VENLAFAXINE HYDROCHLORIDE

Alembic Pharmaceuticals Limited

Chemwatch Hazard Alert Code: **2**

Chemwatch: **4095-60**
Version No: **6.1.1.1**
Safety Data Sheet

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L.GHS.IND.EN

SECTION 1 IDENTIFICATION OF THE SUBSTANCE / MIXTURE AND OF THE COMPANY / UNDERTAKING

Product Identifier

Product name	VENLAFAXINE HYDROCHLORIDE
Chemical Name	venlafaxine hydrochloride
Synonyms	(+/-)-1-[alpha-((dimethylamino)methyl]-p-methoxybenzyl]cyclohexanol, (R/S)-1-[2-(dimethylamino)-1-(4-methoxyphenyl)ethyl]cyclohexanol, C17-H28-Cl-N-O2, Effexor, WY-45030, antidepressant, cyclohexanol, 1-[2-(dimethylamino)-1-(4-methoxyphenyl)ethyl]-,hydrochloride, hydrochloride
Proper shipping name	ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (contains venlafaxine hydrochloride)
Chemical formula	C17H28ClNO2
Other means of identification	Not Available
CAS number	99300-78-4

Relevant identified uses of the substance or mixture and uses advised against

Relevant identified uses	Serotonin-norepinephrine reuptake inhibitors (SNRIs) are a class of antidepressant used in the treatment of major depression and other mood disorders. They are also sometimes used to treat anxiety disorders, obsessive-compulsive disorder, attention deficit hyperactivity disorder (ADHD) and chronic neuropathic pain. They act upon two neurotransmitters in the brain that are known to play an important part in mood, namely, serotonin and norepinephrine. This can be contrasted with the more widely-used selective serotonin reuptake inhibitors (SSRIs), which act only on serotonin. Activity on norepinephrine reuptake is thought necessary for an antidepressant to be effective on neuropathic pain, a property shared with the older tricyclic antidepressants but not with the SSRIs. SNRIs were developed more recently than SSRIs, and there are relatively few of them. Their efficacy as well as their tolerability appear to be somewhat better than the SSRIs', apparently owing to their compound effect Venlafaxine is an antidepressant whose action is believed to be associated with the potentiation of neurotransmitter activity in the CNS. Venlafaxine and its active metabolite desmethylvenlafaxine (ODV) are potent inhibitors of neuronal serotonin and norepinephrine uptake and weak inhibitors of dopamine uptake. Both have no significant affinity for muscarinic, histaminergic, or alpha-1-adrenergic receptors in vitro. Pharmacologic activity at these receptors is hypothesised to be associated with the various anticholinergic, sedative and cardiovascular effects seen with other psychotropic drugs. Venlafaxine and ODV do not possess monoamine oxidase (MAO) inhibitory activity.

Details of the supplier of the safety data sheet

Registered company name	Alembic Pharmaceuticals Limited
Address	Vadadora Gujarat India
Telephone	Not Available
Fax	Not Available
Website	Not Available
Email	Not Available

Emergency telephone number

Association / Organisation	Not Available
Emergency telephone numbers	Not Available
Other emergency telephone numbers	Not Available

SECTION 2 HAZARDS IDENTIFICATION

Classification of the substance or mixture

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NFPA 704 diamond

Note: The hazard category numbers found in GHS classification in section 2 of this SDSs are NOT to be used to fill in the NFPA 704 diamond. Blue = Health Red = Fire Yellow = Reactivity White = Special (Oxidizer or water reactive substances)

Classification	Acute Toxicity (Oral) Category 5, Skin Corrosion/Irritation Category 3, Reproductive Toxicity Category 2, Acute Aquatic Hazard Category 1

Label elements

GHS label elements	
SIGNAL WORD	**WARNING**

Hazard statement(s)

H303	May be harmful if swallowed
H316	Causes mild skin irritation
H361	Suspected of damaging fertility or the unborn child.
H400	Very toxic to aquatic life.

Precautionary statement(s) Prevention

P201	Obtain special instructions before use.
P280	Wear protective gloves/protective clothing/eye protection/face protection.
P273	Avoid release to the environment.

Precautionary statement(s) Response

P308+P313	IF exposed or concerned: Get medical advice/ attention.
P312	Call a POISON CENTER/doctor/physician/first aider/if you feel unwell.
P332+P313	If skin irritation occurs: Get medical advice/attention.
P391	Collect spillage.

Precautionary statement(s) Storage

P405	Store locked up.

Precautionary statement(s) Disposal

P501	Dispose of contents/container in accordance with local regulations.

SECTION 3 COMPOSITION / INFORMATION ON INGREDIENTS

Substances

CAS No	%[weight]	Name	Classification
99300-78-4	>98	venlafaxine hydrochloride	Acute Toxicity (Oral) Category 5, Skin Corrosion/Irritation Category 3, Reproductive Toxicity Category 2, Acute Aquatic Hazard Category 1; H303, H316, H361, H400

Mixtures

See section above for composition of Substances

SECTION 4 FIRST AID MEASURES

Description of first aid measures

Eye Contact	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. ▸ Seek medical attention without delay; if pain persists or recurs seek medical attention. ▸ Removal of contact lenses after an eye injury should only be undertaken by skilled personnel.
Skin Contact	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.
Inhalation	▸ If dust is inhaled, remove from contaminated area. ▸ Encourage patient to blow nose to ensure clear passage of breathing. ▸ If irritation or discomfort persists seek medical attention.

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Ingestion	▸ If swallowed do **NOT** induce vomiting. ▸ If vomiting occurs, lean patient forward or place on left side (head-down position, if possible) to maintain open airway and prevent aspiration. ▸ Observe the patient carefully. ▸ Never give liquid to a person showing signs of being sleepy or with reduced awareness; i.e. becoming unconscious. ▸ Give water to rinse out mouth, then provide liquid slowly and as much as casualty can comfortably drink. ▸ Seek medical advice.

Indication of any immediate medical attention and special treatment needed

Treat symptomatically.
For selective serotonin reuptake inhibitors (SSRIs):
Serotonin toxicity is more pronounced following supra-therapeutic doses and overdoses, and they merge in a continuum with the toxic effects of overdose. The serotonergic toxicity of SSRIs increases with dose, but even in over-dose it is insufficient to cause fatalities from serotonin syndrome in healthy adults. The syndrome occurs in approximately 14 to 16 percent of persons who overdose on SSRIs.
It is usually only when drugs with different mechanisms of action are mixed together that elevations of central nervous system serotonin reach potentially fatal levels.
The symptoms are often described as a clinical triad of abnormalities:

- **Cognitive effects**: mental confusion, hypomania, hallucinations, agitation, headache, coma.
- **Autonomic effects**: shivering, sweating, fever, hypertension, tachycardia, nausea, diarrhea.
- **Somatic effects**: myoclonus/clonus (muscle twitching), hyperreflexia, tremor.

