Material Safety Data Sheet

Developmental Therapeutics Program, DCT
National Cancer Institute
Executive Plaza North, Room 831
6130 Executive Boulevard
Rockville, Maryland 20852

NSC 339555

Revision Date: December 31, 1992

SECTION I. MATERIAL IDENTIFICATION

Common Name: BRYOSTATIN **CAS:** 83314-01-6
Chemical Name: Bryostatin I
Molecular Formula: $C_{47}H_{68}O_{17}$

Manufacturer: Program Resources, Inc.
Fermentation Production Facility
P.O. Box B
Frederick, Maryland 21701
(301) 846-1091 Emergency
(301) 846-1160 Information

SECTION II. INGREDIENTS AND HAZARDS

Ingredient Name	Percent	Exposure Limits
Bryostatin I - Crude organic extract of organism Bugula neritina	100%	NOT YET ESTABLISHED

Toxicity Data: EXTREMELY POWERFUL CYTOTOXIC AGENT.

RTECS Number: EH9455000

Bryostatin is currently undergoing clinical evaluation in studies sponsored by the National Cancer Institute. Preliminary results indicate the following.

A. Intravenous toxicity study in MFI strain mice.
LD_{50}: 0.075 mg/kg body weight; LD_{10}: 0.045 mg/kg body weight.

Observation of the acute toxicity of Bryostatin I showed that death occurred within a few hours of dosing, accompanied by lethargy and coldness. Post mortem findings showed that death was due to haemorrhage into the thoracic cavity and gastro-intestinal tract.

B. Intravenous toxicity study in Wistar rats.
LD_{50}: 0.068 mg/kg body weight; LD_{10}: 0.045 mg/kg body weight.

Following treatment with Bryostatin I most of the rats showed signs of lethargy, unsteady movement and in some cases haematuria which may have been due to the presence of ethanol in the dosing solutions. The majority of deaths occurred within one day of dosing with animals not recovering from the

lethargy and unsteady movement seen at the time of dosing. The significant histological findings were found in animals which died soon after treatment. The main findings in these animals were haemorrhage in the lung, muscle and thymus and perivascular oedema and intrmuscular fibrin deposition in the lung.

C. Repeat intravenous toxicity in MFI strain mice.
LD_{50}: 0.038 mg/kg; LD_{10}: 0.028 mg/kg.

Many mice became lethargic and in some cases had blood stained urine following treatment. At necropsy there were no abnormalities observed which could have been related to the treatment.

SECTION III. PHYSICAL DATA

Appearance & Odor: White powder. No noticeable odor.

MP: 230-235°C **BP:** UNKNOWN
Molecular Weight: 905
Solubility (%): Major solvent-ethyl acetate; minor solvents-methanol, water

SECTION IV. FIRE AND EXPLOSION DATA

Flash Point: UNKNOWN **Autoignition Temperature:** UNKNOWN
Flammability Limits: **LEL %:** UNKNOWN **UEL %:** UNKNOWN
Extinguishing Media: Use materials appropriate to the surrounding fire.

Unusual Fire or Explosion Hazards: Fire may produce irritating or poisonous gases.

Special Fire-fighting Procedures: Evacuate personnel to a safe area. Isolate hazard area and deny entry. Fire fighters should use protective clothing and self-contained breathing apparatus.

Hazardous Combustion Products: Since products of combustion are unknown, as a precaution they should be assumed to be hazardous.

SECTION V. REACTIVITY DATA

Compound Stability: Material is stable under most conditions. Hazardous polymerization is not known to occur.

Chemical Incompatibilities: No unusual chemical incompatibilities are known to exist.

Conditions To Avoid: Avoid exposing Bryostatin to heat.

Hazardous Decomposition Products: Since products of decomposition are unknown, as a precaution, they should be assumed to be hazardous.

