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U.S. Army  
Environmental Hygiene  
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PHASE 1  
ACUTE TOXICITY  
PRELIMINARY ASSESSMENT OF THE RELATIVE TOXICITY  
OF 1,5-DIAZIDO-3-NITRAZAPENTANE  
STUDY NO. 75-51-0856-92  
JANUARY 1989 - FEBRUARY 1992

92-15190

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DEPARTMENT OF THE ARMY  
 U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY  
 ABERDEEN PROVING GROUND, MARYLAND 21010-5422



REPLY TO  
 ATTENTION OF

**EXECUTIVE SUMMARY**  
**PHASE 1**  
**ACUTE TOXICITY**  
**PRELIMINARY ASSESSMENT OF THE RELATIVE TOXICITY**  
**OF 1,5-DIAZIDO-3-NITRAZAPENTANE**  
**STUDY NO. 75-51-0856-92**  
**JANUARY 1989 - FEBRUARY 1992**

1. **GENERAL.** A Preliminary Assessment of the Relative Toxicity of 1,5-Diazido-3-Nitrazapentane (DANPE) was completed in February 1992. The report is enclosed.

2. **ESSENTIAL FINDINGS.** The DANPE is fairly toxic by dermal absorption and by ingestion. The compound has no potential for causing sensitization. The DANPE exhibited increases in chromosomal aberrations and a positive mutagenic response in cell culture.

3. **RECOMMENDATIONS.** The following paragraphs are recommendations based on professional scientific judgment:

a. Conduct further toxicological studies with DANPE in support of the requirement to provide data in establishing guidelines to the occupational health physician for safe workplace conditions.

b. Use extreme caution to prevent DANPE from coming into contact with the skin since studies indicate this material is an effective skin penetrant. In the event of skin contamination, flush immediately with large volumes of water. Abrasive soap may increase absorption through the skin.

c. Protective clothing should be worn by workers when contact is possible and splash guards should prevent splashing onto people or onto equipment that people handle. Work clothing should be changed if it becomes contaminated with DANPE.



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DEPARTMENT OF THE ARMY  
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY  
ABERDEEN PROVING GROUND, MARYLAND 21010-8422



REPLY TO  
ATTENTION OF

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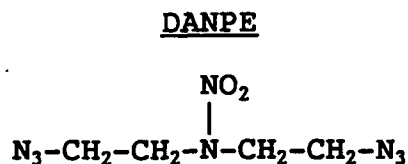
PHASE 1  
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PRELIMINARY ASSESSMENT OF THE RELATIVE TOXICITY  
OF 1,5-DIAZIDO-3-NITRAZAPENTANE  
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1. REFERENCES. See Appendix A for a list of references.
2. AUTHORITY. Memorandum, 1st End, AMC, 31 Oct 88, AMCSG-I, subject: Toxicity Study.
3. PURPOSE. Studies were conducted to obtain information concerning the potential health hazards associated with the use of 1,5-Diazido-3-Nitrazapentane (DANPE). The results will provide information on possible target organs/systems, establish a dose-response order of toxicity for DANPE, and aid the occupational health physician in establishing preliminary guidelines for safe workplace conditions.
4. BACKGROUND. The DANPE, a flammable liquid, is of interest to the U.S. Army for use as an energetic plasticizer in low vulnerability ammunition (LOVA). It generally is present at levels between 5 and 10 percent. The DANPE is unique in its ability to impact good physical parameters to LOVA propellants. No referenced toxicology information on this material was found in searches performed on the National Library of Medicine's Toxicology data network as listed in the Hazardous Substances Databank and in the Registry of Toxic Effects of Chemical Substances (RTECS).

Use of trademarked names does not imply endorsement by the U.S. Army but is intended only to assist in identification of a specific product.

