Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME
Fexofenadine

STATEMENT OF HAZARDOUS NATURE

NFPA

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS

<table>
<thead>
<tr>
<th></th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flammability</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Toxicity</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Body Contact</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Reactivity</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Chronic</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

CANADIAN WHMIS SYMBOLS

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

RISK
May cause SENSITISATION by skin contact.
Possible risk of irreversible effects.
Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED

- Although ingestion is not thought to produce harmful effects, the material may still be damaging to the health of the individual following ingestion, especially where pre-existing organ (e.g. liver, kidney) damage is evident.

EYE

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

SKIN

- The material is not thought to produce adverse health effects or skin irritation following contact (as classified using animal models). Nevertheless, good hygiene practice requires that exposure be kept to a minimum and that suitable gloves be used in an occupational setting.
- Open cuts, abraded or irritated skin should not be exposed to this material.
- Entry into the blood-stream, through, for example, cuts, abrasions or lesions, may produce systemic injury with harmful effects. Examine the skin prior to the use of the material and ensure that any external damage is suitably protected.

INHALED

- The material is not thought to produce adverse health effects or irritation of the respiratory tract (as classified using animal models). Nevertheless, good hygiene practice requires that exposure be kept to a minimum and that suitable control measures be used in an occupational setting.
- Persons with impaired respiratory function, airway diseases and conditions such as emphysema or chronic bronchitis, may incur further disability if excessive concentrations of particulate are inhaled.

CHRONIC HEALTH EFFECTS

- Strong evidence exists that the substance may cause irreversible but non-lethal mutagenic effects following a single exposure. Skin contact with the material is more likely to cause a sensitization reaction in some persons compared to the general population. Limited evidence suggests that repeated or long-term occupational exposure may produce cumulative health effects involving organs or biochemical systems.
- 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.
- Long-term use of antihistamines can cause sugar in the urine, obstructive jaundice, skin discoloration associated with loss of platelets, early periods, loss of milk production, breast development in males and decreased sex drive. Disturbances in the blood include anemia, loss of white blood cells and platelets.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>NAME</th>
<th>CAS RN</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>fexofenadine</td>
<td>83799-24-0</td>
<td>&gt;98</td>
</tr>
</tbody>
</table>

Section 4 - FIRST AID MEASURES

SWALLOWED

- Immediately give a glass of water. · First aid is not generally required. If in doubt, contact a Poisons Information Center or a doctor.

EYE

- If this product comes in contact with eyes: · Wash out immediately with water. · If irritation continues, seek medical attention.

SKIN

- If skin contact occurs: · Immediately remove all contaminated clothing, including footwear · Flush skin and hair with running water (and soap if available).

INHALED
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.

NOTES TO PHYSICIAN
- In severe overdose of antihistamines, the stomach should be emptied by aspiration and lavage. Emetics should not be used.
- Dizziness, drowsiness, and dry mouth have been reported with fexofenadine hydrochloride overdose.
- In the event of overdose, consider standard measures to remove any unabsorbed drug. Symptomatic and supportive treatment is recommended. Following administration of terfenadine, hemodialysis did not effectively remove fexofenadine, the major active metabolite of terfenadine, from blood (up to 1.7% removed).

**Section 5 - FIRE FIGHTING MEASURES**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vapour Pressure (mmHG)</td>
<td>Negligible</td>
</tr>
<tr>
<td>Upper Explosive Limit (%)</td>
<td>Not available</td>
</tr>
<tr>
<td>Specific Gravity (water=1)</td>
<td>Not available</td>
</tr>
<tr>
<td>Lower Explosive Limit (%)</td>
<td>Not available</td>
</tr>
</tbody>
</table>

**EXTINGUISHING MEDIA**
- Foam.
- Dry chemical powder.

**FIRE FIGHTING**
- Alert Emergency Responders and tell them location and nature of hazard.
- Wear breathing apparatus plus protective gloves.
- When any large container (including road and rail tankers) is involved in a fire, consider evacuation by 100 metres in all directions.

**GENERAL FIRE HAZARDS/HAZARDOUS COMBUSTIBLE PRODUCTS**
- Combustible solid which burns but propagates flame with difficulty.
- Avoid generating dust, particularly clouds of dust in a confined or unventilated space as dusts may form an explosive mixture with air, and any source of ignition, i.e. flame or spark, will cause fire or explosion. Dust clouds generated by the fine grinding of the solid are a particular hazard; accumulations of fine dust may burn rapidly and fiercely if ignited.
- Combustion products include: carbon monoxide (CO), carbon dioxide (CO2), nitrogen oxides (NOx), other pyrolysis products typical of burning organic material.

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

**PERSONAL PROTECTION**
- Glasses: Chemical goggles.
- Gloves:
- Respirator: Particulate

**Section 6 - ACCIDENTAL RELEASE MEASURES**

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

**MAJOR SPILLS**
- Environmental hazard - contain spillage.
- Moderate hazard.
- CAUTION: Advise personnel in area.
- Alert Emergency Responders and tell them location and nature of hazard.

