

Phorbol-12,13-didecanoate

sc-202286



The Power is Question

Material Safety Data Sheet

Hazard Alert Code Key: **EXTREME** **HIGH** **MODERATE** **LOW**

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME

Phorbol-12,13-didecanoate

STATEMENT OF HAZARDOUS NATURE

CONSIDERED A HAZARDOUS SUBSTANCE ACCORDING TO OSHA 29 CFR 1910.1200.

NFPA



SUPPLIER

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EMERGENCY:

ChemWatch
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SYNONYMS

C40-H64-O8, "5H-cyclopropa[3, 4]benz[1, 2-e]azulen-5-one, ", "1, 1a-alpha, 1b-beta, 4, 4a, 7a-alpha, 7b, 8, 9, 9a-tetramethyl-, 9, 9a-", didecanoate, "phorbol 12, 13-dicaprylate", PDD, "cyclopropabenzazulene analogue"

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS

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

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



CANADIAN WHMIS SYMBOLS



EMERGENCY OVERVIEW

RISK

Harmful in contact with skin.

Irritating to eyes, respiratory system and skin.

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED

■ The material is not thought to produce adverse health effects following ingestion (as classified using animal models). Nevertheless, adverse systemic effects have been produced following exposure of animals by at least one other route and good hygiene practice requires that exposure be kept to a minimum.

■ Croton oil is a violent purgative. Phorbol esters are thought to be largely responsible for this action.

■ Constant use of purgatives/laxatives may decrease the sensitivity of the intestinal mucosa causing a diminished response to normal stimuli. The redevelopment of a normal habit is thus prevented.

EYE

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

SKIN

■ Skin contact with the material may be harmful; systemic effects may result following absorption.

■ The material may cause mild but significant inflammation of the skin either following direct contact or after a delay of some time. Repeated exposure can cause contact dermatitis which is characterized by redness, swelling and blistering.

■ Externally croton oil is a powerful counter-irritant and vesicant. This action is largely attributed to phorbol esters.

■ The material is a vesicant causing blistering on contact.

■ 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.

There has been some concern that this material can cause cancer or mutations but there is not enough data to make an assessment.

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.

<|p>

Exposure to small quantities may induce hypersensitivity reactions characterized by acute bronchospasm, hives (urticaria), deep dermal wheals (angioneurotic edema), running nose (rhinitis) and blurred vision. Anaphylactic shock and skin rash (non-thrombocytopenic purpura) may occur.

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Phorbol esters (tricyclic diterpene alcohols), a constituent of croton oil, enhance the overall carcinogenic process initiated by genotoxic carcinogens (such as polycyclic aromatic hydrocarbons) when administered after or together with the carcinogen. The "co-carcinogenic" action of phorbol esters is species dependent - it is active in mice but not in rabbits, rats or guinea pigs. The mechanism of action, as an enhancer of the carcinogenic process, depends on tissue damage followed by regeneration and increased rates of DNA synthesis.

Phorbol esters produce enhancement of this effect long after cessation of carcinogenic exposure. This is interpreted as an ability to promote the growth of dormant neoplastic cells (those showing some pre-existing damage to tumours) into tumours. They may also act as promoters during concurrent administration of the carcinogen (if neoplastic conversion is produced) or long after application of the carcinogen.

"Promotion" of carcinogenicity often involves a mechanism which disrupts the normal cell processes which hold latent tumour cells in check.

Free-flow of growth regulators (produced by normal cells), between cells, may be impeded by disruption to membrane integrity (specifically to specified structures known as gap junctions). Numerous studies show that phorbol esters exert various effects on cellular membranes and specifically bind to protein kinase C (PKC). The high biological activity of phorbol esters suggests a structural relationship with a naturally occurring substance involved in signal transduction pathways. Such a structure has been identified in 1,2-diglycerides (1,2-DG), the physiological activators of the enzyme PKC. Activated PKC phosphorylates proteins of the cellular signal cascade, which eventually induces expression of growth regulatory genes. Due to their structural similarity to 1,2-DG, phorbol esters bind and activate PKC. Because phorbol esters have a much longer half-life than 1,2-DG, the activation is stronger and prolonged. The tumour promoting activity of phorbol esters and other diterpene tumour promoters correlates with their affinity to PKC.

Phorbol esters can also produce gene repression and depression. In tissue culture 12-O-tetradecanoyl phorbol 13-acetate (TPA), stimulates cell proliferation and induces gene expression of growth-related genes. It confers a transformed phenotype to normal fibroblasts, supporting growth to higher densities; these effects are fully reversible after withdrawal of the phorbol ester.

In contrast to its esters, phorbol alcohol is ineffective, both as an irritant and as a tumour promoter and even small changes in the ring structure of the esters abolish the tumour-promoting activity. All active promoters have a 4beta-configuration, while 4alpha-phorbol esters are inactive. Modification of fatty acid residues modulates promoting activity. Phorbol 12-myristate 13 acetate (PMA) may also play a role in the

mediation of the immune response. It inhibits the binding of leukotriene B4 and platelet-activating factor and the response they induce in neutrophils. In addition, PMA is a co-inducer of interferon and phytohaemagglutinin.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

NAME	CAS RN	%
phorbol 12,13-didecanoate	24928-17-4	>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 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

■ 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.