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SECTION VI. HEALTH HAZARD INFORMATION

Summary of Risks: UNKNOWN
Primary Entry Routes: Inhalation, ingestion, and skin and/or eye contact.

Target Organs: UNKNOWN **Signs & Symptoms of Overexposure:** UNKNOWN

Acute Effects: UNKNOWN **Chronic Effects:** UNKNOWN

Medical Conditions Which May Be Aggravated By Contact: UNKNOWN

For Eye Contact: Immediately flush eyes with copious amounts of water for at least 15 minutes. Consult an ophthalmologist.

For Skin Contact: Remove contaminated clothing. Wash skin with plenty of soap and water. Consult a physician.

For Inhalation: Remove victim promptly to clean air. If victim is not breathing, administer artificial respiration. Consult a physician.

For Ingestion: Seek medical aid consistent with treatment of accidental injection of poisons.

Although acute and/or chronic effects associated with exposure to Bryostatin are unknown, Bryostatin is known to be a powerful cytotoxic agent.

SECTION VII. SPILL, LEAK AND DISPOSAL PROCEDURES

Spill/Leak Cleanup Procedures: Evacuate area. Wear self-contained breathing apparatus, rubber boots, and heavy rubber gloves. Wear disposable coveralls and discard after use. Avoid raising aerosols by promptly covering the spilled compound with paper towels that are wetted with a 10% solution of sodium hypochlorite. Pick up compound with additional towels, place in a bag, and hold for waste disposal. Expose the contaminated area to the bleach solution for one hour. Afterwards, first wipe the area with paper towels soaked in bleach solution and then with paper towels wet with water. Ventilate area after compound pick-up and decontamination is complete. Dispose of contaminated clean-up materials properly.

Waste Management/Disposal: Bleach decontamination/aqueous base (if using MeOH and EtOAc use >10%). Dispose of as hazardous waste. Incineration is the recommended method of disposal. Observe all federal, state, and local laws concerning the disposal of hazardous materials or waste.

Dissolve solids in a 10% solution of sodium hypochlorite. Add water miscible organic solvent to drug solutions and then treat with the bleach solution. Contaminated glassware, syringes, wipe-up materials, etc., should also be flushed with the bleach solution to reduce residues of toxic materials.

SECTION VIII. SPECIAL PROTECTION INFORMATION

Personal Protective Equipment:

Goggles: Wear chemical safety goggles when handling Bryostatin.
Gloves: Wear rubber or latex gloves when handling Bryostatin.
Respirator: Wear HEPA-type, NIOSH-MSHA approved respirator.
Other: Wear protective laboratory coat or apron.

Workplace Considerations:

Ventilation: Laboratory operations should be conducted in a chemical fume hood, glove box, or ventilated cabinet equipped with mechanical exhaust to the outside.
Safety Stations: Safety shower and eye bath should be accessible.

The personal protective equipment listed above should be worn at all times when handling Bryostatin. Avoid contact and inhalation. Avoid prolonged or repeated exposure. Wash thoroughly after handling.

SECTION IX. SPECIAL PRECAUTIONS

Storage Segregation: Store in tightly-sealed container at -10°C to -20°C. Use of a secondary containers is recommended.

Other Precautions: Wear protective clothing. Avoid contact with dust, mists, or aerosols. Wear approved respirator. Shower after handling. Carry out all manipulations under local exhaust. The user should be made aware that Bryostatin is an investigational substance. It is a highly potent cytotoxin. Handling as solids or solutions should be carried out with extreme care to avoid personal exposure. Hazards associated with exposure to Bryostatin may as yet be unknown. This material should be handled only be those trained in the handling of potentially hazardous material.

For Non-Emergency Information:

Decontamination Procedures 301-496-8780	Chief, Pharmaceutical Resources Branch
Material Safety Data Sheets 301-496-8795	Project Officer, Drug Synthesis And Chemistry Branch
Toxicity Data 301-496-8777	Chief, Toxicology Branch