Symptom onset is usually rapid, often occurring within minutes after self-poisoning or a change in medication. Serotonin syndrome encompasses a wide range of clinical findings. Mild symptoms may only consist of tachycardia, shivering, diaphoresis (sweating), mydriasis (dilated pupils), myoclonus (intermittent tremor or twitching), as well as overactive or over-responsive reflexes.
Moderate intoxication includes additional abnormalities such as hyperactive bowel sounds, hypertension and hyperthermia; a temperature as high as 40 C (104 F) is common in moderate intoxication. The overactive reflexes and clonus in moderate cases may be greater in the lower limbs than in the upper limbs. Mental status changes include hyper-vigilance and agitation. Severe symptoms include severe hypertension and tachycardia that may lead to shock. Severe cases often have agitated delirium as well as muscular rigidity and high muscular tension. Temperature may rise to above 41.1 C (106.0 F) in life-threatening cases. Other abnormalities include metabolic acidosis, rhabdomyolysis, seizures, renal failure, and disseminated intravascular coagulation, these effects usually arise as a consequence of hyperthermia.
SSRIs appear to be safer in overdose when compared with traditional antidepressants such as the tricyclic antidepressants. This relative safety is supported both by case series and studies of deaths per numbers of prescriptions. However, case reports of SSRI poisoning have indicated that severe toxicity can occur and deaths have been reported following massive single ingestions, although this is exceedingly uncommon when compared to the tricyclic antidepressants.
Because of the wide therapeutic index of the SSRIs, most patients will have mild or no symptoms following moderate overdoses. The most commonly reported severe effect following SSRI overdose is serotonin syndrome; serotonin toxicity is usually associated with very high overdoses or multiple drug ingestion. Other reported significant effects include coma, seizures, and cardiac toxicity.
Treatment for SSRI overdose is mainly based on symptomatic and supportive care. Medical care may be required for agitation, maintenance of the airways, and treatment for serotonin syndrome.
ECG monitoring is usually indicated to detect any cardiac abnormalities.
Supportive care includes:

- the control of agitation,
- the administration of serotonin antagonists (cyproheptadine or methysergide),
- the control of autonomic instability, and the control of hyperthermia.

The intensity of therapy depends on the severity of symptoms.
If the symptoms are mild, treatment may only consist of:

- discontinuation of the offending medication or medications,
- offering supportive measures,
- giving benzodiazepines for myoclonus, and waiting for the symptoms to resolve.

Moderate cases should have:

- all thermal and cardiorespiratory abnormalities corrected and
- can benefit from serotonin antagonists such as cyproheptadine.

Critically ill patients should receive the above therapies as well as:

- sedation, neuromuscular paralysis, and
- intubation with artificial ventilation.

Upon initiation of therapy and the discontinuation of serotonergic drugs most cases of serotonin syndrome resolve within 24 hours.although delirium may persist for a number of days. Cases have reported muscle pain and weakness persisting for months although antidepressant withdrawal may contribute to ongoing features. Following appropriate medical management, serotonin syndrome is generally associated with a favorable prognosis.
Many SSRIs are also monoamine oxidase inhibitors (MAOIs):
Special care should be taken with any drug therapy in view of the many hazards of monoamine oxidase inhibitor interactions. In particular metaraminol and other sympathomimetic agents are not suitable for the treatment of hypotension, which should be managed with intravenous fluids and, in severe shock, intravenous hydrocortisone.
Overdose management consists of the general measures associated with antidepressant intoxication. Ensure an adequate airway, oxygenation, and ventilation. Monitor for cardiac rhythm and vital signs. General supportive and symptomatic measures are also recommended. Use of activated
charcoal, emesis, or gastric lavage should be considered. Due to the large volume of distribution of venlafaxine, forced diuresis, dialysis, haemoperfusion, and exchange perfusion are unlikely to be of benefit. No specific antidote is known.

SECTION 5 FIREFIGHTING MEASURES

Extinguishing media

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

Special hazards arising from the substrate or mixture

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

Advice for firefighters

Fire Fighting	▸ Alert Fire Brigade 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 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; it is estimated that most organic dusts are combustible (circa 70%) - according to the circumstances under which the combustion process occurs, such materials may cause fires and / or dust explosions. ▸ Organic powders when finely divided over a range of concentrations regardless of particulate size or shape and suspended in air or some other oxidizing

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	▸ medium may form explosive dust-air mixtures and result in a fire or dust explosion (including secondary explosions). ▸ 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 (420 micron or less) may burn rapidly and fiercely if ignited - particles exceeding this limit will generally not form flammable dust clouds; once initiated, however, larger particles up to 1400 microns diameter will contribute to the propagation of an explosion. ▸ In the same way as gases and vapours, dusts in the form of a cloud are only ignitable over a range of concentrations; in principle, the concepts of lower explosive limit (LEL) and upper explosive limit (UEL) are applicable to dust clouds but only the LEL is of practical use; - this is because of the inherent difficulty of achieving homogeneous dust clouds at high temperatures (for dusts the LEL is often called the "Minimum Explosible Concentration", MEC). ▸ When processed with flammable liquids/vapors/mists,ignitable (hybrid) mixtures may be formed with combustible dusts. Ignitable mixtures will increase the rate of explosion pressure rise and the Minimum Ignition Energy (the minimum amount of energy required to ignite dust clouds - MIE) will be lower than the pure dust in air mixture. The Lower Explosive Limit (LEL) of the vapour/dust mixture will be lower than the individual LELs for the vapors/mists or dusts. ▸ A dust explosion may release of large quantities of gaseous products; this in turn creates a subsequent pressure rise of explosive force capable of damaging plant and buildings and injuring people. ▸ Usually the initial or primary explosion takes place in a confined space such as plant or machinery, and can be of sufficient force to damage or rupture the plant. If the shock wave from the primary explosion enters the surrounding area, it will disturb any settled dust layers, forming a second dust cloud, and often initiate a much larger secondary explosion. All large scale explosions have resulted from chain reactions of this type. ▸ 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. ▸ A sudden release of statically charged materials from storage or process equipment, particularly at elevated temperatures and/ or pressure, may result in ignition especially in the absence of an apparent ignition source. ▸ One important effect of the particulate nature of powders is that the surface area and surface structure (and often moisture content) can vary widely from sample to sample, depending of how the powder was manufactured and handled; this means that it is virtually impossible to use flammability data published in the literature for dusts (in contrast to that published for gases and vapours). ▸ Autoignition temperatures are often quoted for dust clouds (minimum ignition temperature (MIT)) and dust layers (layer ignition temperature (LIT)); LIT generally falls as the thickness of the layer increases. Combustion products include: carbon monoxide (CO) carbon dioxide (CO2) hydrogen chloride phosgene nitrogen oxides (NOx) other pyrolysis products typical of burning organic material.

SECTION 6 ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures

See section 8

Environmental precautions

See section 12

Methods and material for containment and cleaning up

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.

