl]-", 1-butene, Z-toremifene, "toremifene base", chlorotamoxifen, "tamoxifen, chloro-", "anti-oestrogen/ anti-neoplastic"

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS

		Min	Max
Flammability:	1		
Toxicity:	2		
Body Contact:	2		
Reactivity:	1		
Chronic:	3		

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

CANADIAN WHMIS SYMBOLS

EMERGENCY OVERVIEW

RISK

May impair fertility.
May cause harm to the unborn child.
May cause harm to breastfed babies.
Toxic: danger of serious damage to health by prolonged exposure if swallowed.
Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED

■ Although ingestion is not thought to produce harmful effects, the material may still be damaging to the health of the individual following ingestion, especially where pre-existing organ (e.
g.
■ Limited evidence exists that the substance may cause irreversible but non-lethal mutagenic effects following a single exposure.
■ 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.
■ Adverse effects of tamoxifen and its congeners may include hot flushes, oedema, vaginal bleeding, pruritus vulvae, gastrointestinal upsets, dizziness, rashes, hypercalcaemia and tumour pain.
Transient leukopenia and thrombocytopenia have been reported.

EYE

■ There is some evidence to suggest that this material can causeeye irritation and damage in some persons.
■ Systemic tamoxifen may be secreted in tears and deposit on corneal epithelium producing secondary effects.
Subepithelial corneal deposits of granules in a whorl configuration have been described.

SKIN

■ The material is not thought to produce adverse health effects or skin irritation following contact (as classified using animal models).
Nevertheless, good hygiene practice requires that exposure be kept to a minimum and that suitable gloves be used in an occupational setting.
■ 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 adverse health effects or irritation of the respiratory tract (as classified using animal models).
Nevertheless, good hygiene practice requires that exposure be kept to a minimum and that suitable control measures be used in an occupational setting.
■ Limited evidence exists that the substance may cause irreversible but non-lethal mutagenic effects following a single exposure.

CHRONIC HEALTH EFFECTS

■ Toxic: danger of serious damage to health by prolonged exposure if swallowed.
This material can cause serious damage if one is exposed to it for long periods. It can be assumed that it contains a substance which can produce severe defects.
Ample evidence exists from experimentation that reduced human fertility is directly caused by exposure to the material.
Ample evidence exists, from results in experimentation, that developmental disorders are directly caused by human exposure to the material.
There has been some concern that this material can cause cancer or mutations but there is not enough data to make an assessment.
Exposure to the material may result in a possible risk of irreversible effects. The material may produce mutagenic effects in man. This concern is raised, generally, on the basis of
appropriate studies with similar materials using mammalian somatic cells in vivo. Such findings are often supported by positive results from in vitro mutagenicity studies.
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.
Clinical trials in postmenopausal women with metastatic breast cancer, undergoing treatment with tamoxifen, show dose-related decreases in luteinising hormone and follicle-stimulating hormone levels. A rise in sex-hormone-binding globulin levels was also found. All changes occurred within the first three months of therapy.
Perimacular deposits and macular oedema have been reported in patients receiving tamoxifen for more than a year.
Chronic exposure to tamoxifen and its congeners may produce changes in sex organs, intestines and haemopoietic tissues.
Tamoxifen has produced liver tumours in mice and produces endometrial cancer in humans. The risk of an increase in the incidence of endometrial cancer rises from 3 per 10000 to between 6 and 9 per 10000 per year in woman undergoing treatment.
Toremifene was tested for carcinogenicity by oral administration to male and female rats in several studies. No increase in tumour incidence was observed. In one study of long duration, toremifene decreased the incidence of tumours in some hormone-dependent tissues, notably the mammary gland. In another study with female rats, toremifene increased the incidence of kidney tumours and the

proportion of malignant liver tumours induced by N-nitrosodiethylamine. In other studies, toremifene inhibited the development of 7,12-dimethylbenz[a]anthracene or N-methyl-N-
nitrosourea-induced mammary tumours.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

NAME	CAS RN	%
toremifene citrate	89778-27-8	>98

Section 4 - FIRST AID MEASURES

SWALLOWED
· Immediately give a glass of water. · First aid is not generally required. If in doubt, contact a Poisons Information Center or a doctor.

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 or hair contact occurs: · 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 poisons (where specific treatment regime is absent):
----------BASIC TREATMENT

· Establish a patent airway with suction where necessary.
· Watch for signs of respiratory insufficiency and assist ventilation as necessary.
Toremifene is well absorbed in humans with major metabolites (resulting from N-demethylation, hydroxylation and deamination), being excreted in the faeces. The elimination half-life is reportedly six days.

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.
When any large container (including road and rail tankers) is involved in a fire,
consider evacuation by 100 metres in all directions.

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

FIRE INCOMPATIBILITY
■ Avoid contamination with oxidizing agents i.e. nitrates, oxidizing acids,chlorine bleaches, pool chlorine etc. as ignition may result.

PERSONAL PROTECTION
Glasses:
Chemical goggles.
Gloves:
Respirator:

Particulate

Section 6 - ACCIDENTAL RELEASE MEASURES

MINOR SPILLS
■ Environmental hazard - contain spillage.
· Clean up waste regularly and abnormal spills immediately.
· Avoid breathing dust and contact with skin and eyes.
· Wear protective clothing, gloves, safety glasses and dust respirator.
· Use dry clean up procedures and avoid generating dust.
· Vacuum up or sweep up. NOTE: Vacuum cleaner must be fitted with an exhaust micro filter (HEPA type) (consider explosion-proof machines designed to be grounded during storage and use).
· Dampen with water to prevent dusting before sweeping.
· Place in suitable containers for disposal.
MAJOR SPILLS
■ Environmental hazard - contain spillage.
Moderate hazard.
· CAUTION: Advise personnel in area.
· Alert Emergency Responders and tell them location and nature of hazard.

