M A T E R I A L S A F E T Y D A T A S H E E T

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

NSC 615291

Revision Date: December 10, 1992

SECTION I. MATERIAL IDENTIFICATION

Common Name: none **CAS:** 129655-21-6
Chemical Name: BIZELESIN (USAN)
Molecular Formula: $C_{43}H_{36}Cl_2N_8O_5$

Other Designations: U-77,779; CC-1065 analog; NSC 615291

SECTION II. INGREDIENTS AND HAZARDS

Ingredient Name	Percent	Exposure Limits
BIZELESIN	100%	NOT YET ESTABLISHED

Toxicity Data:

Animal Data: LD_{50} in mice is approximately 15 μg/kg as a single intravenous injection. The maximum tolerated dose in mice is 10 μg/kg as a single intravenous dose and 3 μg/kg as five daily doses with the toxicity being cumulative. Dose of 500 ng/kg in dogs is lethal, 100 ng/kg is highly toxic as a single intravenous dose. Deaths in these animal studies occurred 4 to 13 days after drug treatment. The deaths were due to myelosuppression or gastrointestinal toxicity.

The target organs of toxicity in both species are the gastrointestinal tract, bone marrow and lymphoid tissue. Toxicity is delayed following exposure.

Bizelesin is an extremely potent cytotoxin and a DNA damaging agent. Treatment with a 10% solution of sodium hypochlorite will cleave Bizelesin into two relatively nontoxic fragments.

SECTION III. PHYSICAL DATA

Appearance & Odor: Yellow powder

MP: 164.5 - 166.5°C **BP:** decomposes at 180°C
Molecular Weight: 815.72
Solubility (%): 1-2 μg/ml (water); soluble in polar, aprotic organic solvents (DMF, DMA, DMSO)

SECTION IV. FIRE AND EXPLOSION DATA

Flash Point: UNKNOWN **Autoignition Temperature:** UNKNOWN
Flammability Limits: **LEL %:** UNKNOWN **UEL %:** UNKNOWN

Extinguishing Media: Water, carbon dioxide, or dry chemical as appropriate to the surrounding fire.

Unusual Fire or Explosion Hazards: No unusual fire or explosion hazard is known to exist.

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

Hazardous Combustion Products: Thermal decomposition may yield carbon monoxide and other toxic substances. Since specific 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: Because it is an analog of CC-1065, this material is expected to be decomposed by acids, bases, light and air.

Conditions To Avoid: Light; plastic; alkaline pH; storage of aqueous suspensions

Hazardous Decomposition Products: Decomposition products from mild base may retain bioactivity. When, however, this material is exposed to acid, base, light and air, it is expected to pose no long term (>2-3 days) biological hazard.

SECTION VI. HEALTH HAZARD INFORMATION

Summary of Risks: The carcinogenicity and teratogenicity of Bizelesin are unknown. It is, however, very strongly mutagenic.

Primary Entry Routes: Inhalation, ingestion, and skin and/or eye contact.

Target Organs: The target organs of toxicity in animals are the lymphoid tissue, bone marrow and the gastrointestinal tract. Toxicity is delayed following exposure.

Medical Conditions Which May Be Aggravated By Contact: UNKNOWN

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Signs & Symptoms of Overexposure: The effects of overexposure to this drug in the workplace are not known. It is anticipated that acute or chronic overexposure would lead to damage of liver, kidney, lymphoid tissue, and possibly reproductive organs or would be fatal. Bizelesin is cytotoxic and will produce severe toxic effects to rapidly dividing tissues upon overexposure.

Acute Effects: UNKNOWN
Chronic Effects: 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. Chemically decontaminate clothing and then launder before reuse or incinerate.

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

For Ingestion: Remove residual drug. Consult a physician. Provide supportive treatment. No specific antidote exists.

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. Sodium hypochlorite will cleave Bizelesin into two relatively nontoxic fragments. 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: Incineration, at a temperature not less than 1000°C, is the recommended method of disposal. Observe all Federal, state, and local laws concerning the disposal of hazardous material 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 Bizelesin.
Gloves: Wear rubber or latex gloves, not polyvinylchloride, when handling Bizelesin.
Respirator: Wear NIOSH-MSHA approved respirator.
Other: Wear protective laboratory coat.

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 Bizelesin. Avoid contact and inhalation. Avoid prolonged or repeated exposure. Wash thoroughly after handling.

SECTION IX. SPECIAL PRECAUTIONS

Storage Segregation: Store in a tightly-closed container, protected from light, at -20°C. Use of a secondary container is recommended.

Other Precautions: The user should be made aware that Bizelesin 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 Bizelesin may as yet be unknown. This material should be handled only by 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
