

CLOTRIMAZOLE**Hazard Alert Code:
MODERATE**

Chemwatch Material Safety Data Sheet (REVIEW)

Revision No: 5

Chemwatch 69453

Issue Date: 3-Jul-2007

CD 2008/2

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION**PRODUCT NAME:** CLOTRIMAZOLE**SYNONYMS**

C22-H17-CI-N2, "1H-imidazole, 1-[(2-chlorophenyl)diphenylmethyl]-", "1H-imidazole, 1-[(2-chlorophenyl)diphenylmethyl]-", 1-[(2-chlorophenyl)diphenylmethyl]-1H-imidazole, 1-[(2-chlorophenyl)diphenylmethyl]-1H-imidazole, "imidazole, 1-(ortho-chloro-alpha, alpha-diphenylbenzyl)-", "imidazole, 1-(ortho-chloro-alpha, alpha-diphenylbenzyl)-", "1-(ortho-chloro-alpha, alpha-diphenylbenzyl)imidazole", "1-(ortho-chloro-alpha, alpha-diphenylbenzyl)imidazole", "1-(o-chlorotriptyl)imidazole, 1-(o-chlorotriptyl)imidazole, 1-[alpha(2-chlorophenyl)benzhydryl]imidazole, 1-[alpha(2-chlorophenyl)benzhydryl]imidazole, 1-[(ortho-chlorophenyl)diphenylmethyl]imidazole, 1-[(ortho-chlorophenyl)diphenylmethyl]imidazole, diphenyl-(2-chlorophenyl)-1-imidazolylmethane, diphenyl-(2-chlorophenyl)-1-imidazolylmethane, FB-5097, Mycosporin, Lotrimin, Canestan, Mycelex, "azol/ imidazole anti-fungal/ antimycotic agent"

PROPER SHIPPING NAME

ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (contains clotrimazole)

PRODUCT USE

Applied topically as a 1% cream in the treatment of candidiasis, tinea and pityriasis versicolor; as a vaginal cream or in pessaries in treatment of candidal or trichomonal vaginitis; in lozenges for treatment or; prophylaxis of oral candidiasis; in eyedrops. Specific inhibitor of calcium ion activated potassium ion channels.

SUPPLIER

Company: APS Specialty Chemicals

Address:

8 Abbott Road

Seven Hills

NSW, 2147

AUS

Telephone: +61 02 9839 4000

Fax: +61 2 9674 6225

Company: MP Biomedicals Pty Ltd

Address:

Unit 12 , 167 Prospect Highway

Seven Hills

NSW, 2147

AUS

Telephone: +61 2 9838 7422

Telephone: 1800 818 671

Emergency Tel: +61 2 9838 7422

Fax: +61 2 9838 7390

Company: Sigma-Aldrich Pty Ltd

Address:

12 Anella Avenue

Castle Hill

NSW, 2154

AUS

Telephone: +61 2 9841 0555

Telephone: 1800 800 097

Emergency Tel: +44 8701906777

Emergency Tel: 1800 448 456

Fax: +61 2 9841 0500

HAZARD RATINGS

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

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

**Section 2 - HAZARDS IDENTIFICATION****STATEMENT OF HAZARDOUS NATURE****HAZARDOUS SUBSTANCE. DANGEROUS GOODS. According to the Criteria of NOHSC, and the ADG Code.****POISONS SCHEDULE**

S4

RISK

Harmful if swallowed.

May cause SENSITISATION by skin contact.

May produce skin discomfort*.

May possibly affect fertility*.

May possibly be harmful to the foetus/
embryo*.

* (limited evidence).

SAFETY

Avoid exposure - obtain special instructions before use.

To clean the floor and all objects contaminated by this material use water and detergent.

Keep away from food drink and animal feeding stuffs.

Take off immediately all contaminated clothing.

If swallowed IMMEDIATELY contact Doctor or Poisons Information Centre (show this container or label).

