Zanamivir sesquihydrate

sc-358987

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME
Zanamivir sesquihydrate

STATEMENT OF HAZARDOUS NATURE

NFPA

SUPPLIER
Santa Cruz Biotechnology, Inc.
2145 Delaware Avenue
Santa Cruz, California 95060
800.457.3801 or 831.457.3800

EMERGENCY
ChemWatch
Within the US & Canada: 877-715-9305
Outside the US & Canada: +800 2436 2255
(1-800-CHEMCALL) or call +613 9573 3112

SYNONYMS
C12-H20-N4-O7 • 1.5H2O, "(2R, 3R, 4S)-4-[(diaminomethylidene)amino]-3-acetamido-2-[(1R, 2R)-1, 2, "3-trihydroxypropyl]-3, 4-dihydro-2H-pyran-6-carboxylic acid", "5-acetamido-4-guanidino-6-(1, 2, 3-trihydroxypropyl)-5, 6-dihydro-4H-", "pyran-2-carboxylic acid", "5-(acetylamino)-4-[(aminoiminomethyl)-amino]-2, 6-anhydro-3, 4, 5-", "trideoxy-D-glycero-D-galacto-non-2-enonic acid", 4-guanidino-Neu5Ac2en, "4-guanidino-2, 4-dideoxy-2, 3-dehydro-N-acetylenuraminic acid", GG-167, GR-121167X, zanavir, Relenza, "antiviral/ viricidal", "neuraminidase inhibitor"

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>
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<td></td>
</tr>
<tr>
<td>Toxicity</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Body Contact</td>
<td>2</td>
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<tr>
<td>Reactivity</td>
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<td></td>
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<tr>
<td>Chronic</td>
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</table>

CANADIAN WHMIS SYMBOLS

FLAMMABILITY
HEALTH HAZARD
INSTABILITY
EMERGENCY OVERVIEW

RISK

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED

- Accidental ingestion of the material may be damaging to the health of the individual.

EYE

- This material can cause eye irritation and damage in some persons.

SKIN

- Skin contact is not thought to have harmful health effects, however the material may still produce health damage following entry through wounds, lesions or abrasions.
- 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.
- This material can cause inflammation of the skin on contact in some persons.

INHALED

- Inhalation of dusts, generated by the material during the course of normal handling, may be damaging to the health of the individual.
- 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.
- Neuraminidase inhibitors are associated with very little toxicity and are far less likely to promote the development of drug-resistant influenza.

As a class, the neuraminidase inhibitors are effective against all neuraminidase subtypes and, therefore, against all strains of influenza, a key point in epidemic and pandemic preparedness and an important advantage over the adamantanes, which are effective only against sensitive strains of influenza. Adverse effects of neuraminidase inhibitors may include upper respiratory tract symptoms.

CHRONIC HEALTH EFFECTS

- There has been some concern that this material can cause cancer or mutations but there is not enough data to make an assessment.
- There is some evidence that human exposure to the material may result in developmental toxicity. This evidence is based on animal studies where effects have been observed in the absence of marked maternal toxicity, or at around the same dose levels as other toxic effects but which are not secondary non-specific consequences of the 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.
- Exposure to the material for prolonged periods may cause physical defects in the developing embryo (teratogenesis).

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>NAME</th>
<th>CAS RN</th>
<th>%</th>
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<tbody>
<tr>
<td>zanamivir</td>
<td>139110-80-8</td>
<td>&gt;98</td>
</tr>
</tbody>
</table>

Section 4 - FIRST AID MEASURES

SWALLOWED

- 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.

EYE

- If this product comes in contact with the eyes: - Wash out immediately with fresh running water. - Ensure complete irrigation of the eye by keeping eyelids apart and away from eye and moving the eyelids by occasionally lifting the upper and lower lids.

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 fumes or combustion products are inhaled remove from contaminated area. - Other measures are usually unnecessary.

NOTES TO PHYSICIAN

- Treat symptomatically.

