

Phorbol-12,13-dibutyrate

sc-202285

Material Safety Data Sheet



The Power to Question

Hazard Alert Code
Key:

EXTREME

HIGH

MODERATE

LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

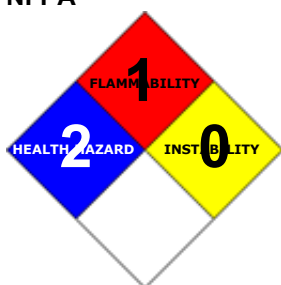
PRODUCT NAME

Phorbol-12,13-dibutyrate

STATEMENT OF HAZARDOUS NATURE

CONSIDERED A HAZARDOUS SUBSTANCE ACCORDING TO OSHA 29 CFR 1910.1200.

NFPA



SUPPLIER

Company: Santa Cruz Biotechnology, Inc.

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Emergency Tel: From outside the US and Canada: +800 2436 2255 (1-800-CHEMCALL) or call +613 9573 3112

PRODUCT USE

Tumour-promoting compound with structural skeleton based on cyclopropabenzazulene. Phorbol myristate acetate (PMA), extracted from croton oil produced by the seeds of *Croton tiglium* Euphorbiaceae, is an active irritant and tumour-promoting agent. PMA is thought to be representative of the family of phorbol esters in the toxic actions it produces. Phorbol 12,13-dibutyrate is commonly used in binding studies or in applications requiring relatively high concentrations of phorbol ester because of its higher solubility in aqueous solutions than other phorbol compounds.

SYNONYMS

C28-H40-O8, "butanoic acid 1, 1a, 1b, 4, 4a, 5, 7a, 7b, 8, 9-decahydro-4a, 7b-dihydroxy-", 3-, "butanoic acid 1, 1a, 1b, 4, 4a, 5, 7a, 7b, 8, 9-decahydro-4a, 7b-dihydroxy-", 3-, "(hydroxymethyl)-1-tetramethyl-5-oxo-9ah-cyclopropa[3, 4]benz[1, 2-e]-", "azulene-9, 9a-diyl ester, (1ar-(1-alpha, 1b-beta, 4a-beta, 7a-alpha, 7b-)", "alpha, 8-alpha, 9-beta, 9a-alpha))-", "(hydroxymethyl)-1-tetramethyl-5-oxo-9ah-cyclopropa[3, 4]benz[1, 2-e]-", "azulene-9, 9a-diyl ester, (1ar-(1-alpha, 1b-beta, 4a-beta, 7a-alpha, 7b-)", "alpha, 8-alpha, 9-beta, 9a-alpha))-", PDBu, "cyclopropabenzazulene analogue"

Section 2 - HAZARDS IDENTIFICATION

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.
- This material can cause inflammation of the skin on contact in some persons.
- The material may accentuate any pre-existing dermatitis condition.
- 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. Prime symptom is breathlessness; lung shadows show on X-ray.

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. An individual may be predisposed to such anti-body mediated reaction if other chemical agents have caused prior sensitization (cross-sensitivity).

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 4 β -configuration, while 4 α -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.

The dibutyrate is moderately active as a tumour promoter when compared with PMA.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

HAZARD RATINGS

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

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



Chronic:

2



Extreme=4



NAME	CAS RN	%
phorbol 12,13-dibutyrate	37558-16-0	>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 fumes or combustion products are inhaled remove from contaminated area.
- Lay patient down. Keep warm and rested.
- Prostheses such as false teeth, which may block airway, should be removed, where possible, prior to initiating first aid procedures.
- Apply artificial respiration if not breathing, preferably with a demand valve resuscitator, bag-valve mask device, or pocket mask as trained. Perform CPR if necessary.
- Transport to hospital, or doctor, without delay.

NOTES TO PHYSICIAN

- 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.
- Administer oxygen by non-rebreather mask at 10 to 15 l/min.
- Monitor and treat, where necessary, for pulmonary edema .
- Monitor and treat, where necessary, for shock.
- Anticipate seizures .
- DO NOT use emetics. Where ingestion is suspected rinse mouth and give up to 200 ml water (5 ml/kg recommended) for dilution where patient is able to swallow, has a strong gag reflex and does not drool.

ADVANCED TREATMENT

- Consider orotracheal or nasotracheal intubation for airway control in unconscious patient or where respiratory arrest has occurred.
- Positive-pressure ventilation using a bag-valve mask might be of use.
- Monitor and treat, where necessary, for arrhythmias.
- Start an IV D5W TKO. If signs of hypovolemia are present use lactated Ringers solution. Fluid overload might create complications.
- Drug therapy should be considered for pulmonary edema.
- Hypotension with signs of hypovolemia requires the cautious administration of fluids. Fluid overload might create complications.
- Treat seizures with diazepam.
- Proparacaine hydrochloride should be used to assist eye irrigation.