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

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

CLOTRIMAZOLE**Hazard Alert Code:
MODERATE**

Chemwatch Material Safety Data Sheet (REVIEW)

Revision No: 5

Chemwatch 69453

Issue Date: 3-Jul-2007

CD 2008/2

NAME	CAS RN	%
clotrimazole	23593-75-1	>98

Section 4 - FIRST AID MEASURES**SWALLOWED**

- IF SWALLOWED, REFER FOR MEDICAL ATTENTION, WHERE POSSIBLE, WITHOUT DELAY.
- For advice, contact a Poisons Information Centre or a doctor.
- Urgent hospital treatment is likely to be needed.
- 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.
- Where medical attention is not immediately available or where the patient is more than 15 minutes from a hospital or unless instructed otherwise:
- 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.

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 oedema .
- 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 hypovolaemia are present use lactated Ringers solution. Fluid overload might create complications.
- Drug therapy should be considered for pulmonary oedema.
- Hypotension with signs of hypovolaemia 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.

Absorbed from the gastrointestinal tract and metabolised in the liver to inactive compounds which are excreted in the urine and faeces.

Section 5 - FIRE FIGHTING MEASURES**EXTINGUISHING MEDIA**

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

FIRE FIGHTING

- Alert Fire Brigade and tell them location and nature of hazard.

CLOTRIMAZOLE**Hazard Alert Code:
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Chemwatch Material Safety Data Sheet (REVIEW)

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CD 2008/2

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

FIRE/EXPLOSION HAZARD

- 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.
- All movable parts coming in contact with this material should have a speed of less than 1-meter/sec

Combustion products include: carbon monoxide (CO), carbon dioxide (CO₂), hydrogen chloride, phosgene, nitrogen oxides (NO_x), other pyrolysis products typical of burning organic material.

FIRE INCOMPATIBILITY

- Avoid contamination with oxidising agents i.e. nitrates, oxidising acids, chlorine bleaches, pool chlorine etc. as ignition may result

HAZCHEM

2X

Personal Protective Equipment

Gas tight chemical resistant suit.

Section 6 - ACCIDENTAL RELEASE MEASURES**EMERGENCY PROCEDURES****MINOR SPILLS**

Environmental hazard - contain spillage.

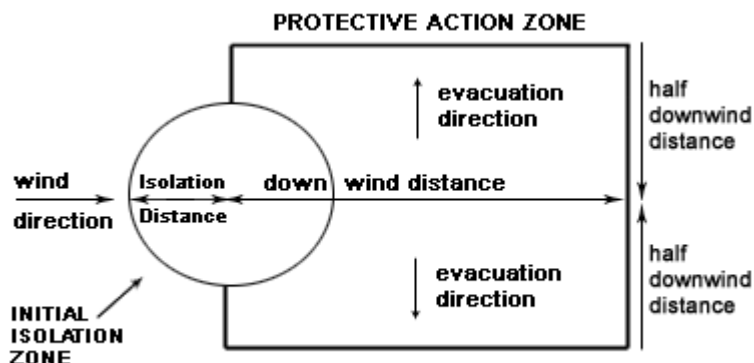
- Clean up waste regularly and abnormal spills immediately.
- Avoid breathing dust and contact with skin and eyes.
- Wear protective clothing, gloves, safety glasses and dust respirator.
- Use dry clean up procedures and avoid generating dust.
- Vacuum up or sweep up. NOTE: Vacuum cleaner must be fitted 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 Services 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

From IERG (Canada/Australia)
 Isolation Distance -
 Downwind Protection Distance 10 metres
 IERG Number 47

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

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Chemwatch Material Safety Data Sheet (REVIEW)

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CD 2008/2

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.

SAFE STORAGE WITH OTHER CLASSIFIED CHEMICALS

+

X

+

X

X

+

*X: Must not be stored together**O: May be stored together with specific preventions**+: May be stored together***Personal Protective Equipment advice is contained in Section 8 of the MSDS.****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.