Section 5 - FIRE FIGHTING MEASURES
Vapour Pressure (mmHG): Negligible
Upper Explosive Limit (%): Not Available
Specific Gravity (water=1): Not Available
Lower Explosive Limit (%): Not Available

EXTINGUISHING MEDIA
· Water spray or fog.
· Foam.

FIRE FIGHTING
· Alert Emergency Responders and tell them location and nature of hazard.
· Wear breathing apparatus plus protective gloves.

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.
· May emit poisonous fumes.
· May emit corrosive fumes.

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

PERSONAL PROTECTION
Glasses:
Chemical goggles.

Gloves:

Respirator:
Particulate

Section 6 - ACCIDENTAL RELEASE MEASURES

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

MAJOR SPILLS
■ Moderate hazard.
· CAUTION: Advise personnel in area.
· Alert Emergency Responders and tell them location and nature of hazard.

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
· Store in original containers.
· Keep containers securely sealed.
· Store at -20º C.

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS
The following materials had no OELs on our records

- zanamivir: CAS:139110-80-8

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 lens or restrictions on use, should be created for each workplace or task. This should include a review of lens absorption and adsorption for the class of chemicals in use and an account of injury experience. Medical and first-aid personnel should be trained in their removal and suitable equipment should be readily available. In the event of chemical exposure, begin eye irrigation immediately and remove contact lens as soon as practicable. Lens should be removed at the first signs of eye redness or irritation - lens should be removed in a clean environment only after workers have washed hands thoroughly. [CDC NIOSH Current Intelligence Bulletin 59].

HANDS/FEET
- Suitability and durability of glove type is dependent on usage. Important factors in the selection of gloves include: such as:
  - frequency and duration of contact,
  - chemical resistance of glove material,
  - glove thickness and
  - dexterity
Select gloves tested to a relevant standard (e.g. Europe EN 374, US F739).
- When prolonged or frequently repeated contact may occur, a glove with a protection class of 5 or higher (breakthrough time greater than 240 minutes according to EN 374) is recommended.
- When only brief contact is expected, a glove with a protection class of 3 or higher (breakthrough time greater than 60 minutes according to EN 374) is recommended.
- Contaminated gloves should be replaced.
Gloves must only be worn on clean hands. After using gloves, hands should be washed and dried thoroughly. Application of a non-perfumed moisturiser is recommended.
  - Rubber gloves (nitrile or low-protein, powder-free latex). Employees allergic to latex gloves should use nitrile gloves in preference.
  - Double gloving should be considered.
  - PVC gloves.
  - Protective shoe covers.
  - Head covering.
Experience indicates that the following polymers are suitable as glove materials for protection against undissolved, dry solids, where abrasive particles are not present.
  - polychloroprene
  - nitrile rubber
  - butyl rubber
  - fluorocaoutchouc
  - 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
Mixes with water.

State | Divided Solid | Molecular Weight | 332.31 (anhydrous basis)
--- | --- | --- | ---
Melting Range (°F) | 493(decomp.) | Viscosity | Not Applicable
Boiling Range (°F) | Not Applicable | Solubility in water (g/L) | Miscible
Flash Point (°F) | Not Available | pH (1% solution) | Not Available
Decomposition Temp (°F) | 493 | pH (as supplied) | Not Available
Autoignition Temp (°F) | Not Available | Vapour Pressure (mmHG) | Negligible
Upper Explosive Limit (%) | Not Available | Specific Gravity (water=1) | Not Available
Lower Explosive Limit (%) | Not Available | Relative Vapor Density (air=1) | Not Applicable
Volatile Component (%vol) | Negligible | Evaporation Rate | Not Applicable

**APPEARANCE**
White to off-white powder; mixes with water (1.8 gm/100 ml). Zwitterionic at physiological pH. Occurs as the sesquihydrate

