

Bifonazole

sc-204652

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

Bifonazole

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

Applied topically as a 1% cream in the treatment of tinea and pityriasis versicolor.

SYNONYMS

C22-H18-N2, "imidazole, 1-[alpha-(4-biphenyl)benzyl]-", "imidazole, 1-[alpha-(4-biphenyl)benzyl]-", bifonazol, 1-[alpha-(4-phenyl)benzyl]imidazole, 1-[alpha-(4-phenyl)benzyl]imidazole, 1-[(4-biphenyl)phenylmethyl]-1H-imidazole, 1-[(4-biphenyl)phenylmethyl]-1H-imidazole, "1H-imidazole, 1-[(1, 1' -biphenyl)-4-ylphenylmethyl]-", "1H-imidazole, 1-[(1, 1' -biphenyl)-4-ylphenylmethyl]-", Amcor, Azolmen, Bifazol, BAY-H-4502, Mycospor, Mycosporan, Trifonazole, "imidazole anti-fungal agent"

Section 2 - HAZARDS IDENTIFICATION

CANADIAN WHMIS SYMBOLS



EMERGENCY OVERVIEW

RISK

Harmful if swallowed.

May cause SENSITIZATION by skin contact.

Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED

- Accidental ingestion of the material may be harmful; animal experiments indicate that ingestion of less than 150 gram may be fatal or may produce serious damage to the health of the individual.
 - Aromatase inhibitors (including triazoles and azoles) produce several side effects including mood swing, depression, weight gain, hot flushes, vaginal dryness, bloating, early onset of menopause. Long-term use may result in bone weakness, increased risk of blood clots, gastrointestinal disturbance, and sweats.
- Aromatase inhibitors lower the level of oestrogen in post-menopausal women who have hormone-receptor-positive breast cancers. Prior to menopause oestrogen is mostly produced in the ovaries. Post-menopausal women produce oestrogen from another hormone, androgen. Aromatase inhibitors prevent the enzyme, aromatase from catalysing this reaction. Breast cancer cell growth in post-menopausal women is stimulated by oestrogen.

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. The material may produce foreign body irritation in certain individuals.

SKIN

- Skin contact is not thought to produce harmful health effects (as classified using animal models). Systemic harm, however, has been identified following exposure of animals by at least one other route and the material may still produce health damage following entry through wounds, lesions or abrasions. 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

- Skin contact with the material is more likely to cause a sensitization reaction in some persons compared to the general population.

Exposure to the material may cause concerns for human fertility, on the basis that similar materials provide some evidence of impaired fertility in the absence of toxic effects, or evidence of impaired fertility occurring at around the same dose levels as other toxic effects, but which are not a secondary non-specific consequence of other toxic effects.

Based on experience with animal studies, there is a possibility that exposure to the material may result in toxic effects to the development of the fetus, at levels which do not cause significant toxic effects to the mother.

Imidazole is structurally related to histamine and has been used as an antagonist to counteract the effects of excess histamine found in certain induced physiological conditions (it therefore acts as an antihistamine).

Imidazoles have been reported to disrupt male fertility through disruption of testicular function.

2-Methylimidazole decreased luteinising hormone secretion and tissue interstitial fluid testosterone concentration two hours after injection into Sprague Dawley rats.

Imidazoles bind to cytochrome P450 haeme, resulting in inhibition of catalysis. However, 2-substituted imidazoles are considered to be poor inhibitors. Imidazole is probably an inducer of cytochrome P4502E1. In general, inducers of this isozyme stabilise the enzyme by preventing phosphorylation of a serine which leads to haeme loss.

Several drugs containing an imidazole moiety were retained and bound in connective tissue when administered to laboratory animals. The bound material was primarily recovered from elastin (70%) and the collagen. It is postulated that reaction with aldehydes gives an aldol condensation product.

Azole fungicides show a broad antifungal activity and are used either to prevent fungal infections or to cure an infection. Therefore, they are important tools in integrated agricultural production. According to their chemical structure, azole compounds are classified into triazoles and imidazoles; however, their antifungal activity is due to the same molecular mechanism. The cell membrane assembly of fungi and yeast is disturbed by blocking the synthesis of the essential membrane component ergosterol. This fundamental biochemical mechanism is the basis for the use of azole fungicides in agriculture and in human and veterinary antimycotic therapies. The enzyme involved is sterol 14[alpha]-demethylase, which is found in several phyla. In mammals, it converts lanosterol into the meiosis-activating sterols (MAS) which regulate or modify cell division. These precursors of cholesterol have been discovered to moderate the development of male and female germ (sexual) cells. Several metabolites of lanosterol have been regarded only as precursors of cholesterol without any biological function in animals. This view dramatically changed recently with the observation that FF-MAS isolated from human follicle fluid and T-MAS isolated from bull testis as well as the MAS-412 and MAS-414 induced resumption of meiosis in cultivated mouse oocytes (Bysskov et al. 1995).