SUITABLE CONTAINER

- Glass container is suitable for laboratory quantities
- Polyethylene or polypropylene container.
- Check all containers are clearly labelled and free from leaks.

STORAGE INCOMPATIBILITY

- Avoid reaction with oxidising agents

STORAGE REQUIREMENTS

- Store in original containers.
- Keep containers securely sealed.
- Store in a cool, dry area protected from environmental extremes.
- 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
- Consider storage in banded areas - ensure storage areas are isolated from sources of community water (including stormwater, ground water, lakes and streams).
- Ensure that accidental discharge to air or water is the subject of a contingency disaster management plan; this may require consultation with local authorities.

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION**EXPOSURE CONTROLS**

The following materials had no OELs on our records

- clotrimazole: CAS:23593-75-1

MATERIAL DATA

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.

Sensory irritants are chemicals that produce temporary and undesirable side-effects on the eyes, nose or throat. Historically occupational exposure standards for these irritants have been based on observation of workers' responses to various airborne concentrations. Present day expectations require that nearly every individual should be protected against even minor sensory irritation and exposure standards are established using uncertainty factors or safety factors of 5 to 10 or more. On occasion animal no-observable-effect-levels (NOEL) are used to determine these limits where human results are unavailable. An additional approach, typically used by the TLV committee (USA) in determining respiratory standards for

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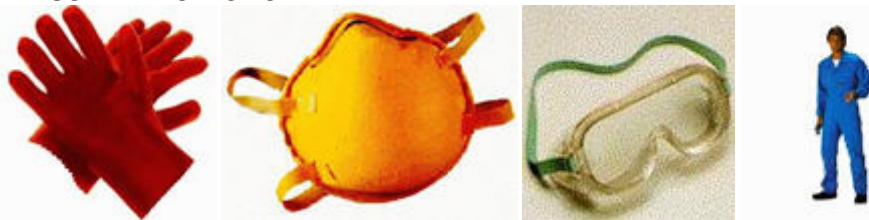
CD 2008/2

this group of chemicals, has been to assign ceiling values (TLV C) to rapidly acting irritants and to assign short-term exposure limits (TLV STELs) when the weight of evidence from irritation, bioaccumulation and other endpoints combine to warrant such a limit. In contrast the MAK Commission (Germany) uses a five-category system based on intensive odour, local irritation, and elimination half-life. However this system is being replaced to be consistent with the European Union (EU) Scientific Committee for Occupational Exposure Limits (SCOEL); this is more closely allied to that of the USA.

OSHA (USA) concluded that exposure to sensory irritants can:

- cause inflammation
- cause increased susceptibility to other irritants and infectious agents
- lead to permanent injury or dysfunction
- permit greater absorption of hazardous substances and
- acclimate the worker to the irritant warning properties of these substances thus increasing the risk of overexposure.

Airborne particulate or vapour 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**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 sensitisation in predisposed individuals. Care must be taken, when removing gloves and other protective equipment, to avoid all possible skin contact.
- Contaminated leather items, such as shoes, belts and watch-bands should be removed and destroyed.

Suitability and durability of glove type is dependent on usage. Factors such as:

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

are important in the selection of gloves.

- 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

RESPIRATOR

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

* - Negative pressure demand ** - Continuous flow.

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

For further information consult site specific CHEMWATCH data (if available), or your Occupational Health and Safety Advisor.

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

CLOTRIMAZOLE**Hazard Alert Code:
MODERATE**

Chemwatch Material Safety Data Sheet (REVIEW)

Revision No: 5

Chemwatch 69453

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CD 2008/2

- 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 vapours.
 - 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**APPEARANCE**

White to pale yellow crystalline powder; does not mix well with water. Soluble in alcohol (1:10), chloroform and ether (1:100).