**Section 7 - HANDLING AND STORAGE**

**PROCEDURE FOR HANDLING**
- Avoid all personal contact, including inhalation.
- Wear protective clothing when risk of exposure occurs.
- Empty containers may contain residual dust which has the potential to accumulate following settling. Such dusts may explode in the presence of an appropriate ignition source.
· Do NOT cut, drill, grind or weld such containers.
· In addition ensure such activity is not performed near full, partially empty or empty containers without appropriate workplace safety authorisation or permit.

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

STORAGE REQUIREMENTS
- Observe manufacturer's storing and handling recommendations.

RECOMMENDED STORAGE METHODS

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

STORAGE REQUIREMENTS
Observe manufacturer's storing and handling recommendations.

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS
The following materials had no OELs on our records

PERSONAL PROTECTION

RESPIRATOR
Particulate
Consult your EHS staff for recommendations

EYE
- When handling very small quantities of the material eye protection may not be required.
For laboratory, larger scale or bulk handling or where regular exposure in an occupational setting occurs:
  - Chemical goggles
  - Face shield. Full face shield may be required for supplementary but never for primary protection of eyes
  - Contact lenses may pose a special hazard; soft contact lenses may absorb and concentrate irritants. A written policy document, describing the wearing of 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].

HANDS/FEET
- NOTE: The material may produce skin sensitization in predisposed individuals. Care must be taken, when removing gloves and other protective equipment, to avoid all possible skin contact.
Suitability and durability of glove type is dependent on usage. Important factors in the selection of gloves include: such as:
  - frequency and duration of contact,
  - chemical resistance of glove material,
  - glove thickness and
  - dexterity
Select gloves tested to a relevant standard (e.g. Europe EN 374, US F739).
- When prolonged or frequently repeated contact may occur, a glove with a protection class of 5 or higher (breakthrough time greater than 240 minutes according to EN 374) is recommended.
- When only brief contact is expected, a glove with a protection class of 3 or higher (breakthrough time greater than 60 minutes according to EN 374) is recommended.
- Contaminated gloves should be replaced.
Gloves must only be worn on clean hands. After using gloves, hands should be washed and dried thoroughly. Application of a non-perfumed moisturiser is recommended.
- Rubber gloves (nitrile or low-protein, powder-free latex). Employees allergic to latex gloves should use nitrile gloves in preference.
- Double gloving should be considered.
- PVC gloves.
- Protective shoe covers.
- Head covering.
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
- fluoroelastomer
- 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.

**ENGINEERING CONTROLS**

- Enclosed local exhaust ventilation is required at points of dust, fume or vapor generation. HEPA terminated local exhaust ventilation should be considered at point of generation of dust, fumes or vapors.

**Section 9 - PHYSICAL AND CHEMICAL PROPERTIES**

**PHYSICAL PROPERTIES**

Solid. Does not mix with water.

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>State</td>
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<tr>
<td>Melting Range °F</td>
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<tr>
<td>Boiling Range °F</td>
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</tr>
<tr>
<td>Flash Point °F</td>
<td>Not available</td>
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<tr>
<td>Decomposition Temp °F</td>
<td>Not available</td>
</tr>
<tr>
<td>Autoignition Temp °F</td>
<td>Not available</td>
</tr>
<tr>
<td>Upper Explosive Limit (%)</td>
<td>Not available</td>
</tr>
<tr>
<td>Lower Explosive Limit (%)</td>
<td>Not available</td>
</tr>
<tr>
<td>Volatile Component (%vol)</td>
<td>Negligible</td>
</tr>
</tbody>
</table>

**APPEARANCE**

White solid; does not mix well with water.

**Section 10 - CHEMICAL STABILITY**

**CONDITIONS CONTRIBUTING TO INSTABILITY**

- Presence of incompatible materials.
- Product is considered stable.

**STORAGE INCOMPATIBILITY**

- Avoid reaction with oxidizing agents.

For incompatible materials - refer to Section 7 - Handling and Storage.

**Section 11 - TOXICOLOGICAL INFORMATION**

**FEXOFENADINE**

**TOXICITY AND IRRITATION**

**FEXOFENADINE:**

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

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Irritation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral (mouse) LD50: &gt;4500 mg/kg *</td>
<td>Nil Reported</td>
</tr>
<tr>
<td>Oral (rat) LD50: &gt;5146 mg/kg * * [Marion Merrell Dow]</td>
<td></td>
</tr>
</tbody>
</table>

- Contact allergies quickly manifest themselves as contact eczema, more rarely as urticaria or Quincke's edema. The pathogenesis of contact eczema involves a cell-mediated (T lymphocytes) immune reaction of the delayed type.

for hydrochloride:

General anaesthesia and EKG changes recorded for parent compound. Fexofenadine hydrochloride, the major active metabolite of terfenadine, is an antihistamine with selective H1-receptor antagonist activity. Both enantiomers of fexofenadine hydrochloride displayed approximately equipotent antihistaminic effects. Fexofenadine hydrochloride inhibited antigen-induced bronchospasm in sensitized guinea pigs and histamine release from peritoneal mast cells in rats. The clinical significance of these findings is unknown. In laboratory animals, no anticholinergic or alpha1-adrenergic blocking effects were observed. Moreover, no sedative or other central nervous system effects were observed. Radio labeled tissue distribution studies in rats indicated that fexofenadine does not cross the blood-brain barrier.

