

sc-203045

Material Safety Data Sheet



The Power is Question

Hazard Alert Code
Key:

EXTREME

HIGH

MODERATE

LOW

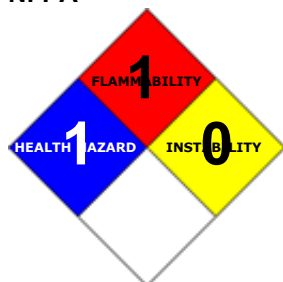
Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME

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

For the treatment of advanced breast cancer in postmenopausal women whose disease has progressed following tamoxifen therapy Irreversible steroidal aromatase inactivator. Breast cancer cell growth may be estrogen-dependent. Aromatase is the principal enzyme that converts androgens to estrogens both in pre- and postmenopausal women. While the main source of estrogen (primarily estradiol) is the ovary in premenopausal women, the principal source of circulating estrogens in postmenopausal women is from conversion of adrenal and ovarian androgens (androstenedione and testosterone) to estrogens (estrone and estradiol) by the aromatase enzyme in peripheral tissues. Estrogen deprivation through aromatase inhibition is an effective and selective treatment for some postmenopausal patients with hormone-dependent breast cancer. Exemestane is an irreversible, steroidal aromatase inactivator, structurally related to the natural substrate androstenedione. It acts as a false substrate for the aromatase enzyme, and is processed to an intermediate that binds irreversibly to the active site of the enzyme causing its inactivation, an effect also known as "suicide inhibition." Exemestane significantly lowers circulating estrogen concentrations in postmenopausal women, but has no detectable effect on adrenal biosynthesis of corticosteroids or aldosterone. Exemestane has no effect on other enzymes involved in the steroidogenic pathway up to a concentration at least 600 times higher than that inhibiting the aromatase enzyme.

SYNONYMS

C20-H24-O2, "androsta-1, 4-diene-3, 17-dione, 6-methylene-", "androsta-1, 4-diene-3, 17-dione, 6-methylene-", "6-methylenandrosta-1, 4-diene-3, 17-dione", "6-methylenandrosta-1, 4-diene-3, 17-dione", "10.13-dimethyl-6-methylidene-7, 8, 9, 10, 11, 12, 13, 14, 15, 16-", decahydrocyclopenta[a]phenanthrene, "10.13-dimethyl-6-methylidene-7, 8, 9, 10, 11, 12, 13, 14, 15, 16-", decahydrocyclopenta[a]phenanthrene, Aromasin, Exemestance, Exemestano, Exemestanum, ATC:L02BG06, "antineoplastic/ steroidal aromatase inactivator"

Section 2 - HAZARDS IDENTIFICATION

CANADIAN WHMIS SYMBOLS



EMERGENCY OVERVIEW

RISK

Harmful if swallowed.

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

■ The material is not thought to be a skin irritant (as classified using animal models). Abrasive damage however, may result from prolonged exposures. Good hygiene practice requires that exposure be kept to a minimum and that suitable gloves be used in an occupational setting.

■ Skin contact with the material may damage the health of the individual; systemic effects may result following absorption.

■ 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 respiratory irritation (as classified using animal models). Nevertheless inhalation of dusts, or fume, especially for prolonged periods, may produce respiratory discomfort and occasionally, distress.

■ Inhalation of dusts, generated by the material during the course of normal handling, may be damaging to the health of the individual.

CHRONIC HEALTH EFFECTS

■ Repeated or long-term occupational exposure is likely to produce cumulative health effects involving organs or biochemical systems.

Ample evidence exists, from results in experimentation, that developmental disorders are directly caused by human exposure to the material.

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

There is some evidence to provide a presumption that human exposure to the material may result in impaired fertility on the basis of: some evidence in animal studies 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 is not a secondary non-specific consequence of other toxic effects.

Long term exposure to high dust concentrations may cause changes in lung function i.e. pneumoconiosis; caused by particles less than 0.5 micron penetrating and remaining in the lung. Prime symptom is breathlessness; lung shadows show on X-ray.

May cause fetal harm when administered to a pregnant woman. Radioactivity related to ¹⁴C-exemestane crossed the placenta of rats following oral administration of 1 mg/kg exemestane. The concentration of exemestane and its metabolites was approximately equivalent in maternal and fetal blood. When rats were administered exemestane from 14 days prior to mating until either days 15 or 20 of gestation, and resuming for the 21 days of lactation, an increase in placental weight was seen at 4 mg/kg/day (approximately 1.5 times the recommended human daily dose on a mg/m² basis). Prolonged gestation and abnormal or difficult labor was observed at doses equal to or greater than 20 mg/kg/day. Increased resorption, reduced number of live fetuses, decreased fetal weight, and retarded ossification were also observed at these doses. No malformations were noted when exemestane was administered to pregnant rats during the organogenesis period at doses up to 810 mg/kg/day (approximately 320 times the recommended human dose on a mg/m² basis). Daily doses of exemestane, given to rabbits during organogenesis caused a decrease in placental weight at 90 mg/kg/day (approximately 70 times the recommended human daily dose on a mg/m² basis). Abortions, an increase in resorptions, and a reduction in fetal body weight were seen at 270 mg/kg/day. There was no increase in the incidence of malformations in rabbits at doses up to 270 mg/kg/day (approximately 210 times the recommended human dose on a mg/m² basis).