PHYSICAL PROPERTIES

Solid.

Does not mix with water.

Molecular Weight: 344.84

Melting Range (°C): Not available

Solubility in water (g/L): Partly miscible

pH (1% solution): Not available

Volatile Component (%vol): Negligible

Relative Vapour Density (air=1): Not applicable

Lower Explosive Limit (%): Not available

Autoignition Temp (°C): Not available.

State: Divided solid

Boiling Range (°C): Not available.

Specific Gravity (water=1): Not available.

pH (as supplied): Not applicable

Vapour Pressure (kPa): Negligible

Evaporation Rate: Not applicable

Flash Point (°C): Not available

Upper Explosive Limit (%): Not available.

Decomposition Temp (°C): 142-149

Viscosity: Not Applicable

Section 10 - CHEMICAL STABILITY AND REACTIVITY INFORMATION**CONDITIONS CONTRIBUTING TO INSTABILITY**

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

Section 11 - TOXICOLOGICAL INFORMATION**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 can cause mood swings, depression, weight gain, hot flushes, vaginal dryness, bloating and early menopause. Long-term use may result in bone weakness, increased risk of blood clots, gastrointestinal disturbance, and sweats.

Aromatase inhibitors reduce the level of oestrogen in post-menopausal women who have breast cancer sensitive to hormones. This reduces the growth of breast cancer in these women.

EYE

Although the material is not thought to be an irritant (as classified by EC Directives), direct contact with the eye may cause transient discomfort characterised 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 under EC Directives 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.

There is some evidence to suggest that the material may cause mild but significant inflammation of the skin either following direct contact or after a delay of some time. Repeated exposure can cause contact dermatitis which is characterised by redness, swelling and blistering.

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 by EC Directives 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 and that suitable control measures be used in an occupational setting.

CHRONIC HEALTH EFFECTS

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

Based on experience with similar materials, there is a possibility that exposure to the material may reduce fertility in humans at levels which do not cause 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 foetus, at levels which do not cause significant toxic effects to the mother.

Imidazole is structurally related, and has been used to counteract the effects of histamine. Imidazoles have been reported to disrupt male fertility, through disruption of the function of the testes.

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

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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 (Byskov et al. 1995).

Aromatase is another target enzyme of azole compounds. In steroidogenesis, it converts androgens into the corresponding estrogens. The importance of androgens and estrogens 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 estrogen-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.

Zam et al; Environmental Health Perspectives - 3/1/2003

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

TOXICITY AND IRRITATION

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

TOXICITY

Intravaginal (woman) TDLo: 28 mg/kg/7 d

Oral (rat) LD50: 708 mg/kg

Intraperitoneal (rat) LD50: 445 mg/kg

Oral (mouse) LD50: 761 mg/kg

Intraperitoneal (mouse) LD50: 108 mg/kg

Oral (dog) LD50: >2000 mg/kg

Oral (cat) LD50: >1000 mg/kg

Oral (rabbit) LD50: >1000 mg/kg

IRRITATION

Nil Reported

Contact allergies quickly manifest themselves as contact eczema, more rarely as urticaria or Quincke's oedema. 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 sensitisation potential: the distribution of the substance and the opportunities for contact with it are equally important. A weakly sensitising substance which is widely distributed can be a more important allergen than one with stronger sensitising 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.

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

Section 12 - ECOLOGICAL INFORMATION

Marine Pollutant: Not Determined

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.

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 metabolizes obtusifolium 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.

Another important P450 enzyme involved in the steroidogenesis is aromatase. Like sterol 14[alpha]-demethylase, aromatase catalyzes the oxidative demethylation of sterols. In contrast to sterol 14[alpha]-demethylase, which has several substrates in different phyla, 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. Estrogens (estrone and estradiol) are products of the androgens (androstenedione and testosterone), and the reaction is catalyzed by aromatase. In mammals, differentiation of the male phenotype depends not only on testosterone but also on estradiol generated from testosterone by neuronal

CLOTRIMAZOLE**Hazard Alert Code:
MODERATE**

Chemwatch Material Safety Data Sheet (REVIEW)

Revision No: 5

Chemwatch 69453

Issue Date: 3-Jul-2007

CD 2008/2

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.
DO NOT discharge into sewer or waterways.