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.

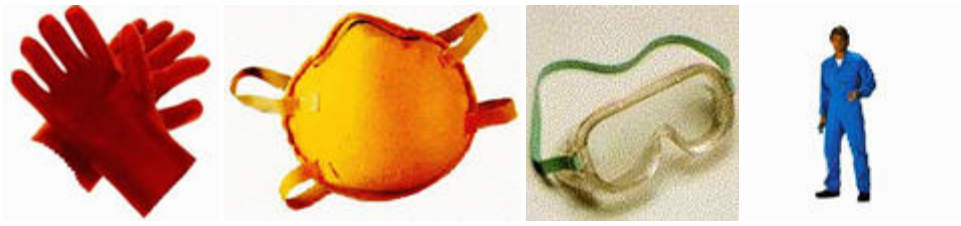
STORAGE REQUIREMENTS
■ Observe manufacturer's storing and handling recommendations.

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS

The following materials had no OELs on our records
• toremifene citrate: CAS:89778-27-8

PERSONAL PROTECTION



RESPIRATOR
•Particulate. (AS/NZS 1716 & 1715, EN 143:2000 & 149:2001, ANSI Z88 or national equivalent)

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], [AS/NZS 1336 or national equivalent].

HANDS/FEET

■ Suitability and durability of glove type is dependent on usage. Important factors in the selection of gloves include:
· 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, AS/NZS 2161.1 or national equivalent).
· 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, AS/NZS 2161.10.1 or national equivalent) 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, AS/NZS 2161.10.1 or national equivalent) 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. [AS/NZS 2210]
· 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.

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	598.14
Melting Range (°F)	320- 324	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)	>1
Volatile Component (%vol)	Negligible	Evaporation Rate	Not applicable

APPEARANCE

Crystalline powder; does not mix well with water (0.44 mg/ml at 37 C.). Sensitive to UV light. Dissociation constant: pKa =~8.0

Log Kow = 3.3

Material	Value

Section 10 - CHEMICAL STABILITY

CONDITIONS CONTRIBUTING TO INSTABILITY

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

STORAGE INCOMPATIBILITY
■ Avoid reaction with oxidizing agents.

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

Section 11 - TOXICOLOGICAL INFORMATION

toremifene citrate

TOXICITY AND IRRITATION
TOREMIFENE CITRATE:
■ unless otherwise specified data extracted from RTECS - Register of Toxic Effects of Chemical Substances.

TOXICITY	IRRITATION
Oral (rat) LD50: 3000 mg/kg	Nil Reported
Oral (monkey) LD50: >2000 mg/kg	

■ NOTE: Substance has been shown to be mutagenic in at least one assay, or belongs to a family of chemicals producing damage or change to cellular DNA.

The substance is classified by IARC as Group 3:
NOT classifiable as to its carcinogenicity to humans.
Evidence of carcinogenicity may be inadequate or limited in animal testing.
Eye effects, incontinence, hair, general depressed activity,
diarrhoea, changes in brain weight, blood changes, changes in uterine
weight, changes in liver weight, changes in ovarian weight recorded.

Section 12 - ECOLOGICAL INFORMATION

Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
This material and its container must be disposed of as hazardous waste.
Avoid release to the environment.
Refer to special instructions/ safety data sheets.

Ecotoxicity

Ingredient	Persistence: Water/Soil	Persistence: Air	Bioaccumulation	Mobility
toremifene citrate	No Data Available	No Data Available		

Section 13 - DISPOSAL CONSIDERATIONS

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

Section 14 - TRANSPORTATION INFORMATION

DOT:
Symbols: G Hazard class or Division: 9
Identification Numbers: UN3077 PG: III
Label Codes: 9 Special provisions: 8, 146,
335, B54,
IB8, IP3,
N20, T1,
TP33
Packaging: Exceptions: 155 Packaging: Non- bulk: 213
Packaging: Exceptions: 155 Quantity limitations: No limit
Passenger aircraft/rail:
Quantity Limitations: Cargo No limit Vessel stowage: Location: A
aircraft only:
Vessel stowage: Other: None
Hazardous materials descriptions and proper shipping names:
Environmentally hazardous substance, solid, n.o.s

Air Transport IATA:
UN/ID Number: 3077 Packing Group: III
Special provisions: A97
Cargo Only
Packing Instructions: 956 Maximum Qty/Pack: 400 kg
Passenger and Cargo Passenger and Cargo
Packing Instructions: Y956 Maximum Qty/Pack: 400 kg
Passenger and Cargo Limited Quantity Passenger and Cargo Limited Quantity
Packing Instructions: 956 Maximum Qty/Pack: 30 kg G
Shipping Name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID,
N.O.S. *(CONTAINS TOREMIFENE CITRATE)

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

Section 15 - REGULATORY INFORMATION

No data for toremifene citrate (CAS: , 89778-27-8)

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE
■ Ingestion may produce health damage*.
■ May produce discomfort of the eyes*.
■ Limited evidence of a carcinogenic effect*.
■ Exposure may produce irreversible effects*.
* (limited evidence).

Germany Hazard classification and labelling of medicines with antineoplastic effects (ATC Code L01 and L02)
INN CAS Danger CMR effects CMR effects Other
Cat 1&2 Cat 3
Torimifen(citrat) 89778- 27- 8 Xn R 22

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■ Classification of the preparation and its individual components has drawn on official and authoritative sources as well as independent

review by the Chemwatch Classification committee using available literature references.
A list of reference resources used to assist the committee may be found at:
www.chemwatch.net/references.

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

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