Personal Protective Equipment advice is contained in Section 8 of the SDS.

SECTION 7 HANDLING AND STORAGE

Precautions for safe handling

Safe 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.

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	▸ 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 storage and handling recommendations contained within this SDS. ▸ Atmosphere should be regularly checked against established exposure standards to ensure safe working conditions are maintained. ▸ Organic powders when finely divided over a range of concentrations regardless of particulate size or shape and suspended in air or some other oxidizing medium may form explosive dust-air mixtures and result in a fire or dust explosion (including secondary explosions) ▸ Minimise airborne dust and eliminate all ignition sources. Keep away from heat, hot surfaces, sparks, and flame. ▸ Establish good housekeeping practices. ▸ Remove dust accumulations on a regular basis by vacuuming or gentle sweeping to avoid creating dust clouds. ▸ Use continuous suction at points of dust generation to capture and minimise the accumulation of dusts. Particular attention should be given to overhead and hidden horizontal surfaces to minimise the probability of a "secondary" explosion. According to NFPA Standard 654, dust layers 1/32 in.(0.8 mm) thick can be sufficient to warrant immediate cleaning of the area. ▸ Do not use air hoses for cleaning. ▸ Minimise dry sweeping to avoid generation of dust clouds. Vacuum dust-accumulating surfaces and remove to a chemical disposal area. Vacuums with explosion-proof motors should be used. ▸ Control sources of static electricity. Dusts or their packages may accumulate static charges, and static discharge can be a source of ignition. ▸ Solids handling systems must be designed in accordance with applicable standards (e.g. NFPA including 654 and 77) and other national guidance. ▸ Do not empty directly into flammable solvents or in the presence of flammable vapors. ▸ The operator, the packaging container and all equipment must be grounded with electrical bonding and grounding systems. Plastic bags and plastics cannot be grounded, and antistatic bags do not completely protect against development of static charges. 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.
Other information	▸ 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 storage and handling recommendations contained within this SDS. For major quantities: ▸ Consider storage in bunded 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.

Conditions for safe storage, including any incompatibilities

Suitable container	▸ Glass container is suitable for laboratory quantities ▸ Packaging as recommended by manufacturer. ▸ Check that containers are clearly labelled. ▸ Tamper-proof containers. ▸ Polyethylene or polypropylene containers. ▸ Metal drum with sealed plastic liner.
Storage incompatibility	▸ Avoid reaction with oxidising agents

SECTION 8 EXPOSURE CONTROLS / PERSONAL PROTECTION

Control parameters

OCCUPATIONAL EXPOSURE LIMITS (OEL)

INGREDIENT DATA

Not Available

EMERGENCY LIMITS

Ingredient	Material name	TEEL-1	TEEL-2	TEEL-3
VENLAFAXINE HYDROCHLORIDE	Not Available	Not Available	Not Available	Not Available

Ingredient	Original IDLH	Revised IDLH
venlafaxine hydrochloride	Not Available	Not Available

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 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.

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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).

Exposure controls

Appropriate engineering controls

Enclosed local exhaust ventilation is required at points of dust, fume or vapour generation.

HEPA terminated local exhaust ventilation should be considered at point of generation of dust, fumes or vapours.

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

A fume hood or vented balance enclosure is recommended for weighing/ transferring quantities exceeding 500 mg.

When handling quantities up to 500 gram in either a standard laboratory with general dilution ventilation (e.g. 6-12 air changes per hour) is preferred. Quantities up to 1 kilogram may require a designated laboratory using fume hood, biological safety cabinet, or approved vented enclosures. Quantities exceeding 1 kilogram should be handled in a designated laboratory or containment laboratory using appropriate barrier/ containment technology.

Manufacturing and pilot plant operations require barrier/ containment and direct coupling technologies.

Barrier/ containment technology and direct coupling (totally enclosed processes that create a barrier between the equipment and the room) typically use double or split butterfly valves and hybrid unidirectional airflow/ local exhaust ventilation solutions (e.g. powder containment booths). Glove bags, isolator glove box systems are optional. HEPA filtration of exhaust from dry product handling areas is required.

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, vapours, 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.

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.

The following protective devices are recommended where exposures exceed the recommended exposure control guidelines by factors of:

10; high efficiency particulate (HEPA) filters or cartridges

10-25; loose-fitting (Tyvek or helmet type) HEPA powered-air purifying respirator.

25-50; a full face-piece negative pressure respirator with HEPA filters

50-100; tight-fitting, full face-piece HEPA PAPR

100-1000; a hood-shroud HEPA PAPR or full face-piece supplied air respirator operated in pressure demand or other positive pressure mode.

Personal protection

Eye and face protection

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 lenses 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], [AS/NZS 1336 or national equivalent]

Skin protection

See Hand protection below

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Hands/feet protection	The selection of suitable gloves does not only depend on the material, but also on further marks of quality which vary from manufacturer to manufacturer. Where the chemical is a preparation of several substances, the resistance of the glove material can not be calculated in advance and has therefore to be checked prior to the application. The exact break through time for substances has to be obtained from the manufacturer of the protective gloves and.has to be observed when making a final choice. Personal hygiene is a key element of effective hand care. Gloves must only be worn on clean hands. After using gloves, hands should be washed and dried thoroughly. Application of a non-perfumed moisturizer is recommended. Suitability and durability of glove type is dependent on usage. Important factors in the selection of gloves include: · 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, AS/NZS 2161.1 or national equivalent). · 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, AS/NZS 2161.10.1 or national equivalent) 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, AS/NZS 2161.10.1 or national equivalent) is recommended. · Some glove polymer types are less affected by movement and this should be taken into account when considering gloves for long-term use. · Contaminated gloves should be replaced. For general applications, gloves with a thickness typically greater than 0.35 mm, are recommended. It should be emphasised that glove thickness is not necessarily a good predictor of glove resistance to a specific chemical, as the permeation efficiency of the glove will be dependent on the exact composition of the glove material. Therefore, glove selection should also be based on consideration of the task requirements and knowledge of breakthrough times. Glove thickness may also vary depending on the glove manufacturer, the glove type and the glove model. Therefore, the manufacturers' technical data should always be taken into account to ensure selection of the most appropriate glove for the task. Note: Depending on the activity being conducted, gloves of varying thickness may be required for specific tasks. For example: · Thinner gloves (down to 0.1 mm or less) may be required where a high degree of manual dexterity is needed. However, these gloves are only likely to give short duration protection and would normally be just for single use applications, then disposed of. · Thicker gloves (up to 3 mm or more) may be required where there is a mechanical (as well as a chemical) risk i.e. where there is abrasion or puncture potential 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, latex/ nitrile). Employees allergic to latex gloves should use nitrile gloves in preference. ▸ Double gloving should be considered. ▸ PVC gloves. ▸ Change gloves frequently and when contaminated, punctured or torn. ▸ Wash hands immediately after removing gloves. ▸ Protective shoe covers. [AS/NZS 2210] ▸ 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. ▸ fluorocaoutchouc. ▸ polyvinyl chloride. Gloves should be examined for wear and/ or degradation constantly.
Body protection	See Other protection below
Other protection	▸ 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
Thermal hazards	Not Available

Respiratory protection

Particulate. (AS/NZS 1716 & 1715, EN 143:000 & 149:001, ANSI Z88 or national equivalent)

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

* - Negative pressure demand ** - Continuous flow
A(All classes) = Organic vapours, B AUS or B1 = Acid gasses, B2 = Acid gas or hydrogen cyanide(HCN), B3 = Acid gas or hydrogen cyanide(HCN), E = Sulfur dioxide(SO2), G = Agricultural chemicals, K = Ammonia(NH3), Hg = Mercury, NO = Oxides of nitrogen, MB = Methyl bromide, AX = Low boiling point organic compounds(below 65 degC)

- **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 protection. 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.**

Continued...

