Tyrphostin A1

sc-3559

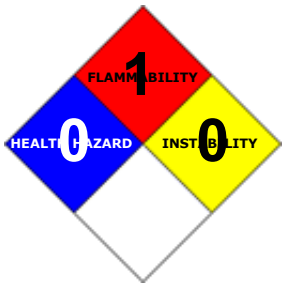
Material Safety Data Sheet

Hazard Alert Code Key:	EXTREME	HIGH	MODERATE	LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME
Tyrphostin A1

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
Selective epidermal growth factor (EGF) receptor tyrosine kinase inhibitor. Negative control IC50 >1250 uM. ■ Epidermal Growth Factor (EGF) results in cellular proliferation, differentiation, and survival. EGF is a low-molecular-weight polypeptide first purified from the mouse submandibular gland, but since then found in many human tissues including submandibular gland, parotid gland. Salivary EGF, which seems also regulated by dietary inorganic iodine, also plays an important physiological role in the maintenance of oro-oesophageal and gastric tissue integrity. The biological effects of salivary EGF include healing of oral and gastroesophageal ulcers, inhibition of gastric acid secretion, stimulation of DNA synthesis as well as mucosal protection from intraluminal injurious factors such as gastric acid, bile acids, pepsin, and trypsin and to physical, chemical and bacterial agents. EGF acts by binding with high affinity to epidermal growth factor receptor (EGFR) on the cell surface and stimulating the intrinsic protein-tyrosine kinase activity of the receptor. The tyrosine kinase activity, in turn, initiates a signal transduction cascade that results in a variety of biochemical changes within the cell - a rise in intracellular calcium levels, increased glycolysis and protein synthesis, and increases in the expression of certain genes including the gene for EGFR - that ultimately lead to DNA synthesis and cell proliferation Stimulation of Epidermal Growth Factor Receptors (EGFR), found on the cell membrane, may result in tumour growth and proliferation, inhibition of apoptosis, stimulation of angiogenesis and the promotion of tissue invasion and metastasis. The receptor is overexpressed in a variety of cancers, including 95% of advanced tumours of the pancreas, up to 90% of tumours in the kidney and the head and the neck, up to 80% of some lung cancers, and up to 70% and 75% of tumours of the ovaries and colon respectively. Ligands such as epidermal growth factor (EGF) and transforming growth factor alpha (TGF alpha) bind to EGFR and turn on a sequence of signalling pathways important to pro-tumour mechanisms. Compounds which interfere with the sequence of pro-tumour events that follow the stimulation of EGFR are thought to be useful as anti-cancer agents. These include monoclonal antibodies directed at this receptor and small molecules targeted at a specific tyrosine kinase, the enzyme responsible for EGFR phosphorylation and downstream signaling.

SYNONYMS
C11-H8-N2-O, "EGF receptor tyrosine/ protein kinase inhibitor"

Section 2 - HAZARDS IDENTIFICATION

CANADIAN WHMIS SYMBOLS

EMERGENCY OVERVIEW
RISK

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. liver, kidney) damage is evident. Present definitions of harmful or toxic substances are generally based on doses producing mortality (death) rather than those producing morbidity (disease, ill-health). Gastrointestinal tract discomfort may produce nausea and vomiting. In an occupational setting however, ingestion of insignificant quantities is not thought to be cause for concern.
■ Considered an unlikely route of entry in commercial/industrial environments.
■ The most common side-effects, associated with the clinical use of Epidermal Growth Factor Receptor (EGFR) inhibitors of tyrosine kinase, in the treatment of non-small cell lung cancers (NSCLC), include diarrhoea, skin rash, nausea, vomiting, headache, dizziness, asthenia, fatigue and loss of appetite. Less common side-effects may include dryness of the mouth, skin dryness, exfoliative dermatitis, pruritus, and itchiness. Rare side-effects may include dryness of the eyes, eye pain and liver injury.
Interstitial pneumonia (sometimes fatal), may also develop as a side-effect of treatment.
High doses of some EGFR inhibitors, administered to dogs, produced decreased body weight, absence of food intake, bloody stools, tremors, emaciation, prostration, ocular changes (palpebral and bulbar conjunctiva redness, partially closed eyes, lachrymation, purulent discharge, corneal opacities, oedema, ulceration and corneal perforation), increased neutrophils and fibrinogen, cachexia, dehydration, abnormal corneal surface, and abnormal surface of the digestive tract. Microscopic findings included diffuse corneal atrophy, corneal ulcers and uveal inflammation, papillary necrosis of kidneys, inflammation and/ or haemorrhage of the digestive tract and degeneration of skeletal muscle.