5. MATERIALS.

a. The DANPE has a slightly irritating odor because of its solvent, ethyl acetate. The sample of DANPE (Lot No. 2316-C) with a stated concentration of 37 percent was received from Ballistics Research Laboratories, Aberdeen Proving Ground, Maryland. The batch sample was analyzed using the Digilab® FTS-15/90 Fourier Transform Infrared Spectrometer filtered with a Mercury Cadmium Telluride detector (Appendix B). See Appendix B for its reference material spectra. The chemical structure of DANPE is as follows:



b. Ethyl acetate is fairly nontoxic and because of its characteristic fruity odor and pleasant taste when diluted, it is primarily used as fruit essences. Pertinent information regarding the mutagenicity, teratogenicity and carcinogenicity was not located in the Integrated Risk Information System.

c. This report and data generated in these studies are stored in the Toxicology Division's files, which are located in the basement of Building 1570, Edgewood Area, Aberdeen Proving Ground, Maryland 21010-5422.

6. ANIMALS.

a. The studies reported were performed with groups of rabbits, rats, and guinea pigs housed in animal facilities fully accredited by the American Association for the Accreditation of Laboratory Animal Care.

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b. Testing for primary skin and eye irritation, and short-term repeated dermal toxicity was conducted using New Zealand White rabbits from Hazleton Research Products, Inc., Denver, Pennsylvania. Albino-Hartley guinea pigs, also from Hazleton Research Products, Inc., were used for sensitization studies. Sprague-Dawley rats from Charles River Laboratories, Wilmington, Massachusetts, were used for oral toxicity testing of the compound.

#### 7. CONTRACT STUDIES.

a. An In Vitro Mutagenicity evaluation of subject compound was performed by means of an Ames/Salmonella plate Mutation Assay and Chinese Hamster Ovary Cells by Integrated Laboratory Systems (ILS), Research Triangle Park, North Carolina, under ILS Project No. A028.\*

b. An In Vitro Bioassay (Sencar Mouse) under Contract No. DAAD-05-89-C-0045 was performed by ILS.\*

c. A dominant lethal study in mice was performed by Omni Research Inc., Baltimore, Maryland, under Contract No. DAAD-05-87-C-0095.\*

d. Acute toxicity testing with DANPE to Bluegill Sunfish, to Rainbow Trout and to Daphnia was performed by Springborn Laboratories, Inc. (SLI), Wareham, Massachusetts, under SLI Report Nos. 90-9-3495, 90-11-3538, and 90-9-3470, respectively.\*

e. A 21-day Acute oral LD<sub>50</sub> study in Bobwhite Quail, an 8-day Acute Dietary LC<sub>50</sub> Study in Bobwhite Quail, and a 9-day Acute Dietary LC<sub>50</sub> Study in Mallard Ducklings was performed by Bio-Life Associates, LTD, Neillsville, Wisconsin.\*

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\* In conducting the studies described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals," U.S. Department of Health, Education and Welfare Publication No. NIH 86-23, 1985.

## 8. METHODS.

a. Skin Irritation. The standard Draize method was utilized to detect the dermal toxic response of a single application of DANPE on the skin of albino rabbits. All hair was clipped from the backs and sides of the animals 24 hours prior to exposure. One-half milliliter of material was applied for a single 24-hour period under a porous gauze patch to the intact and abraded skin of six rabbits. The patches were held in place with surgical adhesive tape and the entire shaved area was covered with a self-adhesive wrap of Coban®. After 24 hours, the wrap and patches were carefully removed; excess material was wiped from the skin; and the test areas were evaluated for irritation. Evaluations were also performed at 72-hour and 7-day intervals. Scoring of irritation effects was based on the Draize method in which erythema and edema were evaluated on a grade of 0 to 4 for severity (Appendices C, D and E).

b. Eye Irritation. A standard Draize test was performed to determine the effect of a single 0.1 mL solution of DANPE and its solvent, ethyl acetate, in one eye of six rabbits each. The other eye, remaining untreated, served as a control. Eyes were examined for gross signs of irritation at 24, 48, 72 hours and 7-day intervals following application. Scoring of irritation was based on the Draize method in which the total score for the eye is the sum of all scores obtained for the cornea, iris, and conjunctiva (Appendices C, D, and E). No gross pathology or histopathology was performed.

c. Sensitization. Sensitization studies were performed to determine the potential of the compound for causing sensitization reactions in humans. Female Hartley guinea pigs weighing between 375 and 425 grams were used for all tests. The test procedure was based on the Buehler technique and was conducted with 10 guinea pigs having 0.3 mL of compound was applied to an occlusive patch which in turn was placed on their backs for a 6-hour exposure time once a week for 3 weeks. They were rested for 2 weeks, then rechallenged to determine if any sensitization had occurred. A positive control, dinitrochlorobenzene (DNCB) at 0.1 percent (w/v) in 80 percent ethanol, was run concurrently with the test compound. The skin responses were scored at 24 and 48 hours post challenge by the Draize method of scoring (Appendices C, D, and E).