Section 13 - DISPOSAL CONSIDERATIONS

- Containers may still present a chemical hazard/ danger when empty.
- Return to supplier for reuse/ recycling if possible.

Otherwise:

- If container can not be cleaned sufficiently well to ensure that residuals do not remain or if the container cannot be used to store the same product, then puncture containers, to prevent re-use, and bury at an authorised landfill.
- Where possible retain label warnings and MSDS and observe all notices pertaining to the product.

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 or process equipment to enter drains.
- It may be necessary to collect all wash water for treatment before disposal.
- In all cases disposal to sewer may be subject to local laws and regulations and these should be considered first.
- Where in doubt contact the responsible authority.
- Recycle wherever possible.
- Consult manufacturer for recycling options or consult local or regional waste management authority for disposal if no suitable treatment or disposal facility can be identified.
- Dispose of by: Burial in a licenced land-fill or Incineration in a licenced apparatus (after admixture with suitable combustible material)
- Decontaminate empty containers. Observe all label safeguards until containers are cleaned and destroyed.

Section 14 - TRANSPORTATION INFORMATION

Environmentally Hazardous Substances meeting the descriptions of UN 3077 or UN 3082 are not subject to this Code when transported by road or rail in;

- (a) packagings;
 - (b) IBCs; or
 - (c) any other receptacle not exceeding 500 kg(L).
- Australian Special Provisions (SP AU01) - ADG Code 7th Ed.

Labels Required: MISCELLANEOUS

HAZCHEM: 2X

UNDG:

Dangerous Goods Class:	9	Subrisk:	None
UN Number:	3077	Packing Group:	III

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

Air Transport IATA:

ICAO/IATA Class:	9	ICAO/IATA Subrisk:	None
UN/ID Number:	3077	Packing Group:	III
Special provisions:	A97		

Shipping Name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID,
N.O.S. *

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	Marine Pollutant:	Not Determined

Shipping Name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID,
N.O.S.

Section 15 - REGULATORY INFORMATION**POISONS SCHEDULE**

S4

REGULATIONS

CLOTRIMAZOLE**Hazard Alert Code:
MODERATE**

Chemwatch Material Safety Data Sheet (REVIEW)

Revision No: 5

Chemwatch 69453

Issue Date: 3-Jul-2007

CD 2008/2

clotrimazole (CAS: 23593- 75- 1) is found on the following regulatory lists;

Australia Hazardous Substances

Australia Inventory of Chemical Substances (AICS)

Australia Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP) - Appendix F (Part 3)

Australia Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP) - Appendix H

Australia Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP) - Schedule 2

Australia Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP) - Schedule 3

Australia Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP) - Schedule 4

Australia Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP) - Schedule 6

OSPAR List of Chemicals for Priority Action

OSPAR List of Substances of Possible Concern

Section 16 - OTHER INFORMATION**Denmark Advisory list for selfclassification of dangerous substances**

Substance CAS Suggested codes clotrimazole 23593- 75- Xn; R22 N; 1 R50/53

Classification of the preparation and its individual components has drawn on official and authoritative sources as well as independent review by the Chemwatch Classification committee using available literature references.

A list of reference resources used to assist the committee may be found at:

www.chemwatch.net/references.

The (M)SDS is a Hazard Communication tool and should be used to assist in the Risk Assessment. Many factors determine whether the reported Hazards are Risks in the workplace or other settings. Risks may be determined by reference to Exposures Scenarios. Scale of use, frequency of use and current or available engineering controls must be considered.

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