EYE
■ Although the material is not thought to be an irritant, direct contact with the eye may produce transient discomfort characterized by tearing or conjunctival redness (as with windburn).

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.

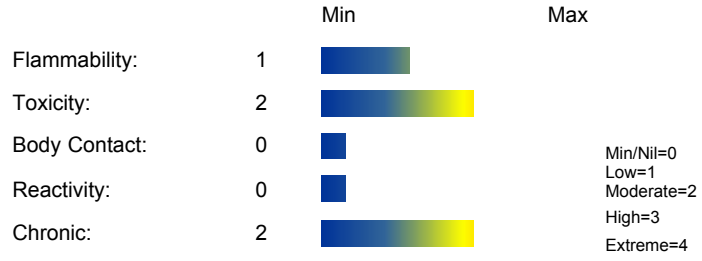
INHALED
■ The material is not thought to produce adverse health effects or irritation of the respiratory tract (as classified using animal models). Nevertheless, good hygiene practice requires that exposure be kept to a minimum and that suitable control measures be used in an occupational setting.
■ 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
■ Principal routes of exposure are usually by skin contact/absorption and inhalation of generated dust.
Animal studies with some Epidermal Growth Factor Receptor (EGFR) inhibitors of tyrosine kinase, indicate that repeated doses may produce adverse effects in many tissues including the eyes.
Repeated exposures may also produce adverse effects on fertility as well as embryo- or foeto-toxicity (generally at maternally toxic levels).
Some chronic administration studies with rats have produced eosinophilic chief cells in the stomach mucosa, haematuria, hair follicular degeneration, papillary necrosis and increased ovarian atrophy, liver necrosis and mononuclear cell infiltration of the liver (in females).
In dogs, chronic studies have produced sporadic emesis, salivation, erythema, decreased absolute red blood cell counts, haematocrit and haemoglobin (in males), increased regeneration of renal proximal tubules, hair loss, ocular changes, and corneal ulceration.
The material may inhibit protein kinase. This family of kinases enzymatically catalyses the phosphorylation of protein . Because phosphorylation triggers a signaling cascade which in turn produces cell growth, inhibition effectively retards the process. There are several different inhibitors which act in this manner but most common are genistein (a naturally occurring steroid-like substance from soybeans), lavendustin (a microbial metabolite) and the tyrphostins (synthetic analogues).
Two families of protein kinase have been identified;
- serine-threonine kinases (also known as PKC) require calcium ion for their activation. The activated PKC phosphorylates proteins of the cellular signal cascade, which eventually induce expression of growth regulatory genes.
- tyrosine kinases which similarly regulate signal transmission to growth regulatory genes

Inhibition may suppress cell or tissue growth or development.
Chronic exposure to cyanides and certain nitriles may result in interference to iodine uptake by thyroid gland and its consequent enlargement. This occurs following metabolic conversion of the cyanide moiety to thiocyanate. Thyroid insufficiency may also occur as a result of metabolic conversion of cyanides to the corresponding thiocyanate. Exposure to small amounts of cyanide compounds over long periods are reported to cause loss of appetite, headache, weakness, nausea, dizziness, abdominal pain, changes in taste and smell, muscle cramps, weight loss, flushing of the face, persistent runny nose and irritation of the upper respiratory tract and eyes. These symptoms are not specific to cyanide exposure and therefore the existence of a chronic cyanide toxicity remains speculative. Repeated minor contact with cyanides produce a characteristic rash with itching, papules (small, superficial raised spots on the skin) and possible sensitization. Concerns have been expressed that low-level, long term exposures may result in damage to the nerves of the eye.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

HAZARD RATINGS



NAME	CAS RN	%
(4-methoxybenzylidene)malonitrile	2826-26-8	>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.
- If pain persists or recurs seek medical attention.
- Removal of contact lenses after an eye injury should only be undertaken by skilled personnel.

SKIN

■ If skin contact occurs:
- Immediately remove all contaminated clothing, including footwear
- Flush skin and hair with running water (and soap if available).
- Seek medical attention in event of irritation.