SECTION 9 PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties

Appearance	White to off-white crystalline powder; mixes with water (572 mg/ml, adjusted to ionic strength of 0.2 M with sodium chloride).

Physical state	Divided Solid	**Relative density (Water = 1)**	Not Available
Odour	Not Available	**Partition coefficient n-octanol / water**	Not Available
Odour threshold	Not Available	**Auto-ignition temperature (°C)**	Not Available
pH (as supplied)	Not Applicable	**Decomposition temperature**	Not available.
Melting point / freezing point (°C)	Not Available	**Viscosity (cSt)**	Not Applicable
Initial boiling point and boiling range (°C)	Not Available	**Molecular weight (g/mol)**	313.87
Flash point (°C)	Not Available	**Taste**	Not Available
Evaporation rate	Not Available	**Explosive properties**	Not Available
Flammability	Not Available	**Oxidising properties**	Not Available
Upper Explosive Limit (%)	Not available.	**Surface Tension (dyn/cm or mN/m)**	Not Applicable
Lower Explosive Limit (%)	Not Available	**Volatile Component (%vol)**	Negligible
Vapour pressure (kPa)	Negligible	**Gas group**	Not Available
Solubility in water (g/L)	Miscible	**pH as a solution (1%)**	Not Available
Vapour density (Air = 1)	>1	**VOC g/L**	Not Available

SECTION 10 STABILITY AND REACTIVITY

Reactivity	See section 7
Chemical stability	▸ Unstable in the presence of incompatible materials. ▸ Product is considered stable. ▸ Hazardous polymerisation will not occur.
Possibility of hazardous reactions	See section 7
Conditions to avoid	See section 7
Incompatible materials	See section 7
Hazardous decomposition products	See section 5

SECTION 11 TOXICOLOGICAL INFORMATION

Information on toxicological effects

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. 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. If prior damage to the circulatory or nervous systems has occurred or if kidney damage has been sustained, proper screenings should be conducted on individuals who may be exposed to further risk if handling and use of the material result in excessive exposures.
Ingestion	Accidental ingestion of the material may be damaging to the health of the individual. for venlafaxine: Since any psychoactive drug may impair judgement, thinking or motor skills, exposed individuals should be cautious in operating machinery. In overdose, somnolence is the most commonly reported symptom. Convulsion and mild sinus tachycardia have also been reported. Treatment is associated with sustained dose-dependent increases in blood pressure. Treatment-related anxiety, nervousness, insomnia and anorexia have also been reported. Significant weight loss may be an undesirable effect of treatment. Hypomania or mania, and seizure has been reported in a small number of patients. Other adverse reactions headache, asthenia, infection, chills, chest pain, trauma, vasodilation, increased blood pressure/ hypertension, tachycardia, postural hypotension, sweating, rash, pruritus, nausea, constipation, diarrhoea, vomiting, dyspepsia, flatulence, somnolence, dry mouth, dizziness, insomnia, nervousness, anxiety, tremor, abnormal dreams, hypertonia, paraesthesia, decreased libido, agitation, confusion, abnormal thoughts, depersonalisation, depression, urinary retention, twitching, yawning, blurred vision, taste perversion, tinnitus, mydriasis, abnormal ejaculation/ orgasm, impotence, urinary frequency, impaired urination, disturbed orgasm, menstrual disorders, dysphagia, eructation, ecchymosis, somnolence, peripheral oedema, weight gain, emotional lability, trismus vertigo, bronchitis, dyspnea, abnormal vision, ear pain, anorgasmia, dysuria, haematuria, metrorrhagia, impaired urination, vaginitis, dry mouth, neck pain, and sweating. Dose-dependent effects included chills, nausea, agitation, dizziness, somnolence, tremor, yawning, sweating, and abnormal ejaculation. A statistically significant increase in serum cholesterol was also reported. Infrequent or rare effects included enlarged abdomen, allergic reactions, cyst, facial oedema, hangover, hernia, moniliasis, neck rigidity, sub- sternal chest pain, pelvic pain, photosensitivity reactions, appendicitis, body odour, halitosis, ulcer, withdrawal symptoms, angina pectoris, extrasystoles, hypotension, peripheral vascular disorder (cold feet and hands), syncope, thrombophlebitis, arrhythmia, first-degree atrioventricular block, bradycardia, bundle branch block, mitral valve disorder, mucocutaneous haemorrhage, sinus bradycardia, varicose vein, colitis, oedema of the tongue, oesophagitis, gastritis, gastroenteritis, gingivitis, glossitis, rectal haemorrhage, hemorrhoids, melena, stomatitis, stomach ulcer, mouth ulcerations, cheilitis, cholecystitis, cholelithiasis, haematemesis, gum haemorrhage, hepatitis, ileitis, jaundice, oral moniliasis, intestinal obstruction, proctitis,

Continued...