There are no studies in pregnant women using exemestane therapy. Exemestane is indicated for postmenopausal women. If there is exposure to the drug during pregnancy, the patient should be apprised of the potential hazard to the fetus and potential risk for loss of the pregnancy.

A 2-year carcinogenicity study in mice at doses of 50, 150 and 450 mg/kg/day exemestane (gavage), resulted in an increased incidence of hepatocellular adenomas and/or carcinomas in both genders at the high dose level. Plasma AUCs(0-24hr) at the high dose were 2575 ± 386 and 5667 ± 1833 ng.hr/ml in males and females (approx. 34 and 75 fold the AUC in post-menopausal patients at the recommended clinical dose). An increased incidence of renal tubular adenomas was observed in male mice at the high dose of 450 mg/kg/day. Since the doses tested in mice did not achieve an MTD, neoplastic findings in organs other than liver and kidneys remain unknown.

A separate carcinogenicity study was conducted in rats at the doses of 30, 100 and 315 mg/kg/day exemestane (gavage) for 92 weeks in males and 2 years in females. No evidence of carcinogenic activity up to the highest dose tested of 315 mg/kg/day was observed in females. The male rat study was inconclusive since it was terminated prematurely at Week 92. At the highest dose, plasma AUC(0-24hr) levels in male (1418 ± 287 ng.hr/ml) and female (2318 ± 1067 ng.hr/ml) rats were 19 and 31 fold higher than those measured in post-menopausal cancer patients, receiving the recommended clinical dose.

Exemestane was not mutagenic in vitro in bacteria (Ames test) or mammalian cells (V79 Chinese hamster lung cells). Exemestane was clastogenic in human lymphocytes in vitro without metabolic activation but was not clastogenic in vivo (micronucleus assay in mouse bone marrow). Exemestane did not increase unscheduled DNA synthesis in rat hepatocytes when tested in vitro.

In a pilot reproductive study in rats, male rats were treated with doses of 125-1000 mg/kg/day exemestane, beginning 63 days prior to and during cohabitation. Untreated female rats showed reduced fertility when mated to males treated with =500 mg/kg/day exemestane (>= 200 times the

recommended human dose on a mg/m² basis). In a separate study, exemestane was given to female rats at 4-100 mg/kg/day beginning 14 days prior to mating and through day 15 or 20 of gestation. Exemestane increased the placental weights at 4 mg/kg/day ($\geq$ 1.5 times the human dose on a mg/m² basis). Exemestane showed no effects on ovarian function, mating behavior, and conception rate in rats given doses up to 20 mg/kg/day (approximately 8 times the recommended human dose on a mg/m² basis), however, decreases in mean litter size and fetal body weight, along with delayed ossification were evidenced at 20 mg/kg/day. In general toxicology studies, changes in the ovary, including hyperplasia, an increase in the incidence of ovarian cysts and a decrease in corpora lutea were observed with variable frequency in mice, rats and dogs at doses that ranged from 3-20 times the human dose on a mg/m² basis.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

HAZARD RATINGS

	Min	Max	
Flammability:	1		
Toxicity:	2		
Body Contact:	2		
Reactivity:	1		
Chronic:	3		
		Min/Nil=0 Low=1 Moderate=2 High=3 Extreme=4	
NAME	CAS RN		%
exemestane	107868-30-4		>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.
- Lay patient down. Keep warm and rested.
- Prostheses such as false teeth, which may block airway, should be removed, where possible, prior to initiating first aid procedures.
- Apply artificial respiration if not breathing, preferably with a demand valve resuscitator, bag-valve mask device, or pocket mask as trained. Perform CPR if necessary.
- Transport to hospital, or doctor.

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.

Clinical trials have been conducted with exemestane given as a single dose to healthy female volunteers at doses as high as 800 mg and daily for 12 weeks to postmenopausal women with advanced breast cancer at doses as high as 600 mg. These dosages were well tolerated. There is no specific antidote to overdosage and treatment must be symptomatic. General supportive care, including frequent monitoring of vital signs and close observation of the patient, is indicated.