INHALED

■
- If 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.

Section 5 - FIRE FIGHTING MEASURES

Upper Explosive Limit (%):	Not available.
Specific Gravity (water=1):	Not available
Lower Explosive Limit (%):	Not available
Relative Vapor Density (air=1):	>1

EXTINGUISHING MEDIA

■
- Foam.
- Dry chemical powder.
- BCF (where regulations permit).
- Carbon dioxide.
- Water spray or fog - Large fires only.

FIRE FIGHTING

■
- 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

■
- Solid which exhibits difficult combustion or is difficult to ignite.
- 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) and nitrogen oxides (NOx).

FIRE INCOMPATIBILITY
■ Avoid contamination with strong oxidizing agents as ignition may result.

PERSONAL PROTECTION
Glasses:
Safety Glasses.
Gloves:
Respirator:
Particulate

Section 6 - ACCIDENTAL RELEASE MEASURES

MINOR SPILLS
■
- Clean up all spills immediately.
- Avoid contact with skin and eyes.
- Wear impervious gloves and safety glasses.
- Use dry clean up procedures and avoid generating dust.
- Sweep up or vacuum up (consider explosion-proof machines designed to be grounded during storage and use).
- Place spilled material in clean, dry, sealable, labeled container.

MAJOR SPILLS
■
- Clear area of personnel and move upwind.
- Alert Emergency Responders and tell them location and nature of hazard.
- Control personal contact by using protective equipment and dust respirator.
- Prevent spillage from entering drains, sewers or water courses.
- Avoid generating dust.
- Sweep, shovel up.
- Recover product wherever possible.
- Put residues in labeled plastic bags or other containers for disposal.
- 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
■
- Limit all unnecessary personal contact.
- Wear protective clothing when risk of exposure occurs.
- Use in a well-ventilated area.
- When handling DO NOT eat, drink or smoke.
- Always wash hands with soap and water after handling.
- Avoid physical damage to containers.
- Use good occupational work practice.
- Observe manufacturer's storing and handling recommendations.

RECOMMENDED STORAGE METHODS
■
- Polyethylene or polypropylene container.
- Packing as recommended by manufacturer
- Check all containers are clearly labeled and free from leaks.

STORAGE REQUIREMENTS
■
- Keep dry.
- Store in original containers.
- Keep containers securely sealed.
- No smoking, naked lights or ignition sources.
- Store in a cool, dry, well-ventilated area.
- Store away from incompatible materials.
- Protect containers against physical damage.
- Check regularly for leaks.
- Observe manufacturer's storing and handling recommendations.

SAFE STORAGE WITH OTHER CLASSIFIED CHEMICALS

+	+	+	+	X	+

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/m³	STEL ppm	STEL mg/m³	Peak ppm	Peak mg/m³	TWA F/CC	Notes
US - Oregon Permissible Exposure Limits (Z3)	(4-methoxybenzylidene)malonitrile (Inert or Nuisance Dust: (d) Total dust)		10						*
US OSHA Permissible Exposure Levels (PELs) - Table Z3	(4-methoxybenzylidene)malonitrile (Inert or Nuisance Dust: (d) Respirable fraction)		5						
US OSHA Permissible Exposure Levels (PELs) - Table Z3	(4-methoxybenzylidene)malonitrile (Inert or Nuisance Dust: (d) Total dust)		15						
US - Hawaii Air Contaminant Limits	(4-methoxybenzylidene)malonitrile (Particulates not other wise regulated - Total dust)		10						
US - Hawaii Air Contaminant Limits	(4-methoxybenzylidene)malonitrile (Particulates not other wise regulated - Respirable fraction)		5						
US - Oregon Permissible Exposure Limits (Z3)	(4-methoxybenzylidene)malonitrile (Inert or Nuisance Dust: (d) Respirable fraction)		5						*
US - Tennessee Occupational Exposure Limits - Limits For Air Contaminants	(4-methoxybenzylidene)malonitrile (Particulates not otherwise regulated Respirable fraction)		5						
US - Wyoming Toxic and Hazardous Substances Table Z1 Limits for Air Contaminants	(4-methoxybenzylidene)malonitrile (Particulates not otherwise regulated (PNOR)(f)- Respirable fraction)		5						
US - Michigan Exposure Limits for Air Contaminants	(4-methoxybenzylidene)malonitrile (Particulates not otherwise regulated, Respirable dust)		5						

MATERIAL DATA

(4-METHOXYBENZYLIDENE)MALONITRILE:

■ These "dusts" have little adverse effect on the lungs and do not produce toxic effects or organic disease. Although there is no dust which does not evoke some cellular response at sufficiently high concentrations, the cellular response caused by P.N.O.C.s has the following characteristics:

- the architecture of the air spaces remain intact,
- scar tissue (collagen) is not synthesised to any degree,
- tissue reaction is potentially reversible.

