U.S. Department
of Transportation
**Research and
Special Programs
Administration**

400 Seventh St., S.W.
Washington, D.C. 20590

APR 15 2004

Mr. Bruce H. Bale
Regulatory/Safety Manager
Molecular Probes, Inc.
4849 Pitchford Avenue
Eugene, OR 97402-9165

Reference No. 03-0107

Dear Mr. Bale:

This is in response to your letter and telephone conversation with a member of my staff asking how to properly classify and describe three fluorescent reagents under the Hazardous Materials Regulations (HMR; 49 CFR Parts 171-180). You describe the reagents as three naturally occurring toxins, phalloidin, phallacidin, and bungarotoxin covalently bonded to fluorescent molecules. Your company offers each product for transportation by aircraft as a dangerous good in excepted quantities and would like to described them as a "Toxic solid, organic, n.o.s., 6.1 (poisonous), UN 2811, PG I or PG II." Your questions are paraphrased and answered below in the order provided.

Q1. From our review of the published data on the toxins, it is our opinion that our solid fluorescent conjugates of these toxins would be appropriately assigned to Packing Group I or Packing Group II. Which is correct?

A1. As provided in § 173.22, it is the shipper's responsibility to properly classify a hazardous material. This Office does not perform that function. However, based on the information and toxicity data you provided, it is this Office's opinion that the classification for this material is, at a minimum, Class 6.1, Packing Group II.

Q2. If the appropriate assignment for the material is Packing Group I, it is our opinion that these reagents would not constitute an inhalation hazard in transport. Is that correct?

A2. It is this Office's opinion that the reagents do not meet the criteria in §173.133(a) for an inhalation hazard.under the HMR.

I hope this information is helpful.

Sincerely,

Hattie L. Mitchell

Hattie L. Mitchell, Chief
Regulatory Review and Reinvention
Office of Hazardous Materials Standards

030107

173.133

Edmonson
§172.101
§173.133
Packing Group

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03-0107

April 17, 2003

Edward T. Mazzullo
US Department of Transportation
Research and Special Program Administration
Office of Hazardous Materials Standards
DHM-10
400 7th St., S.W.
Washington, DC 20590-0001

Dear Mr. Mazzullo,

This morning I spoke with Dr. George Cushmac at the Office of Hazardous Materials Technology and he recommended that I submit my questions to your office to obtain a written interpretation.

Under the Research and Development exemption of TSCA, our company manufactures extremely small quantity, high-purity fluorescent reagents for biochemical research. We sell and distribute approximately 2,500 products worldwide under International Air Transport Regulations (IATA).

A few of these products, the focus of this letter, are fluorescent conjugates of three naturally occurring toxins, phalloidin, phallacidin, and bungarotoxin. Essentially, we covalently bond fluorescent molecules to the toxins. The resulting reagents retain useful properties of the parent toxin while enabling researchers to visualize and quantify them using fluorescence technology. For safety purposes, we conservatively assume that these reagents are toxic.

We sell these products as solids in 1 mg units. We are experienced in safely shipping by air "dangerous goods in excepted quantities." We would like to ship these materials as Toxic solids, organic, n.o.s., UN2811, 6.1. To do that, we need to assign the appropriate Packing Group for these reagents and there is no specific health hazard data available for them. There is toxicological data in the open literature for the toxins. In our conversation today, Dr. Cushmac explained that correlations are made from such data to distinguish between the Packing Groups.

From our review of the published data on the toxins, it is our opinion that our solid fluorescent conjugates of these toxins would be appropriately assigned to:

Packing Group I, or
Packing Group II

1. Which group is correct?

Also, if the appropriate assignment is Packing Group I, it is our opinion that these reagents <u>would not</u> constitute an inhalation hazard in transport.

2. Is that correct?

I am including copies of the references on published health hazard assessments for each of the three toxins. These references were obtained from the Registry of Toxic Effects of Chemical Substances published by the National Institutes of Occupational Safety and Health.

I look forward to your response. Please feel free to contact me at my office at 541-465-8333 if you require any further information.

Thank you.

Sincerely,

Bruce H. Bale
Regulatory/Safety Manager

Encl.