BRONSTEIN, A.C. and CURRANCE, P.L.

EMERGENCY CARE FOR HAZARDOUS MATERIALS EXPOSURE: 2nd Ed. 1994.

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.

- BCF (where regulations permit).
- Carbon dioxide.
- Water spray or fog - Large fires only.

FIRE FIGHTING

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

GENERAL FIRE HAZARDS/HAZARDOUS COMBUSTIBLE PRODUCTS

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

Combustion products include: carbon monoxide (CO), carbon dioxide (CO₂), 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.
- Wear full body protective clothing with breathing apparatus.
- Prevent, by any means available, spillage from entering drains or water course.
- Stop leak if safe to do so.
- Contain spill with sand, earth or vermiculite.
- Collect recoverable product into labeled containers for recycling.
- Neutralize/decontaminate residue.
- Collect solid residues and seal in labeled drums for disposal.
- Wash area and prevent runoff into drains.
- After clean up operations, decontaminate and launder all protective clothing and equipment before storing and re-using.
- If contamination of drains or waterways occurs, advise emergency services.

ACUTE EXPOSURE GUIDELINE LEVELS (AEGl) (in ppm)

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

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

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

Section 7 - HANDLING AND STORAGE

PROCEDURE FOR HANDLING

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

Empty containers may contain residual dust which has the potential to accumulate following settling. Such dusts may explode in the presence of an appropriate ignition source.

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

RECOMMENDED STORAGE METHODS

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

For low viscosity materials

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

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

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

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

STORAGE REQUIREMENTS

-
- Store in original containers.
- Keep containers securely sealed.
- Store in a cool, dry, well-ventilated area.
- Store away from incompatible materials and foodstuff containers.
- Protect containers against physical damage and check regularly for leaks.
- Observe manufacturer's storing and handling recommendations.

SAFE STORAGE WITH OTHER CLASSIFIED CHEMICALS



X: Must not be stored together

O: May be stored together with specific preventions

+: May be stored together

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
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MATERIAL DATA

PHORBOL 12,13-DIBUTYRATE:

■ Airborne particulate or vapor must be kept to levels as low as is practicably achievable given access to modern engineering controls and monitoring hardware. Biologically active compounds may produce idiosyncratic effects which are entirely unpredictable on the basis of literature searches and prior clinical experience (both recent and past).

PERSONAL PROTECTION



Consult your EHS staff for recommendations

EYE

-
- Chemical protective goggles with full seal
- Shielded mask (gas-type)
- Contact lenses may pose a special hazard; soft contact lenses may absorb and concentrate irritants. A written policy document, describing the wearing of lens or restrictions on use, should be created for each workplace or task. This should include a review of lens absorption and adsorption for the class of chemicals in use and an account of injury experience. Medical and first-aid personnel should be trained in their removal and suitable equipment should be readily available. In the event of chemical exposure, begin eye irrigation immediately and remove contact lens as soon as practicable. Lens should be removed at the first signs of eye redness or irritation - lens should be removed in a clean environment only after workers have washed 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.
-
- Respirators may be necessary when engineering and administrative controls do not adequately prevent exposures.
- The decision to use respiratory protection should be based on professional judgment that takes into account toxicity information, exposure measurement data, and frequency and likelihood of the worker's exposure - ensure users are not subject to high thermal loads which may result in heat stress or distress due to personal protective equipment (powered, positive flow, full face apparatus may be an option).
- Published occupational exposure limits, where they exist, will assist in determining the adequacy of the selected respiratory. These may be government mandated or vendor recommended.
- Certified respirators will be useful for protecting workers from inhalation of particulates when properly selected and fit tested as part of a complete respiratory protection program.
- Use approved positive flow mask if significant quantities of dust becomes airborne.
- Try to avoid creating dust conditions.

RESPIRATOR

Protection Factor	Half-Face Respirator	Full-Face Respirator	Powered Air Respirator
10 x PEL	P1	-	PAPR-P1
	Air-line*	-	-
50 x PEL	Air-line**	P2	PAPR-P2
100 x PEL	-	P3	-
		Air-line*	-
100+ x PEL	-	Air-line**	PAPR-P3

* - Negative pressure demand ** - Continuous flow

Explanation of Respirator Codes:

Class 1 low to medium absorption capacity filters.

Class 2 medium absorption capacity filters.

Class 3 high absorption capacity filters.

PAPR Powered Air Purifying Respirator (positive pressure) cartridge.

Type A for use against certain organic gases and vapors.

Type AX for use against low boiling point organic compounds (less than 65°C).

Type B for use against certain inorganic gases and other acid gases and vapors.

Type E for use against sulfur dioxide and other acid gases and vapors.