Aromatase is another target enzyme of azole compounds. In steroidogenesis, it converts androgens into the corresponding oestrogens. The importance of androgens and oestrogens for the development of reproductive organs, for fertility, and in certain sex steroid-dependent diseases is well known. Therefore, azole compounds can be directed against aromatase to treat oestrogen-responsive diseases. Based on the inhibitory activity of azoles on key enzymes involved in sex steroid hormone synthesis, it is likely that effects on fertility, sexual behavior, and reproductive organ development will occur depending on dose level and duration of treatment of laboratory animals. Several azole compounds were shown to inhibit the aromatase and to disturb the balance of androgens and estrogens in vivo. In fact, the clinical use of azole compounds in estrogen-dependent diseases is based on this effect. Additionally, azole antifungals developed to inhibit the sterol 14[alpha]-demethylase of fungi and yeast in agriculture and medicine are also inhibiting aromatase. Therefore, these antifungals may unintentionally disturb the balance of androgens and estrogens. Until now, it is not clear whether this effect is compensated by an increased expression of aromatase or by other unknown mechanisms.

The broad use of biologically active compounds in human therapy as well as in nonhuman applications may involve some risks, as exemplified by emerging antibiotic resistance. In agriculture, fungi and yeast are well known to develop resistance to azoles, and some molecular mechanisms of resistance development have been described. The significance of the agricultural azole resistance for human clinical antimycotic therapies has been discussed in Europe, but is not clarified yet. The actual target enzyme of azole antifungals, the fungal sterol 14[alpha]-demethylase, is expressed in many species including humans, and it is highly conserved through evolution. Hence, it seems reasonable to assume that most of the azole antifungals used in agriculture and medicine as well as azoles used in management of breast cancer also act as inhibitors on human sterol 14[alpha]-demethylase to an unknown extent. The toxicologic profiles of individual azole fungicides provide evidence for endocrine effects. In fact, many of these fungicides have effects on prostate, testis, uterus, and ovaries as well as on fertility, development, and sexual behavior. The current database does not allow us to establish causal relationships of these effects with inhibition of sterol 14[alpha]-demethylase and/or aromatase, but the overall view strongly suggests a connection with disturbed steroidogenesis.

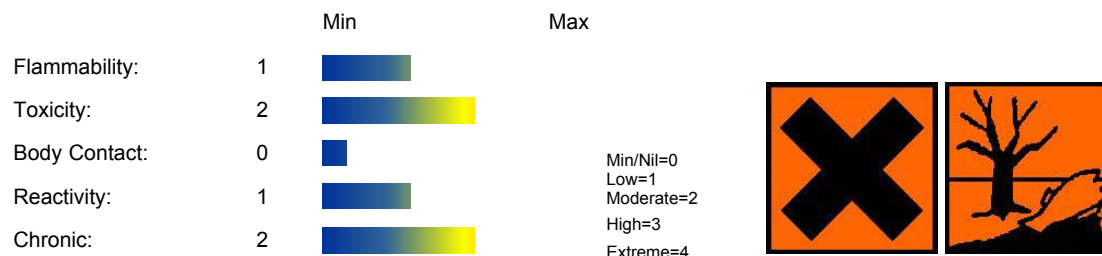
Some azoles have been associated with prolongation of the QT interval on the electrocardiogram.

There is limited evidence that, skin contact with this product is more likely to cause a sensitization reaction in some persons compared to the general population.