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 full body protective clothing with breathing apparatus.

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 (CO₂), 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.
- Phorbol esters may be inactivated with 5% sodium hypochlorite.
- MAJOR SPILLS**
- Clear area of personnel and move upwind.
 - 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.
 - Lined metal can, Lined metal pail/drum
 - Plastic pail.
- 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.
- 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.

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS

Source	Material	TWA ppm	TWA mg/m ³	STEL ppm	STEL mg/m ³	Peak ppm	Peak mg/m ³	TWA F/CC	Notes
Canada - Alberta Occupational Exposure Limits	phorbol 12,13-didecanoate (Turpentine and selected monoterpenes)	20	111						

ENDOELTABLE

PERSONAL PROTECTION



RESPIRATOR

Particulate
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.

· Handle extremely poisonous natural toxins in closed systems such as glove bags or other enclosures, to avoid accidental contact. Workers should wear complete disposable clothing including shoe covers, gloves and mask with an independent air supply.

ENGINEERING CONTROLS

■ Air should be supplied by an independent system.

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	672.9
Melting Range (°F)	Not available	Viscosity	Not Applicable
Boiling Range (°F)	Not available	Solubility in water (g/L)	Partly miscible
Flash Point (°F)	Not available	pH (1% solution)	Not applicable
Decomposition Temp (°F)	Not Available	pH (as supplied)	Not applicable
Autoignition Temp (°F)	Not available	Vapour Pressure (mmHG)	Negligible
Upper Explosive Limit (%)	Not available	Specific Gravity (water=1)	Not available
Lower Explosive Limit (%)	Not available	Relative Vapor Density (air=1)	Not Applicable
Volatile Component (%vol)	Negligible	Evaporation Rate	Not applicable

APPEARANCE

White powder sealed in glass under inert gas; does not mix well with water. Soluble in chloroform.

Section 10 - CHEMICAL STABILITY

CONDITIONS CONTRIBUTING TO INSTABILITY

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

STORAGE INCOMPATIBILITY

■ Avoid strong acids.

Avoid reaction with oxidizing agents.

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

Section 11 - TOXICOLOGICAL INFORMATION

PHORBOL 12,13-DIDECANOATE

TOXICITY AND IRRITATION

PHORBOL 12,13-DIDECANOATE:

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

TOXICITY IRRITATION

Skin (mouse): 7 nanogram - Mild

■ 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.

The material may cause skin irritation after prolonged or repeated exposure and may produce on contact skin redness, swelling, the production of vesicles, scaling and thickening of the skin.

Skin tumours and tumours at site of application recorded.

Equivocal tumourigen by RTECS criteria.

Section 12 - ECOLOGICAL INFORMATION

This material and its container must be disposed of as hazardous waste.

Ecotoxicity

Ingredient	Persistence: Water/Soil	Persistence: Air	Bioaccumulation	Mobility
phorbol 12,13-didecanoate	HIGH		LOW	LOW

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. Special hazard may exist - specialist advice may be required.

Section 14 - TRANSPORTATION INFORMATION

DOT:

Symbols: None Hazard class or Division: 6.1

Identification Numbers: UN3462 PG: II

Label Codes: 6.1 Special provisions: 141, IB8,

IP2, IP4,

T3 TP33

Packaging: Exceptions: None Packaging: Non- bulk: 212

Packaging: Exceptions: None Quantity limitations: 25 kg

Passenger aircraft/rail:

Quantity Limitations: Cargo 100 kg Vessel stowage: Location: B

aircraft only:

Vessel stowage: Other: None

Hazardous materials descriptions and proper shipping names:

Toxins, extracted from living sources, solid, n.o.s.

Air Transport IATA:

ICAO/IATA Class: 6.1 ICAO/IATA Subrisk: None

UN/ID Number: 3462 Packing Group: II

Special provisions: A3

Cargo Only

Packing Instructions: 615 Maximum Qty/Pack: 100 kg

Passenger and Cargo Passenger and Cargo

Packing Instructions: 613 Maximum Qty/Pack: 25 kg

Passenger and Cargo Limited Quantity Passenger and Cargo Limited Quantity

Packing Instructions: Y613 Maximum Qty/Pack: 1 kg

Shipping Name: TOXINS, EXTRACTED FROM LIVING SOURCES, SOLID,

N.O.S. *(CONTAINS PHORBOL 12,13-DIDECAANOATE)

Maritime Transport IMDG:

IMDG Class: 6.1 IMDG Subrisk: None

UN Number: 3462 Packing Group: II

EMS Number: F-A , S-A Special provisions: 210 274

Limited Quantities: 500 g

Shipping Name: TOXINS, EXTRACTED FROM LIVING SOURCES, SOLID, N.O.S.

Section 15 - REGULATORY INFORMATION

phorbol 12,13-didecanoate (CAS: 24928-17-4) is found on the following regulatory lists;

"Canada - Alberta Occupational Exposure Limits", "Canada National Pollutant Release Inventory (NPRI)", "International Fragrance Association (IFRA) Survey: Transparency List"

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE

■ Cumulative effects may result following exposure*.

■ Limited evidence of a carcinogenic effect*.

* (limited evidence).

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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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