

# Atovaquone

sc-217675

Material Safety Data Sheet



The Power is Question

Hazard Alert Code Key:

EXTREME

HIGH

MODERATE

LOW

## Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

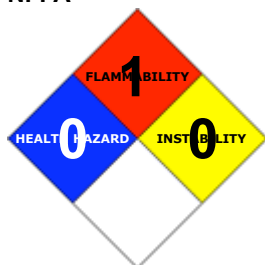
### PRODUCT NAME

Atovaquone

### 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

C22-H19-Cl-O3, "3-[4-(4-chlorophenyl)cyclohexyl]-2-hydroxynaphthalene-1, 4-dione", "2-[trans-4-(4-chlorophenyl)cyclohexyl]-3-hydroxy-1, 4-naphthalenedione", "1, 4-naphthalenedione, 2-[4-(4-chlorophenyl)cyclohexyl]-3-hydroxy-", "trans-", "2-[trans-4-(p-chlorophenyl)cyclohexyl]-3-hydroxy-1, 4-naphthoquinone", Atovachon, BW-566C-80, 566C80, Malarone, Meprone, Wellvone, "antiprotozoal/ anti-malarial"

## Section 2 - HAZARDS IDENTIFICATION

### CHEMWATCH HAZARD RATINGS

		Min	Max
Flammability:	1		
Toxicity:	2		
Body Contact:	0		
Reactivity:	1		
Chronic:	2		

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



### CANADIAN WHMIS SYMBOLS



## EMERGENCY OVERVIEW

### RISK

Very toxic to aquatic organisms.

### POTENTIAL HEALTH EFFECTS

#### ACUTE HEALTH EFFECTS

##### SWALLOWED

- Accidental ingestion of the material may be damaging to the health of the individual.
- The substance and/or its metabolites may bind to hemoglobin inhibiting normal uptake of oxygen. This condition, known as "methemoglobinemia", is a form of oxygen starvation (anoxia).

##### EYE

- Although the material is not thought to be an irritant, direct contact with the eye may cause transient discomfort characterized by tearing or conjunctival redness (as with windburn). Slight abrasive damage may also result.

##### 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 either adverse health effects or irritation of the respiratory tract following inhalation (as classified using animal models). Nevertheless, adverse 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 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

- Limited evidence suggests that repeated or long-term occupational exposure may produce cumulative health effects involving organs or biochemical systems.

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

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.

Some anthraquinone (also known as anthracenedione) dyes are carcinogenic while others are positive allergens which cause hypersensitivity responses in unsensitised humans or cause or cause immunotoxic responses. Some of these dyes cause dermatitis whilst others produce slight teratogenic effects when administered intraperitoneally to pregnant mice. Information on the neurotoxic effects and metabolism on most members of this class of dyes is missing.

Anthraquinones are classified with a large number of other quinone molecules that can be derived from aromatic molecules such as benzene, naphthalene, and anthracene. Reactive oxygen species generated by metabolism of a variety of quinones may be associated with DNA damage or activation of signaling pathways involved in initiation, promotion, and progression of carcinogenesis. A high percentage (36/80) of phenolic anthraquinones have been reported to be mutagenic in Salmonella.

Quinone molecules can be reduced to a relatively stable hydroquinone, which usually is not associated with oxidative stress, or they may be reduced in a one-electron reduction to semiquinone free radicals that give rise to superoxide anions, hydrogen peroxide, and other reactive oxygen species. Quinones may be produced from benzene, polycyclic aromatic hydrocarbons, estrogens, and catecholamines and give rise to reactive oxygen species that can damage DNA and other cellular macromolecules and activate signaling pathways. These molecular events may be associated with the initiation, promotion, and progression of carcinogenesis.

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.

## Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

NAME	CAS RN	%
atovaquone	95233-18-4	>98

## Section 4 - FIRST AID MEASURES

## SWALLOWED

· If swallowed do NOT induce vomiting. · If vomiting occurs, lean patient forward or place on left side (head-down position, if possible) to maintain open airway and prevent aspiration.

## 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 fumes or combustion products are inhaled remove from contaminated area. · Other measures are usually unnecessary.

## 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.

The bioavailability of atovaquone is low and variable and is highly dependent on formulation and diet. Bioavailability of the suspension increases two-fold when administered with meals. When administered with food, bioavailability is approximately 47%. Without food, the bioavailability is 23%.

Atovaquone is extensively bound to plasma proteins (99.9%) over the concentration range of 1 to 90 µg/mL. Some evidence suggests limited metabolism (although no metabolites have been identified).

Greater than 90% of atovaquone is eliminated unchanged in the faeces with negligible excretion in urine.

The elimination half-life of atovaquone is about 2-3 days in adults and 1-2 days in children. Following oral administration, the clearance of atovaquone in adults and children (weighing 40 kg) is approximately 0.04 to 0.05 L/h/Kg. In children (weighing 11 - 40 kg), the clearance is approximately 0.12 to 0.05 L/h/Kg, respectively.

## 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<sub>2</sub>), hydrogen chloride, phosgene, 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

- atovaquone: CAS:95233-18-4

### PERSONAL PROTECTION



### RESPIRATOR

Particulate

Consult your EHS staff for recommendations

### EYE

- When handling very small quantities of the material eye protection may not be required.

For laboratory, larger scale or bulk handling or where regular exposure in an occupational setting occurs:

- Chemical goggles
- Face shield. Full face shield may be required for supplementary but never for primary protection of eyes
- Contact lenses may pose a special hazard; soft contact lenses may absorb and concentrate irritants. A written policy document, describing the wearing of lens or restrictions on use, should be created for each workplace or task. This should include a review of lens absorption and adsorption for the class of chemicals in use and an account of injury experience. Medical and first-aid personnel should be trained in their removal and suitable equipment should be readily available. In the event of chemical exposure, begin eye irrigation immediately and remove contact lens as soon as practicable. Lens should be removed at the first signs of eye redness or irritation - lens should be removed in a clean environment only after workers have washed hands thoroughly. [CDC NIOSH Current Intelligence Bulletin 59].