Chronic administration of the congener, clotrimazole, has produced central nervous system toxicity. Repeated high oral doses of clotrimazole (50-120 mg/kg) in rats and mice produced embryotoxicity (secondary to maternal toxicity), impairment of mating, decreased litter size and number of viable young, and a decrease of pups surviving to weaning.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

HAZARD RATINGS



NAME	CAS RN	%
bifonazole	60628-96-8	>98

Section 4 - FIRST AID MEASURES

SWALLOWED

-
- IF SWALLOWED, REFER FOR MEDICAL ATTENTION, WHERE POSSIBLE, WITHOUT DELAY.
- Where Medical attention is not immediately available or where the patient is more than 15 minutes from a hospital or unless instructed otherwise:
- For advice, contact a Poisons Information Center or a doctor.
- Urgent hospital treatment is likely to be needed.
- If conscious, give water to drink.
- INDUCE vomiting with fingers down the back of the throat, ONLY IF CONSCIOUS. Lean patient forward or place on left side (head-down position, if possible) to maintain open airway and prevent aspiration.

NOTE: Wear a protective glove when inducing vomiting by mechanical means.

- In the mean time, qualified first-aid personnel should treat the patient following observation and employing supportive measures as indicated by the patient's condition.
- If the services of a medical officer or medical doctor are readily available, the patient should be placed in his/her care and a copy of the MSDS should be provided. Further action will be the responsibility of the medical specialist.
- If medical attention is not available on the worksite or surroundings send the patient to a hospital together with a copy of the MSDS.

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.
- Other measures are usually unnecessary.

NOTES TO PHYSICIAN

- 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.

Treat symptomatically.

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 breathing apparatus plus protective gloves.
- Prevent, by any means available, spillage from entering drains or water course.
- 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

-
- 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), nitrogen oxides (NO_x), 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.

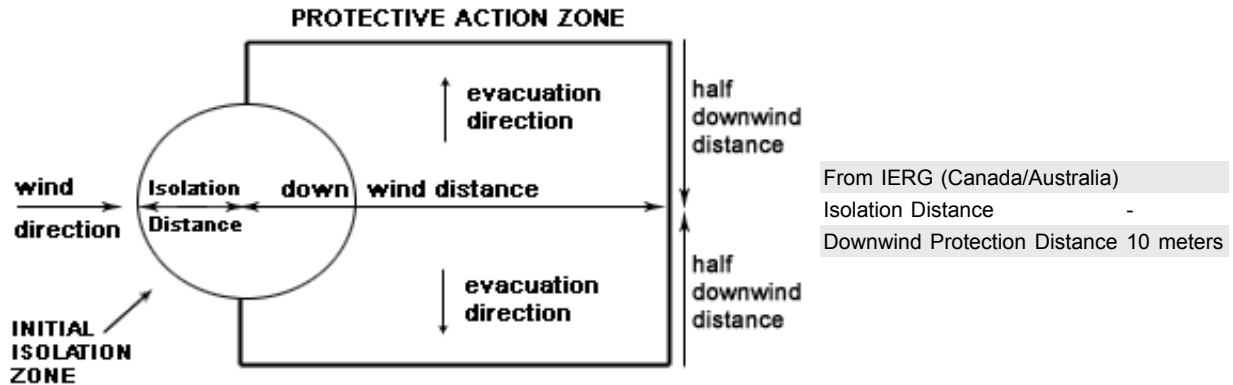
MAJOR SPILLS

- Environmental hazard - contain spillage.

Moderate hazard.

- CAUTION: Advise personnel in area.
- Alert Emergency Responders and tell them location and nature of hazard.
- Control personal contact by wearing protective clothing.
- Prevent, by any means available, spillage from entering drains or water courses.
- Recover product wherever possible.
- IF DRY: Use dry clean up procedures and avoid generating dust. Collect residues and place in sealed plastic bags or other containers for disposal. IF WET: Vacuum/shovel up and place in labelled containers for disposal.
- ALWAYS: Wash area down with large amounts of water and prevent runoff into drains.
- If contamination of drains or waterways occurs, advise emergency services.

PROTECTIVE ACTIONS FOR SPILL



FOOTNOTES

- 1 PROTECTIVE ACTION ZONE is defined as the area in which people are at risk of harmful exposure. This zone assumes that random changes in wind direction confines the vapour plume to an area within 30 degrees on either side of the predominant wind direction, resulting in a crosswind protective action distance equal to the downwind protective action distance.
- 2 PROTECTIVE ACTIONS should be initiated to the extent possible, beginning with those closest to the spill and working away from the site in the downwind direction. Within the protective action zone a level of vapour concentration may exist resulting in nearly all unprotected persons becoming incapacitated and unable to take protective action and/or incurring serious or irreversible health effects.
- 3 INITIAL ISOLATION ZONE is determined as an area, including upwind of the incident, within which a high probability of localised wind reversal may expose nearly all persons without appropriate protection to life-threatening concentrations of the material.
- 4 SMALL SPILLS involve a leaking package of 200 litres (55 US gallons) or less, such as a drum (jerrican or box with inner containers). Larger packages leaking less than 200 litres and compressed gas leaking from a small cylinder are also considered "small spills". LARGE SPILLS involve many small leaking packages or a leaking package of greater than 200 litres, such as a cargo tank, portable tank or a "one-tonne" compressed gas cylinder.
- 5 Guide 171 is taken from the US DOT emergency response guide book.
- 6 IERG information is derived from CANUTEC - Transport Canada.