increased salivation, soft stools, discolouration of the tongue, oesophageal ulcer, peptic ulcer syndrome, goiter, hyperthyroidism, hypothyroidism, leukocytosis, leukopenia, lymphadenopathy, lymphocytosis, thrombocytopenia, thrombocythemia, basophilia, cyanosis, eosinophilia, abnormal erythrocytes and WBC, diabetes mellitus, glycosuria, hypercholesteraemia, hyperglycaemia, hyperlipaemia, hyperrubicaemia, hypoglycaemia, hypokalaemia, increased thirst, alcohol intolerance, bilirubinaemia, gout, haemochromatosis, hyperkalaemia, hyperphosphataemia, hypoglycaemic reaction, hyponatraemia, hypophosphataemia, hypoproteinaemia, uraemia, arthritis, arthrosis, bone pain, bone spurs, bursitis, joint disorder, myasthenia, tenosynovitis, osteoporosis, apathy, ataxia, circumoral paraesthesia, CNS stimulation, euphoria, hallucinations, hostility, hyperaesthesia, hyperkinaesia, hypertonia, hypotonia, incoordination, increased libido, manic reactions, myoclonus, neuralgia, neuropathy, paranoid reaction, psychosis, psychotic depression, sleep disturbance, abnormal speech, stupor, torticollis, akathisia, alkinaesia, alcohol abuse, aphasia, bradykinaesia, cerebrovascular accident, loss of consciousness, delusions, dementia, dystonia, hypokinaesia, neuritis, nystagmus, increased reflexes, seizures, acne, alopecia, brittle nails, contact dermatitis, dry skin, herpes simplex, herpes zoster, maculopapular rash, urticaria, dermal atrophy, exfoliative dermatitis, fungal dermatitis, lichenoid dermatitis, discolouration of the hair, eczema, furuncolosis, hirsutism, skin hypertrophy, leukoderma, psoriasis, pustular rash, vesiculobullous rash, asthma, chest congestion, epistaxis, hyperventilation, laryngismus, laryngitis, pneumonia, voice alterations, atelectasis, haemoptysis, hypoxia, pleurisy, pulmonary embolus, sleep apnea, increased sputum, cataract, conjunctivitis, corneal lesion, diplopia, dry eyes, exophthalmos, eye pain, otitis media, parosmia, photophobia, subconjunctival haemorrhage, loss of taste, visual field defect, blepharitis, chromatopsia, conjunctival oedema, deafness, glaucoma, hyperacusis, keratitis labrynthitis, miosis, papilloedema, decreased pupillary reflex, schleritis, albuminuria, amenorrhoea, kidney calculus, cystitis, leukorrhea, menorrhagia, nocturia, bladder pain, breast pain, kidney pain, polyuria, prostatitis, pyelonephritis, pyuria, urinary incontinence,urinary urgency, uterine fibroids, enlarged uterine haemorrhage, vaginal haemorrhage, vaginal moniliasis, abortion, breast engorgement, breast enlargement, calcium crystalluria, female lactation, hypomenorrhea, menopause, prolonged erection, uterine spasm.
Adverse reactions, some serious, have been reported in patients who have recently discontinued monoamine oxidase inhibitor (MAOI) therapy or who have discontinued venlafaxine therapy prior to initiation of an MAOI.
Reactions include tremor, myoclonus, diaphoresis, nausea, vomiting, flushing, dizziness, hyperthermia, with features resembling neuroleptic malignant syndrome, seizures, and death. In patients receiving antidepressants with similar action to venlafaxine in combination there have been reports of serious, sometimes fatal reactions. For a selective serotonin reuptake inhibitor, these include hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuation of vital signs, and mental status changes that include extreme agitation progressing to delirium and coma.
Certain cases present with features resembling neuroleptic malignant syndrome. Severe hypothermia and sometimes fatal seizures have been reported with combined use of tricyclics and MAOIs.
Because one of the actions of the SNRIs is to block the reuptake (and hence extracellular accumulation) of serotonin as the SSRIs do, it has many of the same side effects. The most common include nausea, drowsiness, headache, changes in appetite, vivid dreams, and sexual side effects. There are two common sexual side effects: diminished interest in sex (libido) and difficulty reaching climax (orgasm). These drugs typically do not cause problems with erection, but the sexual side effects are the most common reason people stop taking this type of antidepressant even if it is working well.
One rarely mentioned side effect which is hardly mentioned in the literature is a decreased ability to perform normal physical activities. Examples of this include exhaustion following house chores or inability to complete even an easy work-out routine without napping afterwards.
Serotonin accumulation may lead to severe reactions known as serotonin syndrome - this may be life-threatening. Symptom onset is usually rapid, often occurring within minutes. Serotonin syndrome encompasses a wide range of clinical findings. Mild symptoms may only consist of increased heart rate, shivering, sweating, dilated pupils, myoclonus (intermittent tremor or twitching), as well as overresponsive reflexes. Moderate intoxication includes additional abnormalities such as hyperactive bowel sounds, high blood pressure and hyperthermia; a temperature as high as 40 deg C (104 deg F) is common in moderate intoxication. Mental status changes include hypervigilance and agitation.Severe symptoms include severe increases in heart rate and blood pressure that may lead to shock. Temperature may rise to above 41.1 deg C (106.0 deg F) in life-threatening cases. Other abnormalities include metabolic acidosis, rhabdomyolysis, seizures, renal failure, and disseminated intravascular coagulation; these effects usually arising as a consequence of hyperthermia
The side effects of norepinephrine reuptake inhibition (NRI) use arise from the over-stimulation of metabolic processes. Migraines, restlessness, and nausea can develop as a reaction to the medication. The drug's appetite-suppressing effects might also lead to the development of anorexia. When the drug is used beyond normal levels, the problems escalate; the patient's brain can suffer from severe toxicity, resulting in comas or death. Numerous experts support the use of norepinephrine reuptake inhibitors, however, saying that there is little to no risk of developing an addiction to the drugs. Activity at the norepinephrine transporter can sometimes cause anxiety, activation, and elevated blood pressure, leading to the recommendation that everyone who takes these medications should have their blood pressure monitored. Severe, throbbing headaches occur in most people with elevated norepinephrine levels. The headaches typically correlate to the marked elevation in blood pressure caused by norepinephrine
SNRIs should be taken with caution when using St John's wort, and should never be taken with MAOI antidepressants.
As with the SSRIs, abrupt discontinuation of SNRI-medication usually leads to a discontinuation syndrome which could include states of anxiety and further symptoms
SNRIs may be monoamine oxidase inhibitors (MAOIs). Monoamine oxidase inhibitors produce postural hypotension, dizziness, drowsiness, weakness and fatigue, dryness of the mouth, constipation and other gastrointestinal disturbances (including nausea and vomiting) and oedema. Other symptoms may include agitation and tremors, insomnia and restless sleep, blurred vision, difficulty in urinating, convulsions, skin rashes, leucopenia, sexual disturbances and weight gain with inappropriate appetite. Psychotic episodes may be characterised by hypomanic behavior, confusion and hallucinations. Jaundice has been reported and infrequently this may lead to fatal progressive hepatocellular necrosis.
Serotonin syndrome (serious changes to how the brain, muscles and digestive system works due to high levels of serotonin in the body) may occur in therapy.
Signs and symptoms of serotonin syndrome include:

- restlessness
- fast heart beat
- fast changes in blood pressure
- diarrhoea and vomiting
- nausea
- hallucinations
- increased body temperature
- coma
- loss of coordination
- overactive reflexes

General side effects of serotonin reuptake inhibitors (SSRIs) are mostly present during the first 1-4 weeks while the body adapts to the drug (with the exception of sexual side effects, which tend to occur later in treatment). In fact, it often takes 6-8 weeks for the drug to begin reaching its full potential (the slow onset is considered a downside to treatment with SSRIs). Almost all SSRIs are known to cause one or more of these symptoms:

- anhedonia (inability to experience pleasure from normally pleasurable life events such as eating, exercise, and social or sexual interaction.)
- nausea
- drowsiness or somnolence
- headache
- clenching of teeth
- extremely vivid and strange dreams
- dizziness
- changes in appetite
- weight loss/gain (measured by a change in bodyweight of 7 pounds)
- may result in a double risk of bone fractures and injuries
- changes in sexual behaviour
- increased feelings of depression and anxiety (which may sometimes provoke panic attacks)
- tremors
- autonomic dysfunction including orthostatic tension, increased or reduced sweating
- akathisia (a syndrome characterised by unpleasant sensations of "inner" restlessness that manifests itself with an inability to sit still or remain motionless)
- liver or renal impairment
- thoughts of suicide
- Photosensitivity (increased risk of sunburn) (Use protective clothing, such as long sleeves and hats, and sunscreen to decrease the risk of sunburn.)