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* R T E C S (R) *
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* Supplied by : MDL Information Systems, Inc. *
* Provided by : Canadian Centre for Occupational Health and Safety *
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*** CHEMICAL IDENTIFICATION ***

RTECS NUMBER : EL6100500
CHEMICAL NAME :
Bungarotoxin
CAS REGISTRY NUMBER : 37209-28-2
LAST UPDATED : 199703
DATA ITEMS CITED : 1
COMPOUND DESCRIPTOR : Natural Product

*** HEALTH HAZARD DATA ***

** ACUTE TOXICITY DATA **

TYPE OF TEST : LD50 - Lethal dose, 50 percent kill
ROUTE OF EXPOSURE : Intraperitoneal
SPECIES OBSERVED : Rodent - mouse
DOSE/DURATION : 100 ug/kg
TOXIC EFFECTS :
Details of toxic effects not reported other than lethal dose value
REFERENCE :
TOXIA6 Toxicon. (Pergamon Press Ltd., Headington Hill Hall, Oxford OX3 OBW, UK) V.1- 1962- Volume(issue)/page/year: 10,227,1972

*** END OF RECORD ***

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* R T E C S(R) *
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* Supplied by : MDL Information Systems, Inc. *
* Provided by : Canadian Centre for Occupational Health and Safety *
* Issue : 2002-4 (November, 2002) *

*** CHEMICAL IDENTIFICATION ***

RTECS NUMBER : GT8943000
CHEMICAL NAME :
cyclic(L-Alanyl-2-mercapto-L-tryptophyl-4,5-dihydroxy-L-leucyl-L-valyl-ery thro-3-hydroxy-D-alpha-aspartyl-L-cysteinyl-cis-4-hydroxy-L-prolyl) cyclic (2-6)-sulfide
CAS REGISTRY NUMBER : 26645-35-2
BEILSTEIN REFERENCE NO. : 0604129
LAST UPDATED : 199612
DATA ITEMS CITED : 2
MOLECULAR FORMULA : C37-H50-N8-O13-S
MOLECULAR WEIGHT : 847.01
SYNONYMS/TRADE NAMES :
* Phallacidin

*** HEALTH HAZARD DATA ***

** ACUTE TOXICITY DATA **

TYPE OF TEST : LD50 - Lethal dose, 50 percent kill
ROUTE OF EXPOSURE : Intraperitoneal
SPECIES OBSERVED : Rodent - mouse
DOSE/DURATION : 2 mg/kg
TOXIC EFFECTS :
Details of toxic effects not reported other than lethal dose value
REFERENCE :
CRBCAI CRC Critical Reviews in Biochemistry. (CRC Press, Inc., 2000 Corporate Blvd., NW, Boca Raton, FL 33431) V.1- 1972- Volume(issue)/page/year: 5,185,1978

TYPE OF TEST : LD50 - Lethal dose, 50 percent kill
ROUTE OF EXPOSURE : Unreported
SPECIES OBSERVED : Rodent - mouse
DOSE/DURATION : 2500 ug/kg
TOXIC EFFECTS :
Details of toxic effects not reported other than lethal dose value
REFERENCE :
ARZNAD Arzneimittel-Forschung. Drug Research. (Editio Cantor Verlag, Postfach 1255, W-7960 Aulendorf, Fed. Rep. Ger.) V.1- 1951- Volume(issue)/page/year: 22,2142,1972

*** END OF RECORD ***

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 * Supplied by : MDL Information Systems, Inc.
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 * Provided by : Canadian Centre for Occupational Health and Safety
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2002) *
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*** CHEMICAL IDENTIFICATION ***

RTECS NUMBER : SE9800000
CHEMICAL NAME :
Phalloidin
CAS REGISTRY NUMBER : 17466-45-4
OTHER CAS REGISTRY NOS. : 63-24-1
BEILSTEIN REFERENCE NO. : 4347460
LAST UPDATED : 200003
DATA ITEMS CITED : 10
MOLECULAR FORMULA : C35-H48-N8-O11-S
MOLECULAR WEIGHT : 788.97
COMPOUND DESCRIPTOR : Mutagen
Natural Product
SYNONYMS/TRADE NAMES :
* Phalloidine

*** HEALTH HAZARD DATA ***

** ACUTE TOXICITY DATA **

TYPE OF TEST : LDLo - Lowest published lethal dose
ROUTE OF EXPOSURE : Intraperitoneal
SPECIES OBSERVED : Rodent - rat
DOSE/DURATION : 1 mg/kg
TOXIC EFFECTS :
Details of toxic effects not reported other than lethal dose value
REFERENCE :
TOXIA6 Toxicon. (Pergamon Press Ltd., Headington Hill Hall, Oxford OX3 OBW, UK) V.1- 1962- Volume(issue)/page/year: 10,357,1972