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.
- Polyethylene or polypropylene container.
- Check all containers are clearly labelled and free from leaks.

STORAGE REQUIREMENTS

- 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

The following materials had no OELs on our records

- bifonazole: CAS:60628-96-8

MATERIAL DATA

BIFONAZOLE:

- It is the goal of the ACGIH (and other Agencies) to recommend TLVs (or their equivalent) for all substances for which there is evidence of health effects at airborne concentrations encountered in the workplace.

At this time no TLV has been established, even though this material may produce adverse health effects (as evidenced in animal experiments or clinical experience). Airborne concentrations must be maintained as low as is practically possible and occupational exposure must be kept to a minimum.

NOTE: The ACGIH occupational exposure standard for Particles Not Otherwise Specified (P.N.O.S) does NOT apply.

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

- 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

- NOTE: The material may produce skin sensitization in predisposed individuals. Care must be taken, when removing gloves and other protective equipment, to avoid all possible skin contact.

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
-
- 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

- 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.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES

Solid.

Does not mix with water.

State	Divided solid	Molecular Weight	310.4
Melting Range (°F)	287.6	Viscosity	Not Applicable
Boiling Range (°F)	Not available.	Solubility in water (g/L)	Partly miscible
Flash Point (°F)	Not available	pH (1% solution)	Not available
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 <0.1 mg/100 ml, pH 6). Soluble in alcohols, DMF and DMSO. Very lipophilic. Stable in aqueous solution at pH 1-12.

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

bifonazole

TOXICITY AND IRRITATION

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

TOXICITY	IRRITATION
Oral (rat) LD50: 1463 mg/kg	Nil Reported
Subcutaneous (rat) LD50: >10000 mg/kg	
Intravenous (rat) LD50: 63 mg/kg	
Oral (mouse) LD50: 2629 mg/kg	
Subcutaneous (mouse) LD50: >15000 mg/kg	
Intravenous (mouse) LD50: 57 mg/kg	
Oral (dog) LD50: >500 mg/kg	
Oral (rabbit) LD50: 4000 mg/kg	

■ Contact allergies quickly manifest themselves as contact eczema, more rarely as urticaria or Quincke's edema. The pathogenesis of contact eczema involves a cell-mediated (T lymphocytes) immune reaction of the delayed type. Other allergic skin reactions, e.g. contact urticaria, involve antibody-mediated immune reactions. The significance of the contact allergen is not simply determined by its sensitization potential: the distribution of the substance and the opportunities for contact with it are equally important. A weakly sensitizing substance which is widely distributed can be a more important allergen than one with stronger sensitizing potential with which few individuals come into contact. From a clinical point of view, substances are noteworthy if they produce an allergic test reaction in more than 1% of the persons tested.

Somnolence, convulsions, ataxia, respiratory depression, effects on fertility recorded.

Section 12 - ECOLOGICAL INFORMATION

Refer to data for ingredients, which follows:

BIFONAZOLE:

- Very toxic to aquatic organisms.
- Do NOT allow product to come in contact with surface waters or to intertidal areas below the mean high water mark. Do not

contaminate water when cleaning equipment or disposing of equipment wash-waters.
Wastes resulting from use of the product must be disposed of on site or at approved waste sites.

■ For azole-containing substances.

Azole fungicides and systemically used antifungal drugs directly interfere with steroidogenesis by acting as potent inhibitors of steroidogenic enzymes and are known to cause endocrine disruption mainly via this mechanism.