Continued...

	Common gastrointestinal side effects include nausea, vomiting, and diarrhoea, which are brought about by the actions of serotonin on the gastrointestinal tract. Most side effects usually disappear after the adaptation phase, when the antidepressive effects begin to show. However, despite being called general, the side effects and their durations are highly individual and drug-specific. Usually the treatment is begun with a small dose to see how the patient's body reacts to the drug, after that either the dose can be adjusted. Mania or hypomania is a possible side-effect. Users with some type of bipolar disorder are at a much higher risk, however SSRI-induced mania in patients previously diagnosed with unipolar depression can trigger a bipolar diagnosis. **Sexual dysfunction:** SSRIs can cause various types of sexual such as anorgasmia, erectile dysfunction, and diminished libido. Initial studies found that such side effects occur in less than 10% of patients, but since these studies relied on unprompted reporting, the frequency was probably underestimated. In more recent studies, doctors have specifically asked about sexual difficulties, and found that they are present in between 17% and 41% of patients. This dysfunction occasionally disappears spontaneously without stopping the SSRI, and in most cases resolves after discontinuation. In some cases, however, it does not; this is known as Post SSRI Sexual Dysfunction (PSSD). It is believed that sexual dysfunction is caused by an SSRI induced reduction in dopamine. Stimulation of postsynaptic 5-HT2 and 5-HT3 receptors decreases dopamine release from the Substantia nigra. **Cardiovascular side effects** are very rare with SSRI use, with a reported incidence of less than 0.0003 percent. SSRIs inhibit cardiac and vascular sodium, calcium and potassium channels and prolong QT intervals. However, a number of large studies of patients without known pre-existing heart disease have reported no EKG changes related to SSRI use. In overdose, fluoxetine has been reported to cause sinus tachycardia, myocardial infarction, junctional rhythms and trigeminy. Some authors have suggested electrocardiographic monitoring in patients with severe pre-existing cardiovascular disease who are taking SSRI's. **Discontinuation syndrome:** SSRIs are addictive as discontinuing their use is known to produce both somatic and psychological withdrawal symptoms. **Suicidality and aggression:** Similarly to other antidepressants, SSRIs can cause suicidality in children. A 2004 Food and Drug Administration (FDA) analysis of clinical trials on children with major depressive disorder found statistically significant increases of the risks of "possible suicidal ideation and suicidal behavior" by about 80%, and of agitation and hostility by about 130%. An additional analysis by the FDA also indicated 1.5-fold increase of suicidality in the 18–24 age group. This resulted in a black box warning on SSRI and other antidepressant medications regarding the increased risk of suicidality in patients younger than 24. In 2004, the Medicines and Healthcare products Regulatory Agency (MHRA) in the United Kingdom judged fluoxetine (Prozac) to be the only antidepressant that offered a favorable risk-benefit ratio in children with depression, though it was also associated with a slight increase in the risk of self-harm and suicidal ideation. Only two SSRIs are licensed for use with children in the UK, sertraline (Zoloft) and fluvoxamine (Luvox), and only for the treatment of obsessive-compulsive disorder. Fluoxetine, despite having a favorable risk-benefit ratio for use with depression in adolescents and children, is not licensed for this use. Other studies on SSRIs and suicide among adolescents are equivocal; rates of suicide attempts in high-risk populations appear to be unaffected by SSRI prescriptions in adults. There is also evidence that higher rates of SSRI prescriptions are associated with lower rates of suicide in children, though since the evidence is correlational, the true nature of the relationship is unclear. The introduction of a warning regarding the association between SSRIs and suicide led to a decrease in prescriptions for the medications in 2003 and 2004, and these decreases in prescriptions were associated with an increase in actual number of teenage suicide. **Interaction with carbohydrate metabolism:** Serotonin is also involved in regulation of carbohydrate metabolism. Few analyses of the role of SSRIs in treating depression cover the effects on carbohydrate metabolism from intervening in serotonin handling by the body. **Pregnancy:** When taken by pregnant women, selective serotonin reuptake inhibitors (SSRIs) cross the placenta and have the potential to affect newborns. Sertraline and paroxetine have been associated with congenital malformations. Some evidence suggests that SSRIs are associated with neonatal complications such as neonatal abstinence syndrome (NAS) and persistent pulmonary hypertension (PPHN). **Neonatal abstinence syndrome** is a withdrawal syndrome in newborn babies which has been documented in SSRI treatment. **Persistent pulmonary hypertension** (PPHN) is a serious and life-threatening, but rare, lung condition that occurs soon after birth of the newborn. Newborn babies with PPHN have high pressure in their lung blood vessels and are not able to get enough oxygen into their bloodstream. About 1 to 2 babies per 1000 babies born in the U.S. develop PPHN shortly after birth, and often they need intensive medical care. One study has found that PPHN is six times more common in babies whose mothers take an SSRI antidepressant after the 20th week of the pregnancy compared to babies whose mothers do not take an antidepressant. SSRIs may be monoamine oxidase inhibitors (MAOIs). Monoamine oxidase inhibitors produce postural hypotension, dizziness, drowsiness, weakness and fatigue, dryness of the mouth, constipation and other gastrointestinal disturbances (including nausea and vomiting) and oedema. Other symptoms may include agitation and tremors, insomnia and restless sleep, blurred vision, difficulty in urinating, convulsions, skin rashes, leucopenia, sexual disturbances and weight gain with inappropriate appetite. Psychotic episodes may be characterised by hypomanic behavior, confusion and hallucinations. Jaundice has been reported and infrequently this may lead to fatal progressive hepatocellular necrosis.
Skin Contact	Skin contact is not thought to have harmful health effects (as classified under EC Directives); the material may still produce health damage following entry through wounds, lesions or abrasions. Limited evidence exists, or practical experience predicts, that the material either produces inflammation of the skin in a substantial number of individuals following direct contact, and/or produces significant inflammation when applied to the healthy intact skin of animals, for up to four hours, such inflammation being present twenty-four hours or more after the end of the exposure period. Skin irritation may also be present after prolonged or repeated exposure; this may result in a form of contact dermatitis (nonallergic). The dermatitis is often characterised by skin redness (erythema) and swelling (oedema) which may progress to blistering (vesiculation), scaling and thickening of the epidermis. At the microscopic level there may be intercellular oedema of the spongy layer of the skin (spongiosis) and intracellular oedema of the epidermis. **PHOTOSENSITISER:** Certain individuals working with this substance may show an abnormally heightened or allergic reaction of the skin to the influence of sunlight. This results in sensitivity to sun, which may be severe, unless protective covering and 15+SPF sunblock cream are used. Responses may vary from sunburn-like responses to edematous, vesiculated lesions or bullae. Open cuts, abraded or irritated skin should not be exposed to this material Entry into the blood-stream through, for example, cuts, abrasions, puncture wounds 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.
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.
Chronic	Long-term exposure to the product is not thought to produce chronic effects adverse to health (as classified by EC Directives using animal models); nevertheless exposure by all routes should be minimised as a matter of course. Exposure to the material may cause concerns for humans owing to possible developmental toxic effects, generally on the basis that results in appropriate animal studies provide strong suspicion of developmental toxicity in the absence of signs of marked maternal toxicity, or at around the same dose levels as other toxic effects but which are 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. A prime symptom is breathlessness. Lung shadows show on X-ray. Venlafaxine given by gavage to mice for 18 months (up to 120 mg/kg/day) and to rats for 24 months (up to 120 mg/kg/day) did not induce tumours. Venlafaxine and the major metabolite desvenlafaxine were not mutagenic in the Ames reverse mutation assay in Salmonella or the CHO/HGPRT mammalian cell forward gene mutation assay, the in vitro BALB/c-3T3 mouse cell transformation assay, the sister chromatid exchange assay in cultured CHO cells, or in the in vivo chromosomal aberration assay in rat bone marrow. desvenlafaxine was not mutagenic in the in vitro CHO cell chromosomal aberration assay. There was a clastogenic response in th in vitro chromosomal aberration assay in rat bone marrow in male rats receiving 200 times, on a mg/kg basis, or 50 times on a mg/m2 basis, the maximum human daily dose. The no-effect dose was 67 times (mg/kg) or 17 times (mg/m2) the human dose. Reproduction and fertility studies in rats showed no effects on male and female fertility up to oral doses 8 times that of the maximum recommended human dose (mg/kg basis). Venlafaxine did not cause malformations in offspring of rats and rabbits given 11 times (rat) or 12 times (rabbit) the maximum recommended human daily dose on a mg/kg basis. In rats, however, there was a decrease in pup weight, and an increase in stillborn pups and an increase in pup deaths during the first 5 days of lactation, when dosing began during pregnancy and continued until weaning. These effects occurred at 10 times the maximum human