### 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

**zanamivir**

#### TOXICITY AND IRRITATION

**ZANAMIVIR:**

- unless otherwise specified data extracted from RTECS - Register of Toxic Effects of Chemical Substances.
- Allergic-like reactions, including oropharyngeal oedema, serious skin rashes, and anaphylaxis have been reported

**Carcinogenesis, Mutagenesis, Impairment of Fertility**

Carcinogenesis: In 2-year carcinogenicity studies conducted in rats and mice using a powder formulation administered through inhalation, zanamivir induced no statistically significant increases in tumours over controls. The maximum daily exposures in rats and mice were approximately 23 to 25 and 20 to 22 times, respectively, greater than those in humans at the proposed clinical dose based on AUC comparisons.

Mutagenesis: Zanamivir was not mutagenic in in vitro and in vivo genotoxicity assays which included bacterial mutation assays in S. typhimurium and E. coli, mammalian mutation assays in mouse lymphoma, chromosomal aberration assays in human peripheral blood lymphocytes, and the in vivo mouse bone marrow micronucleus assay.

Reproductive toxicity: The effects of zanamivir on fertility and general reproductive performance were investigated in male (dosed for 10 weeks prior to mating, and throughout mating, gestation/lactation, and shortly after weaning) and female rats (dosed for 3 weeks prior to mating through Day 19 of pregnancy, or Day 21 post partum) at IV doses 1, 9, and 90 mg/kg/day. Zanamivir did not impair mating or fertility of male or female rats, and did not affect the sperm of treated male rats. The reproductive performance of the F1 generation born to female rats given zanamivir was not affected. Based on a subchronic study in rats at a 90 mg/kg/day IV dose, AUC values ranged between 142 and 199 mcghr/mL ( > 300 times the human exposure at the proposed clinical dose).

Developmental toxicity: Embryo/foetal development studies were conducted in rats (dosed from days 6 to 15 of pregnancy) and rabbits (dosed from days 7 to 19 of pregnancy) using the same IV doses (1, 9, and 90 mg/kg/day). Pre- and post-natal developmental studies were performed in rats (dosed from day 16 of pregnancy until litter day 21 to 23). No malformations, maternal toxicity, or embryotoxicity were observed in pregnant rats or rabbits and their foetuses. Because of insufficient blood sampling timepoints in rat and rabbit reproductive toxicity studies, AUC values were not available. In a subchronic study in rats at the 90 mg/kg/day IV dose, the AUC values were greater than 300 times the human exposure at the proposed clinical dose.

An additional embryo/foetal study, in a different strain of rat, was conducted using subcutaneous administration of zanamivir, 3 times daily, at doses of 1, 9, or 80 mg/kg during days 7 to 17 of pregnancy. There was an increase in the incidence rates of a variety of minor skeletal alterations and variants in the exposed offspring in this study. Based on AUC measurements, the 80 mg/kg dose produced an exposure greater than 1,000 times the human exposure at the proposed clinical dose. However, in most instances, the individual incidence rate of each skeletal alteration or variant remained within the background rates of the historical occurrence in the strain studied.

Zanamivir has been shown to cross the placenta in rats and rabbits. In these animals, fetal blood concentrations of zanamivir were significantly lower than zanamivir concentrations in the maternal blood.

### Section 12 - ECOLOGICAL INFORMATION

**Ecotoxicity**

<table>
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<tr>
<th>Ingredient</th>
<th>Persistence: Water/Soil</th>
<th>Persistence: Air</th>
<th>Bioaccumulation</th>
<th>Mobility</th>
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<td>zanamivir</td>
<td>No Data Available</td>
<td>No Data Available</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

No data
Section 13 - DISPOSAL CONSIDERATIONS

Disposal Instructions
All waste must be handled in accordance with local, state and federal regulations.
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
NOT REGULATED FOR TRANSPORT OF DANGEROUS GOODS: DOT, IATA, IMDG

Section 15 - REGULATORY INFORMATION
No data for zanamivir (CAS: , 139110-80-8)

Section 16 - OTHER INFORMATION

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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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