An important P450 enzyme involved in the steroidogenesis is aromatase. Aromatase demethylates C10 and specifically converts androstenedione and testosterone. On the protein level, the amino acid sequence homology between aromatase from fish and humans is about 50% and between rats and humans is about 78%. In mammals, aromatase is mainly expressed in the brain and the gonads, but it is also found in placental, adipose, and bone tissue. The physiologic balance between different sex steroid hormones is crucial for the development, maintenance, and function of the reproductive system as well as for the differentiation of the sexual phenotype during ontogeny. Oestrogens (estrone and estradiol) are products of the androgens (androstenedione and testosterone), and the reaction is catalysed by aromatase. In mammals, differentiation of the male phenotype depends not only on testosterone but also on estradiol generated from testosterone by neuronal aromatase in central nervous system. Therefore, disturbances in aromatase expression and/or changes in its catalytic activity are expected to exhibit negative effects on reproduction parameters.

Azole-containing compounds produce profound effects in the environment. In part this is due to inhibition of several enzyme systems including those involving sterol 14[alpha]-demethylase. Sterol 14[alpha]-demethylase is a member of the superfamily of haeme-containing cytochrome P450 enzymes involved in metabolism of endogenous and xenobiotic substances. The antifungal effect of azoles is due to inhibition of sterol 14[alpha]-demethylase in fungi and yeast, thereby blocking the biosynthesis of ergosterol. The subsequent lack of ergosterol is detrimental because ergosterol is an essential sterol component in the membranes of fungi and yeast. Sterol 14[alpha]-demethylase is not only expressed in fungi and yeast but is also found in many other species ranging from bacteria to mammals. In plants, the sterol 14[alpha]-demethylase reaction metabolises obtusifoliol and provides precursors for biosynthesis of phytosterols. In animals, the sterol 14[alpha]-demethylase reaction is part of the metabolic pathway leading to biosynthesis of cholesterol. Cholesterol in turn is the substrate for the production of many other sterols (e.g., the sex steroid hormones).

The DNA sequences encoding sterol 14[alpha]-demethylase of many fungi and yeast are known, as well as the sequences of mice, rats, pigs, and humans. On the protein level, the amino acid sequences are highly conserved along the phylogenetic tree. This fact is considered by many authors as an indication of the pivotal role of sterol 14[alpha]-demethylase in all organisms. The homology of the amino acid sequence level between rats and humans is 93% and 40% between fungi and humans. In humans, the sterol 14[alpha]-demethylase is expressed in many different tissues.

■ DO NOT discharge into sewer or waterways.

Ecotoxicity

Ingredient bifonazole	Persistence: Water/Soil HIGH	Persistence: Air	Bioaccumulation LOW	Mobility LOW
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Section 13 - DISPOSAL CONSIDERATIONS

Disposal Instructions

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

! Puncture containers to prevent re-use and bury at an authorized landfill.

Legislation addressing waste disposal requirements may differ by country, state and/ or territory. Each user must refer to laws operating in their area. In some areas, certain wastes must be tracked.

A Hierarchy of Controls seems to be common - the user should investigate:

- Reduction
- Reuse
- Recycling
- Disposal (if all else fails)

This material may be recycled if unused, or if it has not been contaminated so as to make it unsuitable for its intended use. Shelf life considerations should also be applied in making decisions of this type. Note that properties of a material may change in use, and recycling or reuse may not always be appropriate.

DO NOT allow wash water from cleaning equipment to enter drains. Collect all wash water for treatment before disposal.

- Recycle wherever possible.
- Consult manufacturer for recycling options or consult Waste Management Authority for disposal if no suitable treatment or disposal facility can be identified.
- Dispose of by: Burial in a licensed land-fill or Incineration in a licensed apparatus (after admixture with suitable combustible material)
- Decontaminate empty containers. Observe all label safeguards until containers are cleaned and destroyed.

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: Passenger aircraft/rail:	No limit
Quantity Limitations: Cargo	No limit	Vessel stowage: Location:	A

aircraft only:

NO LIMIT

VESSEL STOWAGE: LOCATION:

A

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:	藥
UN/ID Number:	3077	Packing Group:	III
Special provisions:	A97		

Shipping Name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. *(CONTAINS BIFONAZOLE)

Maritime Transport IMDG:

IMDG Class:	9	IMDG Subrisk:	None
UN Number:	3077	Packing Group:	III
EMS Number:	F-A,S-F	Special provisions:	274 909 944

Limited Quantities: 5 kg

Shipping Name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S.(contains bifonazole)

Section 15 - REGULATORY INFORMATION

No data for bifonazole (CAS: , 60628-96-8)

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE

- May possibly affect fertility*.
- May possibly be harmful to the fetus/ embryo*.

* (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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