Continued...

	dose (mg/kg basis).

venlafaxine hydrochloride	**TOXICITY**	**IRRITATION**
	Not Available	Not Available

Legend:	*1. Value obtained from Europe ECHA Registered Substances - Acute toxicity 2.* Value obtained from manufacturer's SDS. Unless otherwise specified data extracted from RTECS - Register of Toxic Effect of chemical Substances*

VENLAFAXINE HYDROCHLORIDE	Oral (human) LDLo: 235 mg/kg/12d - I Nil reported Oral (woman) TDLo: 315 mg/kg/30w - I Oral (man) TDLo: 32 mg/kg/9w - I Oral (woman) TDLo: 360 mg/kg/17w - I Fibrosis, acute pulmonary oedema, gastrointestinal changes, mydriasis, spasticity, sweating, withdrawal, diarrhoea, nausea, vomiting, headache,

Acute Toxicity	✔	**Carcinogenicity**	⊘
Skin Irritation/Corrosion	✔	**Reproductivity**	✔
Serious Eye Damage/Irritation	⊘	**STOT - Single Exposure**	⊘
Respiratory or Skin sensitisation	⊘	**STOT - Repeated Exposure**	⊘
Mutagenicity	⊘	**Aspiration Hazard**	⊘

Legend: ✘ *– Data available but does not fill the criteria for classification*
✔ *– Data required to make classification available*
⊘ *– Data Not Available to make classification*

SECTION 12 ECOLOGICAL INFORMATION

Toxicity

Ingredient	Endpoint	Test Duration (hr)	Species	Value	Source
Not Available	Not Applicable	Not Applicable	Not Applicable	Not Applicable	Not Applicable
Legend:	*Extracted from 1. IUCLID Toxicity Data 2. Europe ECHA Registered Substances - Ecotoxicological Information - Aquatic Toxicity 3. EPIWIN Suite V3.12 - Aquatic Toxicity Data (Estimated) 4. US EPA, Ecotox database - Aquatic Toxicity Data 5. ECETOC Aquatic Hazard Assessment Data 6. NITE (Japan) - Bioconcentration Data 7. METI (Japan) - Bioconcentration Data 8. Vendor Data*				