Type K for use against ammonia and organic ammonia derivatives

Class P1 intended for use against mechanically generated particulates of sizes most commonly encountered in industry, e.g. asbestos, silica.

Class P2 intended for use against both mechanically and thermally generated particulates, e.g. metal fume.

Class P3 intended for use against all particulates containing highly toxic materials, e.g. beryllium.

The local concentration of material, quantity and conditions of use determine the type of personal protective equipment required.

Use appropriate NIOSH-certified respirator based on informed professional judgement. In conditions where no reasonable estimate of exposure can be made, assume the exposure is in a concentration IDLH and use NIOSH-certified full face pressure demand SCBA with a minimum service life of 30 minutes, or a combination full facepiece pressure demand SAR with auxiliary self-contained air supply. Respirators provided only for escape from IDLH atmospheres shall be NIOSH-certified for escape from the atmosphere in which they will be used.

ENGINEERING CONTROLS

■ For potent pharmacological agents:

Powders

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

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

Solutions Handling:

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

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

- For Laboratory-scale handling of Substances assessed to be toxic by inhalation. Quantities of up to 25 grams may be handled in Class II biological safety cabinets *; Quantities of 25 grams to 1 kilogram may be handled in Class II biological safety cabinets* or equivalent containment systems. Quantities exceeding 1 kg may be handled either using specific containment, a hood or Class II biological safety cabinet*.
- HEPA terminated local exhaust ventilation should be considered at point of generation of dust, fumes or vapors.
- The need for respiratory protection should also be assessed where incidental or accidental exposure is anticipated. Dependent on levels of contamination, PAPR, full face air purifying devices with P2 or P3 filters or air supplied respirators should be evaluated. When handling: Quantities of up to 25 grams, an approved respirator with HEPA filters or cartridges should be considered. Quantities of 25 grams to 1 kilogram, a half-face negative pressure, full negative pressure, or powered helmet-type air purifying respirator should be considered. Quantities in excess of 1 kilogram, a full face negative pressure, helmet-type air purifying, or supplied air respirator should be considered.

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

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

Air should be supplied by an independent system.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES

Solid.

Does not mix with water.

State	Divided solid	Molecular Weight	504.6
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.
- Hazardous polymerization will not occur.

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-dibutyrate

TOXICITY AND IRRITATION

- unless otherwise specified data extracted from RTECS - Register of Toxic Effects of Chemical Substances.
 - 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.
- No significant acute toxicological data identified in literature search.

Section 12 - ECOLOGICAL INFORMATION

Refer to data for ingredients, which follows:

PHORBOL 12,13-DIBUTYRATE:

- Some antioestrogens such as tamoxifen inhibit protein kinase C activity while phorbol esters enhance protein kinase C activity by mimicking the diacylglycerol pathway. Consequently, because of the diverse pathways of endocrine disruption, the net result of all influences on hormone receptor function and feedback must be considered in sex hormone regulation. Steroidogenic enzymes are responsible for the biosynthesis from cholesterol of various steroid hormones including glucocorticoids, mineralocorticoids, progestins, androgens, and oestrogens. The adrenal gland is the most important steroidogenic tissue in the human body and, unlike the gonads, essential for survival. All steroidogenic processes take place in the adrenal cortex. Steroid production is regulated by specific external stimuli, such as adrenocorticotrophic hormone (ACTH) which selectively increases mineralocorticoid synthesis via the inositol triphosphate/diacylglycerol-mediated protein kinase C (PKC) pathway. Mineralocorticoids are essential for survival as they tightly regulate the Na⁺/K⁺ balance in extracellular fluids. Steroid 21-hydroxylase (CYP21), an enzyme unique to the adrenal cortex, is essential for the biosynthesis of mineralo- and glucocorticoids and is responsible for the conversion of progesterone and 17-hydroxyprogesterone to 11-deoxycorticosterone (mineralocorticoid pathway).
- Substances containing unsaturated carbons are ubiquitous in indoor environments. They result from many sources (see below). Most are reactive with environmental ozone and many produce stable products which are thought to adversely affect human health. The potential for surfaces in an enclosed space to facilitate reactions should be considered.