A male child (age unknown) accidentally ingested a 25-mg tablet of exemestane. The initial physical examination was normal, but blood tests performed 1 hour after ingestion indicated leucocytosis (WBC 25000/mm³ with 90% neutrophils). Blood tests were repeated 4 days after the incident and were normal. No treatment was given.

Following oral administration to healthy postmenopausal women, exemestane is rapidly absorbed. After maximum plasma concentration is reached, levels decline polyexponentially with a mean terminal half-life of about 24 hours. Exemestane is extensively distributed and is cleared from the systemic circulation primarily by metabolism. The pharmacokinetics of exemestane are dose proportional after single (10 to 200 mg) or repeated oral doses (0.5 to 50 mg). Following repeated daily doses of exemestane 25 mg, plasma concentrations of unchanged drug are similar to levels measured after a single dose.

Pharmacokinetic parameters in postmenopausal women with advanced breast cancer following single or repeated doses have been compared with those in healthy, postmenopausal women. Exemestane appeared to be more rapidly absorbed in the women with breast cancer than in the healthy women, with a mean t_{max} of 1.2 hours in the women with breast cancer and 2.9 hours in the healthy women. After repeated dosing, the average oral clearance in women with advanced breast cancer was 45% lower than the oral clearance in healthy postmenopausal women, with corresponding higher systemic exposure. Mean AUC values following repeated doses in women with breast cancer (75.4 ng×h/mL) were about twice those in healthy women (41.4 ng×h/mL). Absorption: Following oral administration of radiolabeled exemestane, at least 42% of radioactivity was absorbed from the gastrointestinal tract. Exemestane plasma levels increased by approximately 40% after a high-fat breakfast.

Distribution: Exemestane is distributed extensively into tissues. Exemestane is 90% bound to plasma proteins and the fraction bound is independent of the total concentration. Albumin and a1-acid glycoprotein both contribute to the binding. The distribution of exemestane and its metabolites into blood cells is negligible.

Metabolism and Excretion: Following administration of radiolabeled exemestane to healthy postmenopausal women, the cumulative amounts of radioactivity excreted in urine and feces were similar (42 ± 3% in urine and 42 ± 6% in feces over a 1-week collection period). The amount of drug excreted unchanged in urine was less than 1% of the dose. Exemestane is extensively metabolized, with levels of the unchanged drug in plasma accounting for less than 10% of the total radioactivity. The initial steps in the metabolism of exemestane are oxidation of the methylene group in position 6 and reduction of the 17-keto group with subsequent formation of many secondary metabolites. Each metabolite accounts only for a limited amount of drug-related material. The metabolites are inactive or inhibit aromatase with decreased potency compared with the parent drug. One metabolite may have androgenic activity (see Pharmacodynamics, Other Endocrine Effects). Studies using human liver preparations indicate that cytochrome P-450 3A4 (CYP 3A4) is the principal isoenzyme involved in the oxidation of exemestane.

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), other pyrolysis products typical of burning organic material.

May emit poisonous fumes.

FIRE INCOMPATIBILITY

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

PERSONAL PROTECTION

Glasses:

Chemical goggles.

Gloves:

Respirator:

Particulate

Section 6 - ACCIDENTAL RELEASE MEASURES

MINOR SPILLS

-
- Clean up waste regularly and abnormal spills immediately.
- Avoid breathing dust and contact with skin and eyes.
- Wear protective clothing, gloves, safety glasses and dust respirator.
- Use dry clean up procedures and avoid generating dust.
- Vacuum up or sweep up. NOTE: Vacuum cleaner must be fitted with an exhaust micro filter (HEPA type) (consider explosion-proof machines designed to be grounded during storage and use).
- Dampen with water to prevent dusting before sweeping.
- Place in suitable containers for disposal.

MAJOR SPILLS

-
- 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.

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.

RECOMMENDED STORAGE METHODS

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

STORAGE REQUIREMENTS

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

SAFE STORAGE WITH OTHER CLASSIFIED CHEMICALS



X: Must not be stored together

O: May be stored together with specific preventions

+: May be stored together

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS

The following materials had no OELs on our records

- exemestane: CAS:107868-30-4

MATERIAL DATA

EXEMESTANE:

■ 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

- 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.

Experience indicates that the following polymers are suitable as glove materials for protection against undissolved, dry solids, where abrasive particles are not present.

- polychloroprene
- nitrile rubber
- butyl rubber
- fluorocautchouc
- polyvinyl chloride

Gloves should be examined for wear and/ or degradation constantly.

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 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

- 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.

Barrier protection or laminar flow cabinets should be considered for laboratory scale handling. 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.