In dogs (30 mg/kg/orally twice daily for 5 days) and rabbits (10 mg/kg, intravenously over 1 hour), fexofenadine hydrochloride did not prolong
QTc. In dogs, the plasma fexofenadine concentration was approximately 9 times the therapeutic plasma concentrations in adults receiving the maximum recommended human daily oral dose of 180 mg. In rabbits, the plasma fexofenadine concentration was approximately 20 times the therapeutic plasma concentration in adults receiving the maximum recommended human daily oral dose of 180 mg. No effect was observed on calcium channel current, delayed K⁺ channel current, or action potential duration in guinea pig myocytes, or on the delayed rectifier K⁺ channel cloned from human heart at concentrations up to 1 x 10⁻⁵ M of fexofenadine.

No deaths occurred at oral doses of fexofenadine hydrochloride up to 5000 mg/kg in mice (110 times the maximum recommended daily oral dose in adults and children based on mg/m²) and up to 5000 mg/kg in rats (230 times the maximum recommended daily oral dose in adults and 210 times the maximum recommended daily oral dose in children based on mg/m²). Additionally, no clinical signs of toxicity or gross pathological findings were observed. In dogs, no evidence of toxicity was observed at oral doses up to 2000 mg/kg (300 times the maximum recommended daily oral dose in adults and 280 times the maximum recommended daily oral dose in children based on mg/m²).

Carcinogenesis, Mutagenesis, Impairment of Fertility
The carcinogenic potential of fexofenadine was assessed using terfenadine studies with adequate fexofenadine exposure (based on plasma area-under-the-concentration vs. time [AUC] values). No evidence of carcinogenicity was observed in an 18-month study in mice and in a 24-month study in rats at oral doses up to 150 mg/kg of terfenadine (which led to fexofenadine exposures that were approximately 3 and 5 times the exposure at the maximum recommended daily oral dose of fexofenadine hydrochloride in adults [180 mg] and children [60 mg] respectively).

In in vitro (Bacterial Reverse Mutation, CHO/HGPRT Forward Mutation, and Rat Lymphocyte Chromosomal Aberration assays) and in vivo (Mouse Bone Marrow Micronucleus assay) tests, fexofenadine hydrochloride revealed no evidence of mutagenicity.

In rat fertility studies, dose-related reductions in implants and increases in postimplantation loss were observed at an oral dose of 150 mg/kg of terfenadine (which led to fexofenadine exposures that were approximately 3 times the exposure at the maximum recommended human daily oral dose of 180 mg of fexofenadine hydrochloride based on comparison of AUCs). In mice, fexofenadine hydrochloride produced no effect on male or female fertility at average oral doses up to 4438 mg/kg (which led to fexofenadine exposures that were approximately 13 times the exposure at the maximum recommended human daily oral dose of 180 mg of fexofenadine hydrochloride based on comparison of AUCs).

There was no evidence of teratogenicity in rats or rabbits at oral doses of terfenadine up to 300 mg/kg (which led to fexofenadine exposures that were approximately 4 and 30 times, respectively, the exposure at the maximum recommended human daily oral dose of 180 mg of fexofenadine hydrochloride based on comparison of AUCs).

In mice, no adverse effects and no teratogenic effects during gestation were observed with fexofenadine hydrochloride at oral doses up to 3730 mg/kg (which led to fexofenadine exposures that were approximately 15 times the exposure at the maximum recommended human daily oral dose of 180 mg of fexofenadine hydrochloride based on comparison of AUCs).

Dose-related decreases in pup weight gain and survival were observed in rats exposed to an oral dose of 150 mg/kg of terfenadine (which led to fexofenadine exposures that were approximately 3 times the exposure at the maximum recommended human daily oral dose of 180 mg of fexofenadine hydrochloride based on comparison of AUCs).

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Section 12 - ECOLOGICAL INFORMATION

Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment. This material and its container must be disposed of as hazardous waste. Avoid release to the environment. Refer to special instructions/ safety data sheets.

Section 13 - DISPOSAL CONSIDERATIONS

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

Section 14 - TRANSPORTATION INFORMATION
Section 15 - REGULATORY INFORMATION

No data for fexofenadine (CAS: 83799-24-0, 76815-58-2, 159389-12-5)

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE

- Cumulative effects may result following exposure*.
  * (limited evidence).

Ingredients with multiple CAS Nos

Ingredient Name CAS fexofenadine 83799-24-0, 76815-58-2, 159389-12-5

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- Classification of the preparation and its individual components has drawn on official and authoritative sources as well as independent review by the Chemwatch Classification committee using available literature references. A list of reference resources used to assist the committee may be found at: www.chemwatch.net/references.

- 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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