Source of unsaturated substances	Unsaturated substances (Reactive Emissions)	Major Stable Products produced following reaction with ozone.
Occupants (exhaled breath, ski oils, personal care products)	Isoprene, nitric oxide, squalene, unsaturated sterols, oleic acid and other unsaturated fatty acids, unsaturated oxidation products	Methacrolein, methyl vinyl ketone, nitrogen dioxide, acetone, 6MHQ, geranyl acetone, 4OPA, formaldehyde, nonanal, decanal, 9-oxo-nonanoic acid, azelaic acid, nonanoic acid.
Soft woods, wood flooring, including cypress, cedar and silver fir boards, houseplants	Isoprene, limonene, alpha-pinene, other terpenes and sesquiterpenes	Formaldehyde, 4-AMC, pinoaldehyde, pinic acid, pinonic acid, formic acid, methacrolein, methyl vinyl ketone, SOAs

houseplants		including ultrafine particles
Carpets and carpet backing	4-Phenylcyclohexene, 4-vinylcyclohexene, styrene, 2-ethylhexyl acrylate, unsaturated fatty acids and esters	Formaldehyde, acetaldehyde, benzaldehyde, hexanal, nonanal, 2-nonenal
Linoleum and paints/polishes containing linseed oil	Linoleic acid, linolenic acid	Propanal, hexanal, nonanal, 2-heptenal, 2-nonenal, 2-decenal, 1-pentene-3-one, propionic acid, n-butyric acid
Latex paint	Residual monomers	Formaldehyde
Certain cleaning products, polishes, waxes, air fresheners	Limonene, alpha-pinene, terpinolene, alpha-terpineol, linalool, linalyl acetate and other terpenoids, longifolene and other sesquiterpenes	Formaldehyde, acetaldehyde, glycoaldehyde, formic acid, acetic acid, hydrogen and organic peroxides, acetone, benzaldehyde, 4-hydroxy-4-methyl-5-hexen-1-al, 5-ethenyl-dihydro-5-methyl-2(3H)-furanone, 4-AMC, SOAs including ultrafine particles
Natural rubber adhesive	Isoprene, terpenes	Formaldehyde, methacrolein, methyl vinyl ketone
Photocopier toner, printed paper, styrene polymers	Styrene	Formaldehyde, benzaldehyde
Environmental tobacco smoke	Styrene, acrolein, nicotine	Formaldehyde, benzaldehyde, hexanal, glyoxal, N-methylformamide, nicotinaldehyde, cotinine
Soiled clothing, fabrics, bedding	Squalene, unsaturated sterols, oleic acid and other saturated fatty acids	Acetone, geranyl acetone, 6MHO, 40PA, formaldehyde, nonanal, decanal, 9-oxo-nonanoic acid, azelaic acid, nonanoic acid
Soiled particle filters	Unsaturated fatty acids from plant waxes, leaf litter, and other vegetative debris; soot; diesel particles	Formaldehyde, nonanal, and other aldehydes; azelaic acid; nonanoic acid; 9-oxo-nonanoic acid and other oxo-acids; compounds with mixed functional groups (=O, -OH, and -COOH)
Ventilation ducts and duct liners	Unsaturated fatty acids and esters, unsaturated oils, neoprene	C5 to C10 aldehydes
"Urban grime"	Polycyclic aromatic hydrocarbons	Oxidized polycyclic aromatic hydrocarbons
Perfumes, colognes, essential oils (e.g. lavender, eucalyptus, tea tree)	Limonene, alpha-pinene, linalool, linalyl acetate, terpinene-4-ol, gamma-terpinene	Formaldehyde, 4-AMC, acetone, 4-hydroxy-4-methyl-5-hexen-1-al, 5-ethenyl-dihydro-5-methyl-2(3H) furanone, SOAs including ultrafine particles
Overall home emissions	Limonene, alpha-pinene, styrene	Formaldehyde, 4-AMC, pinonaldehyde, acetone, pinic acid, pinonic acid, formic acid, benzaldehyde, SOAs including ultrafine particles

Abbreviations: 4-AMC, 4-acetyl-1-methylcyclohexene; 6MHQ, 6-methyl-5-heptene-2-one, 4OPA, 4-oxopentanal, SOA, Secondary Organic Aerosols
Reference: Charles J Weschler; Environmental Health Perspectives, Vol 114, October 2006.
■ DO NOT discharge into sewer or waterways.

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.
- Consult manufacturer for recycling options.
- Consult Waste Management Authority for disposal.
- Bury or incinerate residue at an approved site.
- Decontaminate empty containers. Observe all label safeguards until containers are cleaned and destroyed.
- Puncture containers to prevent re-use and bury at an authorized landfill.

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: Passenger aircraft/rail:	25 kg
Quantity Limitations: Cargo aircraft only:	100 kg	Vessel stowage: Location:	B
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		

Shipping Name: TOXINS, EXTRACTED FROM LIVING SOURCES, SOLID, N.O.S. *(CONTAINS PHORBOL 12,13-DIBUTYRATE)

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.(contains phorbol 12,13-dibutyrate)

Section 15 - REGULATORY INFORMATION

phorbol 12,13-dibutyrate (CAS: 37558-16-0) is found on the following regulatory lists;

"Canada - Alberta Occupational Exposure Limits", "Canada National Pollutant Release Inventory (NPRI)"

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 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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