Entecavir

sc-204738

Material Safety Data Sheet

Hazard Alert Code Key:	EXTREME	HIGH	MODERATE	LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME
Entecavir

STATEMENT OF HAZARDOUS NATURE
CONSIDERED A HAZARDOUS SUBSTANCE ACCORDING TO OSHA 29 CFR 1910.1200.

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-H15-N5-O3.H2O, "[1S-(1alpha, 3alpha, 4beta)]-2-amino-1, 9-dihydro-9-[", 4-hydroxy-3-(hydroxymethyl)-2-methylenecyclopentyl, "]-6H-purin-6-one monohydrate", "EMS 200475-01", "SQ 34676", BMS-200475-01, "Hepatitis B API", Baraclude, "nucleoside analogue"

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS

		Min	Max
Flammability:	1		
Toxicity:	2		
Body Contact:	0		
Reactivity:	1		
Chronic:	3		

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

CANADIAN WHMIS SYMBOLS


EMERGENCY OVERVIEW

RISK
Harmful if swallowed.
Limited evidence of a carcinogenic effect.
May impair fertility.
May cause harm to the unborn child.
Harmful to aquatic organisms.

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED
■ Accidental ingestion of the material may be damaging to the health of the individual.
■ At sufficiently high doses the material may be hepatotoxic(i.
e.

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 either adverse health effects or irritation of the respiratory tract following inhalation (as classified using animal models).
Nevertheless, adverse 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.

CHRONIC HEALTH EFFECTS
■ There has been concern that this material can cause cancer or mutations, but there is not enough data to make an assessment.
Ample evidence exists from experimentation that reduced human fertility is directly caused by exposure to the material.
Ample evidence exists, from results in experimentation, that developmental disorders are directly caused by human exposure to the material.
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.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

NAME	CAS RN	%
entecavir	142217-69-4	>98

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 or hair contact occurs: · Flush skin and hair with running water (and soap if available). · Seek medical attention in event of irritation.

INHALED
· If fumes or combustion products are inhaled remove from contaminated area. · Other measures are usually unnecessary.

NOTES TO PHYSICIAN
■ Treat symptomatically.
A pre-placement physical examination and history for employees with potential exposure to this substance is recommended.. Base line testing would include: a blood test for liver function.
Based on the opportunity for exposure and duration of exposure, a periodic followup examination should be considered. This exam is overseen by a physician thoroughly knowledgeable about both the toxicity of the substance and the extent
of workplace exposure. It is recommended that the content be similar to the pre-placement exam.
Employees who are pregnant are breast-funding, or who are concerned with other reproductive issues should be encouraged to consult with the occupational physician responsible for monitoring the health of workers.

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 (CO_2), nitrogen oxides (NOx), other pyrolysis products typical of burning organic material.
May emit poisonous fumes.
Dusts which exhibit a Minimum Ignition Energy (MIE) above 100 mJ show a low sensitivity to ignition.
Minimum Ignition Energy MIE >500 mJ
Volume Resistivity (ambient) 1.7e13 ohm.m
Charge decay time (ambient) 33 minute
Material is highly susceptible to accumulating static charges during processing.
The material has low sensitivity to ignition as a dust cloud.

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
■ Observe manufacturer's storing and handling recommendations.

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS

The following materials had no OELs on our records

• entecavir: CAS:142217-69-4

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	277.28
Melting Range (°F)	460.4- 471.2	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)	Not Available	pH (as supplied)	Not Applicable
Autoignition Temp (°F)	Not Available	Vapour Pressure (mmHG)	Negligible
Upper Explosive Limit (%)	Not Available	Specific Gravity (water=1)	Not Available
Lower Explosive Limit (%)	Not Available	Relative Vapor Density (air=1)	Not Applicable
Volatile Component (%vol)	Negligible	Evaporation Rate	Not Applicable

APPEARANCE

White crystalline solid; mixes with water (2.2-3 g/l)

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

ENTECAVIR

TOXICITY AND IRRITATION

ENTECAVIR:

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

TOXICITY	IRRITATION
Oral (Rat) LD50: >1000 mg/kg *	
Oral (Mouse) LD50: >1000 mg/kg *	