Fume-hoods and other open-face containment devices are acceptable when face velocities of at least 1 m/s (200 feet/minute) are achieved. Partitions, barriers, and other partial containment technologies are required to prevent migration of the material to uncontrolled areas. For non-routine emergencies maximum local and general exhaust are necessary. Air contaminants generated in the workplace possess varying "escape" velocities which, in turn, determine the "capture velocities" of fresh circulating air required to effectively remove the contaminant.

Type of Contaminant:	Air Speed:
solvent, vapors, etc. evaporating from tank (in still air)	0.25-0.5 m/s (50-100 f/min.)
aerosols, fumes from pouring operations, intermittent container filling, low speed conveyer transfers (released at low velocity into zone of active generation)	0.5-1 m/s (100-200 f/min.)
direct spray, drum filling, conveyer loading, crusher dusts, gas discharge (active generation into zone of rapid air motion)	1-2.5 m/s (200-500 f/min.)

Within each range the appropriate value depends on:

Lower end of the range	Upper end of the range
1: Room air currents minimal or favourable to capture	1: Disturbing room air currents
2: Contaminants of low toxicity or of nuisance value only.	2: Contaminants of high toxicity
3: Intermittent, low production.	3: High production, heavy use
4: Large hood or large air mass in motion	4: Small hood-local control only

Simple theory shows that air velocity falls rapidly with distance away from the opening of a simple extraction pipe. Velocity generally decreases with the square of distance from the extraction point (in simple cases). Therefore the air speed at the extraction point should be adjusted, accordingly, after reference to distance from the contaminating source. The air velocity at the extraction fan, for example, should be a minimum of 1-2.5 m/s (200-500 f/min.) for extraction of gases discharged 2 meters distant from the extraction point. Other mechanical considerations, producing performance deficits within the extraction apparatus, make it essential that theoretical air velocities are multiplied by factors of 10 or more when extraction systems are installed or used.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES

Does not mix with water.

State	Divided Solid	Molecular Weight	296.41
Melting Range (°F)	311.234	Viscosity	Not Applicable
Boiling Range (°F)	Not Applicable	Solubility in water (g/L)	Immiscible
Flash Point (°F)	Not Available	pH (1% solution)	Not Applicable
Decomposition Temp (°F)	Not Available	pH (as supplied)	Not Applicable
Autoignition Temp (°F)	Not Available	Vapour Pressure (mmHG)	Negligible
Upper Explosive Limit (%)	Not Available	Specific Gravity (water=1)	Not Available
Lower Explosive Limit (%)	Not Available	Relative Vapor Density (air=1)	Not Applicable
Volatile Component (%vol)	Negligible	Evaporation Rate	Not Applicable

APPEARANCE

White to slightly yellow crystalline powder; does not mix with water. Soluble in N,N-dimethylformamide, methanol.

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

exemestane

TOXICITY AND IRRITATION

■ unless otherwise specified data extracted from RTECS - Register of Toxic Effects of Chemical Substances. In mice, mortality was observed after a single oral dose of exemestane of 3200 mg/kg, the lowest dose tested (about 640 times the recommended human dose on a mg/m2 basis). In rats and dogs, mortality was observed after single oral doses of exemestane of 5000 mg/kg (about 2000 times the recommended human dose on a mg/m2 basis) and of 3000 mg/kg (about 4000 times the recommended human dose on a mg/m2 basis), respectively.

Convulsions were observed after single doses of exemestane of 400 mg/kg and 3000 mg/kg in mice and dogs (approximately 80 and 4000 times the recommended human dose on a mg/m2 basis), respectively.

Section 12 - ECOLOGICAL INFORMATION

Refer to data for ingredients, which follows:

EXEMESTANE:

- DO NOT discharge into sewer or waterways.

Section 13 - DISPOSAL CONSIDERATIONS

Disposal Instructions

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

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

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

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

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

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

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

- Recycle wherever possible.
- 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

NOT REGULATED FOR TRANSPORT OF DANGEROUS GOODS: DOT, IATA, IMDG

Section 15 - REGULATORY INFORMATION

No data for exemestane (CAS: , 107868-30-4)

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE

- Inhalation and/or skin contact may produce health damage*.
- Cumulative effects may result following exposure*.
- Limited evidence of a carcinogenic effect*.
- May affect fertility*.
- May be harmful to the fetus/ embryo*.

* (limited evidence).

Germany Hazard classification and labelling of medicines with antineoplastic effects (ATC Code L01 and L02)

INN	CAS	Danger	CMR effects	CMR effects	Other
			Cat 1&2	Cat 3	
Exemestan	107868- 30- 4	T	R 61		R 22

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

A list of reference resources used to assist the committee may be found at:
www.chemwatch.net/references.

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

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