Extensive concentrations of P.N.O.C.s may:

- seriously reduce visibility,
- cause unpleasant deposits in the eyes, ears and nasal passages,
- contribute to skin or mucous membrane injury by chemical or mechanical action, per se, or by the rigorous skin cleansing procedures necessary for their removal. [ACGIH]

This limit does not apply:

- to brief exposures to higher concentrations
- nor does it apply to those substances that may cause physiological impairment at lower concentrations but for which a TLV has as yet to be determined.

This exposure standard applies to particles which

- are insoluble or poorly soluble* in water or, preferably, in aqueous lung fluid (if data is available) and
- have a low toxicity (i.e.. are not cytotoxic, genotoxic, or otherwise chemically reactive with lung tissue, and do not emit ionizing radiation, cause immune sensitization, or cause toxic effects other than by inflammation or by a mechanism of lung overload)

PERSONAL PROTECTION



Consult your EHS staff for recommendations

EYE

■

- Safety glasses.
- Safety glasses with side shields.
- Chemical goggles.
- Contact lenses pose a special hazard; soft lenses may absorb irritants and all lenses concentrate them.

HANDS/FEET

■ Wear general protective gloves, e.g.. light weight rubber gloves.

OTHER

■ Overalls.

- Impervious protective clothing
- Eyewash unit.

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 65ºC).
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

■ General exhaust is adequate under normal operating conditions. If risk of overexposure exists, wear an approved respirator. Correct fit is essential to obtain adequate protection. Provide adequate ventilation in warehouse or closed storage areas. 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, degreasing 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, welding, spray drift, plating acid fumes, pickling (released at low velocity into zone of active generation)	0.5-1 m/s (100-200 f/min.)
direct spray, spray painting in shallow booths, 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)
grinding, abrasive blasting, tumbling, high speed wheel generated dusts (released at high initial velocity into zone of very high rapid air motion).	2.5-10 m/s (500-2000 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 favorable 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 m/s (200-400 f/min.) for extraction of solvents generated in a tank 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	184.2
Melting Range (°F)	Not available	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 available		

APPEARANCE

Solid; does not mix well with water.

Section 10 - CHEMICAL STABILITY

CONDITIONS CONTRIBUTING TO INSTABILITY

■

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

STORAGE INCOMPATIBILITY

■ Avoid reaction with oxidizing agents.

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

Section 11 - TOXICOLOGICAL INFORMATION

(4-methoxybenzylidene)malonitrile

TOXICITY AND IRRITATION

■ No significant acute toxicological data identified in literature search.

Section 12 - ECOLOGICAL INFORMATION

Refer to data for ingredients, which follows:
(4-METHOXYBENZYLIDENE)MALONITRILE:

Ecotoxicity

Ingredient	Persistence: Water/Soil	Persistence: Air	Bioaccumulation	Mobility
(4-methoxybenzylidene)malonitrile	HIGH		LOW	MED

Section 13 - DISPOSAL CONSIDERATIONS

Disposal Instructions

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

- Consult manufacturer for recycling options and recycle where possible .
- Consult Waste Management Authority for disposal.
- Incinerate residue at an approved site.
- Recycle containers where possible, or dispose of in an authorized landfill.

Section 14 - TRANSPORTATION INFORMATION

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

Section 15 - REGULATORY INFORMATION

(4-methoxybenzylidene)malonitrile (CAS: 2826-26-8) is found on the following regulatory lists;
"US - Hawaii Air Contaminant Limits","US - Oregon Permissible Exposure Limits (Z3)","US OSHA Permissible Exposure Levels (PELs) - Table Z3"

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE
■ Ingestion may produce health damage*.
■ Cumulative effects may result following exposure*.
■ May possibly affect fertility*.
* (limited evidence).

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 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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