TYPE OF TEST : LD50 - Lethal dose, 50 percent kill
ROUTE OF EXPOSURE : Intraperitoneal
SPECIES OBSERVED : Rodent - mouse
DOSE/DURATION : 2 mg/kg
TOXIC EFFECTS :
Details of toxic effects not reported other than lethal dose value
REFERENCE :
NEJMAG New England Journal of Medicine. (Massachusetts Medical Soc., 10 Shattuck St., Boston, MA 02115) V.198- 1928- Volume(issue)/page/year: 269,223,1963

TYPE OF TEST : LDLo - Lowest published lethal dose
ROUTE OF EXPOSURE : Intravenous
SPECIES OBSERVED : Rodent - mouse
DOSE/DURATION : 6600 ug/kg

TOXIC EFFECTS :
Behavioral - muscle weakness
Liver - fatty liver degeneration
REFERENCE :
AEPPAE Naunyn-Schmiedeberg's Archiv fuer Experimentelle Pathologie und Pharmakologie. (Berlin, Ger.) V.110-253, 1925-66. For publisher information, see NSAPCC. Volume(issue)/page/year: 190,406,1938

TYPE OF TEST : LD50 - Lethal dose, 50 percent kill
ROUTE OF EXPOSURE : Unreported
SPECIES OBSERVED : Rodent - mouse
DOSE/DURATION : 2 mg/kg
TOXIC EFFECTS :
Details of toxic effects not reported other than lethal dose value
REFERENCE :
ARZNAD Arzneimittel-Forschung. Drug Research. (Editio Cantor Verlag, Postfach 1255, W-7960 Aulendorf, Fed. Rep. Ger.) V.1-1951- Volume(issue)/page/year: 22,2142,1972

TYPE OF TEST : LD - Lethal dose
ROUTE OF EXPOSURE : Intravenous
SPECIES OBSERVED : Mammal - dog
DOSE/DURATION : >10 mg/kg
TOXIC EFFECTS :
Details of toxic effects not reported other than lethal dose value
REFERENCE :
ARTODN Archives of Toxicology. (Springer-Verlag, Heidelberger Pl. 3, D-1000 Berlin 33, Fed. Rep. Ger.) V.32- 1974- Volume(issue)/page/year: 48,61,1981

TYPE OF TEST : LDLo - Lowest published lethal dose
ROUTE OF EXPOSURE : Oral
SPECIES OBSERVED : Mammal - species unspecified
DOSE/DURATION : 1000 ug/kg
TOXIC EFFECTS :
Details of toxic effects not reported other than lethal dose value
REFERENCE :
CTOXAO Clinical Toxicology. (New York, NY) V.1-18, 1968-81. For publisher information, see JTCTDW. Volume(issue)/page/year: 17,45,1980

** OTHER MULTIPLE DOSE TOXICITY DATA **

TYPE OF TEST : TDLo - Lowest published toxic dose
ROUTE OF EXPOSURE : Intraperitoneal
SPECIES OBSERVED : Rodent - rat
DOSE/DURATION : 2500 ug/kg/5D-I
TOXIC EFFECTS :
Liver - other changes
REFERENCE :
JOGAET Journal of Gastroenterology. (Japanese Society of Gastroenterology, Ginza Orient BLDG, 9-13 Ginza 8, Chuo-ku, Tokyo 104 Japan) V.29- 1994- Volume(issue)/page/year: 29,172,1994

TYPE OF TEST : TDLo - Lowest published toxic dose
ROUTE OF EXPOSURE : Intraperitoneal
SPECIES OBSERVED : Rodent - rat
DOSE/DURATION : 3500 ug/kg/7D-I

TOXIC EFFECTS :
Liver - jaundice, cholestatic
Liver - other changes
Liver - changes in liver weight
REFERENCE :
GASTAB Gastroenterology. (Academic Press, Inc., 1 E. First St., Duluth, MN 55802) V.1- 1943- Volume(issue)/page/year: 75,450,1978

** MUTATION DATA **

TYPE OF TEST : Morphological transformation
TEST SYSTEM : Rodent - rat Liver
DOSE/DURATION : 1 umol/L
REFERENCE :
CYTZAM Cytobiologie. (Stuttgart, Fed. Rep. Ger.) V.1-18, 1969-79. For publisher information, see EJCBDN. Volume(issue)/page/year: 17,73,1978

TYPE OF TEST : DNA inhibition
TEST SYSTEM : Rodent - rat Liver
DOSE/DURATION : 100 nmol/L
REFERENCE :
TOXIA6 Toxicon. (Pergamon Press Ltd., Headington Hill Hall, Oxford OX3 OBW, UK) V.1- 1962- Volume(issue)/page/year: 25,1265,1987

*** END OF RECORD ***