### HANDS/FEET

- Suitability and durability of glove type is dependent on usage. Important factors in the selection of gloves include: such as:

- frequency and duration of contact,
- chemical resistance of glove material,
- glove thickness and
- dexterity

Select gloves tested to a relevant standard (e.g. Europe EN 374, US F739).

- When prolonged or frequently repeated contact may occur, a glove with a protection class of 5 or higher (breakthrough time greater than 240 minutes according to EN 374) is recommended.
- When only brief contact is expected, a glove with a protection class of 3 or higher (breakthrough time greater than 60 minutes according to EN 374) is recommended.
- Contaminated gloves should be replaced.

Gloves must only be worn on clean hands. After using gloves, hands should be washed and dried thoroughly. Application of a non-perfumed moisturiser is recommended.

- Rubber gloves (nitrile or low-protein, powder-free latex). Employees allergic to latex gloves should use nitrile gloves in preference.
- Double gloving should be considered.
- PVC gloves.
- Protective shoe covers.
- Head covering.

#### 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

State	Divided Solid	Molecular Weight	366.84
Melting Range (°F)	Not Available	Viscosity	Not Applicable
Boiling Range (°F)	Not Applicable	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

Crystalline solid; does not mix well with water (2x10<sup>-4</sup> mg/ml)

### 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

#### ATOVAQUONE

#### TOXICITY AND IRRITATION

##### ATOVAQUONE:

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

The median lethal dose is higher than the maximum oral dose tested in mice and rats (1825 mg/kg per day). Overdoses up to 31,500 mg of atovaquone have been reported. In one such patient who also took an unspecified dose of dapsone, methemoglobinemia occurred. Rash has also been reported after overdose.

Oncogenicity studies of atovaquone alone in mice showed an increased incidence of hepatocellular adenomas and carcinomas at all dose levels tested, yielding exposures approximately 5 to 8 times the average steady-state plasma concentrations in humans during prophylaxis of malaria. The pattern of associated histological findings observed in the liver, is consistent with a species specific, non genotoxic, neoplastic response. Studies in rats at oral dose levels of up to 500 mg/kg/day were negative. Atovaquone is unlikely to present a carcinogenic risk to humans at therapeutic doses.

There was no evidence that either atovaquone is mutagenic in bacterial and mammalian cell gene mutation assays in vitro, and in mouse

bone marrow micronucleus assays for chromosome damage in vivo.

There are no data on the effect of atovaquone on human fertility. Data from animal studies show that atovaquone does not affect reproductive potential or performance at oral doses of up to 1000 mg/kg (approximately 6.5 times human exposure at the maximum recommended clinical treatment dose, based on AUC).

Therapeutic doses /of atovaquone/ can cause maternal toxicity and interfere with normal foetal development in rabbits

Atovaquone was not teratogenic and did not cause reproductive toxicity in rats with plasma concentrations up to 2 to 3 times the estimated human exposure. It did cause maternal toxicity in rabbits with plasma concentrations that were approximately equal to the estimated human exposure; mean foetal body lengths and weights were decreased and there were higher numbers of early resorption and post-implantation losses per dam. It is not clear whether these effects were caused by atovaquone or were secondary to maternal toxicity. Concentrations in rabbit fetuses averaged 30% of the concurrent maternal plasma concentrations. After a single (14)C-radiolabeled dose, concentrations of radiocarbon in rat fetuses were 18% (middle gestation) and 60% (late gestation) of concurrent maternal plasma concentrations

It is not known whether atovaquone is excreted into human milk. In a rat study, the atovaquone concentrations in milk were 30% of the concurrent atovaquone concentrations in maternal plasma.

In clinical studies of atovaquone in the treatment of diseases other than malaria, small decreases in plasma concentrations were associated with concomitant use of paracetamol, benzodiazepines, aciclovir, opiates, cephalosporins, antidiarrhoeal agents and laxatives

## Section 12 - ECOLOGICAL INFORMATION

Very toxic to aquatic organisms.

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

Avoid release to the environment.

Refer to special instructions/ safety data sheets.

## Section 13 - DISPOSAL CONSIDERATIONS

### Disposal Instructions

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

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:**

ICAO/IATA Class: 9 ICAO/IATA Subrisk: None  
UN/ID Number: 3077 Packing Group: III  
Special provisions: A97  
Cargo Only  
Packing Instructions: 911 Maximum Qty/Pack: 400 kg  
Passenger and Cargo Passenger and Cargo  
Packing Instructions: 911 Maximum Qty/Pack: 400 kg  
Passenger and Cargo Limited Quantity Passenger and Cargo Limited Quantity  
Packing Instructions: Y911 Maximum Qty/Pack: 30 kg G  
Shipping Name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID,  
N.O.S. \*(CONTAINS ATOVAQUONE)

**Maritime Transport IMDG:**

IMDG Class: 9 IMDG Subrisk: None  
UN Number: 3077 Packing Group: III  
EMS Number: F-A , S-F Special provisions: 179 274 335 909  
Limited Quantities: 5 kg Marine Pollutant: Yes  
Shipping Name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S.

**Section 15 - REGULATORY INFORMATION**

**No data for atovaquone (CAS: , 95233-18-4)**

**Section 16 - OTHER INFORMATION****LIMITED EVIDENCE**

- Ingestion may produce health damage\*.
- 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](http://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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