Target organs include liver, spleen, thymus, prostate, muscle bone marrow, testes, lymph nodes, gastrointestinal tract, kidney, heart, lungs, pancreas,blood, embryo/ foetus.
LOAEL 2 week oral daily (rat): 20 mg/kg (males and females)
Effects included death, decreased body weight, decreased food consumption, increased urine volume, changes in red blood cell parameters, decreased white blood cell count, decreased platelets, decreased organ weights including thymus, spleen, prostate, uterus/ cervix.
LOAEL 6 months oral daily (rat): 0.02 mg/kg (males and females): microscopic changes were observed in liver centrilobular region, muscle.
NOAEL 2 weeks oral daily (dog): 1 mg/kg (males and females): effects included death, vomiting, decreased body weight, decreased food consumption, changes in clinical pathology parameters, decreased organ weights including testes. Microscopic changes were observed in the testes, bone marrow, lymph nodes, gastrointestinal tract, thymus, spleen, kidney.
LOAEL 3 month dietary daily (rat): 1 mg/kg (males and females): effects included decreased body weight, increase in blood cholesterol, death, increased platelets, changes in white blood cell parameters, decreased food consumption, gastrointestinal tract toxicity, degeneration of skeletal muscle, increased organ weights including spleen, decreased organ organ weights included testes, uterus/ cervix. Microscopic changes were observed in the gastrointestinal tract, thymus, lymph nodes, testes, heart, lungs, kidney, muscle, bone marrow, spleen.
LOAEL 3 months oral daily (dog): 0.3 mg/kg (males and females): effects included central nervous system toxicity, decreased body weigh, decreased food consumption, decreased white blood cell count, decreased platelets, decreased organ weights including testes, prostate, ovary.. Microscopic changes were observed in pancreas, testes, prostate, bone marrow, kidney, liver, lymph node.
NOAEL 1 year oral daily (monkey): 40 mg/kg (males and females) changes observed

in blood.

Genetic toxicity:

In vitro
Ames reverse-mutation assay - negative
Chromosome aberration test - positive
In vivo
Oral, mutagenicity (micronucleus test) (rat) - negative
Oral DNA repair assay (rat) - negative
Mutagenic assessment: did not show mutagenic effects in animals.

Carcinogenicity:

NOAEL 2 years oral (mouse): 0.4 mg/kg (males and females) tumour organs: lungs, cardiovascular, liver. Effects include increase in food consumption, death, decreased weight gain, decreased body weight. Effects considered species specific and may not be relevant for humans. The relevance for human risk assessment is unknown.
NOAEL 2 years oral (rat): 0.2 mg/kg (male and female) tumour organs: liver, brain, skin, uterus/ cervix. Effects included decreased body weight. Microscopic changes were observed in the following organs; pancreas, kidneys, testes.
Carcinogenicity Assessment: Limited evidence of carcinogenic potential.

Reproductive Toxicity:

NOAEL Oral Study of fertility and early embryonic development (rat): 1 mg/kg (males). Paternal effects include decreased body weight, decreased weight gain. No effects were found on mating or fertility. No effects were observed in the foetus/ embryo.
Assessment Reproductive Toxicity
No effects were found in mating or fertility. Substance may cause injury to male reproductive organs at high doses.
Developmental Toxicity
NOAEL Oral study of embryo-foetal development (rat): 2 mg/kg (embryo/ foetus females). Foetal effects include death, decreased body weight, malformations. Maternal effects include decreased body weight gain, decreased body weight, death, decreased food consumption, foetal changes. Teratogenic doses occur only at doses which also produce adverse effects in the maternal animal.
NOAEL Oral study of embryo/ foetal development (rabbit): 4 mg/kg (embryo/ foetus, females) Foetal effects include death, developmental delay, malformations. No adverse maternal effects were observed. Selective developmental toxicant.
NOAEL Oral study pre- and post- natal development (rat): 3 mg/kg (parent, females) Maternal effects include decreased weight gain. No effects were observed in the foetus/ membryo
Developmental Toxicity Assessments
Birth defects were observed in animal studies.
* Bristol-Myers Squibb MSDS

Section 12 - ECOLOGICAL INFORMATION

Harmful to aquatic organisms.

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

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

Section 15 - REGULATORY INFORMATION

No data for entecavir (CAS: , 142217-69-4)

Section 16 - OTHER INFORMATION

Reasonable care has been taken in the preparation of this information, but the author makes no warranty of merchantability or any other warranty, expressed or implied, with respect to this information. The author makes no representations and assumes no liability for any direct, incidental or consequential damages resulting from its use. For additional technical information please call our toxicology department on +800 CHEMCALL.

■ 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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