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®Coban is a registered tradename of the Minnesota Mining and Manufacturing Co., St. Paul, Minnesota.

d. Acute Toxicity Studies. Acute toxicity studies were performed to determine the adverse effects occurring within a short period of time following a single dose of a substance. This type of study identifies the relative toxicity of a compound, investigates its mode of action and specific toxic effect, and determines the existence of species differences. In the present study, single doses of the compound were administered to male and female rats by gavage, intraperitoneal injection, and to male and female rabbits by skin application in order to determine the Approximate Lethal Dose (ALD) for this compound. A 14-day observation period was used to observe death or clinical signs. Animals were weighed at 1, 3, 7, and 14-day intervals after exposure. All survivors were euthanized at 14 days and submitted for gross necropsy.

e. In Vitro Mutagenicity Assay. The DANPE chemical was evaluated for mutagenic activity in the Ames Salmonella/Microsome Plate assay. The Ames test was used with Salmonella typhimurium indicator strains TA-100, TA-1535, TA-1537, TA-1538, and TA-98. The assays were conducted in duplicate in the presence and absence of metabolic activation. The assays were conducted at doses which had been selected on a preliminary toxicity test with the strain TA-100. For the actual assay, doses were selected with the highest doses exhibiting  $\leq 90$  percent toxicity and ranged over a series of six doses from 0.005  $\mu\text{L}/\text{plate}$  to 10  $\mu\text{L}/\text{plate}$  (reference 2).

## 9. RESULTS.

a. Primary Dermal Irritation Studies. A group of six female rabbits was used to determine the primary dermal irritation to intact and abraded skin of ethyl acetate and ethyl acetate DANPE solution. No erythema, edema, or necrosis was observed in any of the rabbits upon examination following 24-hour dermal contact with DANPE or its solvent ethyl acetate. Subsequent observations at 72-hour and 7-day intervals were negative in all respects. The Draize scoring system was used for the evaluation of skin reactions (Appendices C, D, and E). The U.S. Environmental Protection Agency (EPA) hazard indicator index placed these skin responses in grade IV (Appendix F).

b. Eye Irritation. Very mild conjunctival redness was observed in the eyes of rabbits treated with DANPE (Lot No. 2316-C). Similar conjunctival redness was present in rabbit eyes treated with the solvent ethyl acetate. None of the rabbits showed any inflammation or irritation of the iris or the cornea. All of the mild irritative effects of the two samples were resolved within 72 hours following treatment.

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c. Sensitization. Guinea pigs were challenged with the DANPE and ethyl acetate solvent 2 weeks after the third sensitization induction treatment. None of the animals displayed any signs of sensitization to the test agents (i.e., no erythema or edema was present on the challenge sites at 24 and 48 hours). Concurrent studies with the positive control DNCB showed a marked sensitization response of eight out of ten guinea pigs.

d. Acute Studies. Tabular presentation of the oral, intraperitoneal and dermal approximate lethal values follows:

TABLE 1. ACUTE LETHAL STUDIES

Sex	ALD mg/kg	Lot No.
<u>Oral Administration of DANPE/Ethyl Acetate</u>		
Male rats	1,498	2316-C
Female rats	617	2316-C
Female guinea pigs	5,824	2316-C
<u>Intraperitoneal Administration of DANPE/Ethyl Acetate</u>		
Male rats	653	2316-C
Female rats	603	2316-C
<u>Dermal Administration of DANPE/Ethyl Acetate</u>		
Male Rabbits	2,129	2316-C
Female Rabbits	3,192	2316-C
<u>Oral Administration of Ethyl Acetate</u> J.T. Baker 44066		
Male Rats	>3,333	
Female Rats	>3,333	
<u>Intraperitoneal Administration of Ethyl acetate</u>		
Male Rats	1,400	
Female Rats	2,222	