|
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 selective serotonin reuptake inhibitors (SSRIs):
Selective serotonin reuptake inhibitors (SSRIs) are a major class of widely prescribed antidepressants and obsessive-compulsive regulators that includes Prozac, Zoloft, Luvox, and Paxil.
The function of serotonin in a wide array of aquatic creatures could prove highly significant in any discussion of the importance of low levels of pharmaceuticals in the environment. The potential for dramatic physiologic effects on nontarget species (such as invertebrates) by low (ppb) concentrations of pharmaceuticals is the subject of many studies. Serotonin is a biogenic amine common in both vertebrate and invertebrate nervous systems. SSRIs increase serotonin neurotransmission by inhibiting its reuptake at the synapses by inhibiting the transporter enzymes. In addition to playing a key role in mammalian neurotransmission, serotonin is involved in a wide array of physiologic regulatory roles in molluscs, among most other creatures. For bivalves, reproductive functions including spawning, oocyte maturation, and parturition are regulated by serotonin Serotonin controls a wide spectrum of additional behaviors and reflexes in molluscs, including heartbeat rhythm, feeding/biting, swimming motor patterns, beating of cilia, and induction of larval metamorphosis. It also stimulates release of various neurohormones in crustaceans (hyperglycemic hormone, red pigment-dispersing hormone, neurodepressing hormone, and molt-inhibiting hormone) and ovarian maturation. It has long been known that serotonin at concentrations of 10-4 to 10-3 M (~0.18-1.8 g/L) induces spawning in bivalves. Some commercial farmers make use of this by adding serotonin to induce spawning. Prozac (fluoxetine) and Luvox (fluvoxamine) are the most potent inducers ever found, eliciting spawning behavior in zebra mussels at aqueous concentrations many orders of magnitude lower than serotonin. Fluoxetine elicited significant spawning in male mussels at concentrations of 10-7 M (~150 ug/L); females were an order of magnitude less sensitive at 10-6 M. Fluvoxamine was the most potent of the SSRIs, eliciting significant spawning in male mussels, at 10-9 M (~0.318 ug/L); females were two orders of magnitude less sensitive, at 10-7 M. In males, spawning was complete in the first hour, while females were slower (within 2 hr). Paxil (paroxetine) was the least potent of these three SSRIs, eliciting male spawning, but to a lesser degree, at 10-6 M, and having no inducing effect on females at any concentration. It should be noted that the evidence is not clear whether these compounds are indeed acting as SSRIs, or via some other mechanism. It is also unknown how these compounds are taken up by molluscs. In another study, fluvoxamine induces significant parturition in fingernail clams at 1 nM; 1 nM fluvoxamine also potentiated the effect of 10 uM 5-hydroxytryptophan (5-HT, a precursor of serotonin) by almost 5-fold. Paroxetine was less potent, requiring a concentration of 10 uM to effect significant parturition. In contrast, even at concentrations of 100 uM, fluoxetine displayed no effect, although it was capable at 5 uM of potentiating 5-HT at concentrations that were otherwise subthreshold. It is interesting that the order of potency for inducing parturition in clams differs from the order for induction of spawning in mussels (above). This points to the complexity of considering any approach involving extrapolations from one species to another or from one drug to another within a given class.
In crustaceans, fluoxetine significantly potentiates the effect of 5-HT in crayfish, enhancing the release of ovary-stimulating hormone, which results in larger oocytes with enhanced amounts of vitellin; any ecologic consequences of higher vitellin protein levels are unknown.
Similarly, in fiddler crabs, fluoxetine at a dose of 125 nmol stimulates (through 5-HT) the production of gonad-stimulating hormone, which accelerates testicular maturation . It is clear that aquatic life can be exquisitely sensitive to at least some of this class of compounds.
Although some SSRIs are extremely potent, others have almost no effect, which possibly makes the approach of assessing ecologic risk on a class-by-class basis infeasible.
Concentration of SSRIs plays a complicated role with respect to effects. For example, while injected fluoxetine induced significant metamorphosis in a gastropod, 10-4 M induced less metamorphosis than 10-6 M. Simple extrapolations of effects from higher concentrations do not necessarily have any relevance to effects at lower concentrations.
The potential for SSRIs to elicit subtle effects on aquatic life is further extended by serotonin reuptake mechanisms that also are a factor in snails and squids , particularly in the regulation of aggression . Yet another example of a subtle effect that would go unnoticed is the fighting behavior of lobsters, in which serotonin causes behavior reversal by stimulating subordinates to engage in fighting against dominants by reducing their propensity to retreat .
DO NOT discharge into sewer or waterways.
log Kow 0.43 (0.2 M sodium chloride)

Persistence and degradability

Ingredient	Persistence: Water/Soil	Persistence: Air
	No Data available for all ingredients	No Data available for all ingredients

Bioaccumulative potential

Ingredient	Bioaccumulation
	No Data available for all ingredients

Continued...

Mobility in soil

Ingredient	Mobility
	No Data available for all ingredients

SECTION 13 DISPOSAL CONSIDERATIONS

Waste treatment methods

Product / Packaging disposal	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. In most instances the supplier of the material should be consulted. ▸ **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 land-fill specifically licenced to accept chemical and / or pharmaceutical wastes 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 TRANSPORT INFORMATION

Labels Required

	
Marine Pollutant	

Land transport (UN)

UN number	3077
UN proper shipping name	ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (contains venlafaxine hydrochloride)
Transport hazard class(es)	Class: 9 Subrisk: Not Applicable
Packing group	III
Environmental hazard	Not Applicable
Special precautions for user	Special provisions: 274; 331; 335; 375 Limited quantity: 5 kg

Air transport (ICAO-IATA / DGR)

UN number	3077
UN proper shipping name	Environmentally hazardous substance, solid, n.o.s. * (contains venlafaxine hydrochloride)
Transport hazard class(es)	ICAO/IATA Class: 9 ICAO / IATA Subrisk: Not Applicable ERG Code: 9L
Packing group	III
Environmental hazard	Not Applicable
Special precautions for user	Special provisions: A97 A158 A179 A197 Cargo Only Packing Instructions: 956 Cargo Only Maximum Qty / Pack: 400 kg Passenger and Cargo Packing Instructions: 956 Passenger and Cargo Maximum Qty / Pack: 400 kg

Continued...

	Passenger and Cargo Limited Quantity Packing Instructions	Y956
	Passenger and Cargo Limited Maximum Qty / Pack	30 kg G

Sea transport (IMDG-Code / GGVSee)

UN number	3077
UN proper shipping name	ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (contains venlafaxine hydrochloride)
Transport hazard class(es)	IMDG Class: 9 IMDG Subrisk: Not Applicable
Packing group	III
Environmental hazard	Marine Pollutant
Special precautions for user	EMS Number: F-A, S-F Special provisions: 274 335 966 967 969 Limited Quantities: 5 kg

Transport in bulk according to Annex II of MARPOL and the IBC code

Not Applicable

SECTION 15 REGULATORY INFORMATION

Safety, health and environmental regulations / legislation specific for the substance or mixture

VENLAFAXINE HYDROCHLORIDE(99300-78-4) IS FOUND ON THE FOLLOWING REGULATORY LISTS

Not Applicable

National Inventory	Status
Australia - AICS	N (venlafaxine hydrochloride)
Canada - DSL	N (venlafaxine hydrochloride)
Canada - NDSL	N (venlafaxine hydrochloride)
China - IECSC	N (venlafaxine hydrochloride)
Europe - EINEC / ELINCS / NLP	N (venlafaxine hydrochloride)
Japan - ENCS	N (venlafaxine hydrochloride)
Korea - KECI	N (venlafaxine hydrochloride)
New Zealand - NZIoC	N (venlafaxine hydrochloride)
Philippines - PICCS	N (venlafaxine hydrochloride)
USA - TSCA	N (venlafaxine hydrochloride)
Legend:	*Y = All ingredients are on the inventory* *N = Not determined or one or more ingredients are not on the inventory and are not exempt from listing(see specific ingredients in brackets)*

SECTION 16 OTHER INFORMATION

Other information

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
The 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.

Definitions and abbreviations

PC—TWA: Permissible Concentration-Time Weighted Average
PC—STEL: Permissible Concentration-Short Term Exposure Limit
IARC: International Agency for Research on Cancer
ACGIH: American Conference of Governmental Industrial Hygienists
STEL: Short Term Exposure Limit
TEEL: Temporary Emergency Exposure Limit。
IDLH: Immediately Dangerous to Life or Health Concentrations
OSF: Odour Safety Factor
NOAEL :No Observed Adverse Effect Level
LOAEL: Lowest Observed Adverse Effect Level
TLV: Threshold Limit Value
LOD: Limit Of Detection
OTV: Odour Threshold Value
BCF: BioConcentration Factors
BEI: Biological Exposure Index

Continued...

end of SDS