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TABLE 2. ACUTE TOXICITY RESPONSES OF VARIOUS COMPOUNDS

	Rabbit		Rat	
	LD <sub>50</sub> (mg/kg)		LD <sub>50</sub> (mg/kg)	
Han (Hydroxylammonium Nitrate)	Oral ALD	101	Male oral	882
	Dermal	70	Female oral	520
Malathion	Dermal	4,100	Male oral	290
Benzene	Dermal	500	Male oral	4,900
Deet	Dermal	3,180	Male oral	1,950
DANPE			Male oral ALD	1,498
			Female oral ALD	617

e. Contract Studies.

(1) In Vitro Mutagenicity evaluation with an Ames/Salmonella plate assay test system indicated a positive mutagenic response in strains TA100 and TA1535 both with and without metabolic activation (reference 2).

(2) Cytogenetic testing of DANPE employing the rodent bone marrow micronucleus assay in male B6C3F1 mice concluded: Multiple treatment with DANPE caused a small but significant increase in MN-PCE frequency without significantly depressing the percent of PCE (reference 3).

(3) Mouse Lymphoma Mutagenesis Assay on DANPE: The results indicate that, under the conditions of these mutagenicity tests, DANPE showed a negative response in the absence of exogenous metabolic activation and an equivocal response in the presence of exogenous metabolic activation (reference 4).

(4) In Vitro Cytogenetic testing on DANPE employing the Chromosome Aberration Assay in Chinese Hamster Ovary (CHO) Cells concluded: In the presence but not the absence of metabolic activation, treatment with DANPE induced a significant increase in chromosomal aberrations in CHO cells (reference 5).

(5) Dominant lethal effects of DANPE in mice were negative (reference 6).

(6) In Vitro Mutagenicity test on ethyl acetate employing the Ames/Salmonella Plate Assay Test System indicated a lack of mutagenic activity in all five bacterial strains both with and without metabolic activation. The test sample was evaluated for mutagenic activity in the salmonella typhimurium plate incorporation assay with five tester strains. The sample was tested directly and in the presence of liver homogenates (S9 fraction) from rats treated with Aroclor® 1254 (reference 7).

(7) Dominant lethal effects of ethyl acetate were negative (reference 8).

(8) The 8-Day Acute Dietary LC<sub>50</sub> Study in Bobwhite Quail resulted in a No-Observed-effect level of 625 ppm a.i.† The 8-day acute dietary LC<sub>50</sub> was determined to be 2,975 ppm a.i. with 95 percent confidence limits of 2,479 to 3,570 ppm a.i. (reference 9).

(9) The 9-Day Acute Dietary LC<sub>50</sub> Study in Mallard Ducklings resulted in a No-Observed-effect level to be 312 ppm a.i. The 9-day acute dietary LC<sub>50</sub> was determined to be 2,370 ppm a.i. with 95 percent confidence limits of 508 to 1,601 ppm a.i. (reference 10).

(10) The 21-Day Acute Oral LD<sub>50</sub> Study in Bobwhite Quail resulted in a No-Observed-effect level to be less than 316 mg a.i./kg body weight. The 21-day acute oral median lethal dose was determined to be 860 mg a.i./kg of body weight with 95 percent confidence limits of 723 to 1,023 mg a.i./kg of body weight (reference 11).

(11) The DANPE-Acute toxicity to Bluegill Sunfish (*Lepomis Macrochirus*) under static conditions resulted in a 96-hour LC<sub>50</sub> value by nonlinear interpolation to be 67 mg a.i./L with a 95 percent confidence interval calculated by binomial probability of 36-100 mg a.i./L. The No-Observed-effect concentration established for this study was 22 mg a.i./L (reference 12).

(12) In Vitro Skin Bioassay (Sencar Mouse), contract No. DAAD05-89-0045, demonstrated DANPE negative when administered as an initiator for an increased incidence of skin tumor formation (reference 13).

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®Aroclor is a tradename of the Monsanto Company, St. Louis, Missouri.

† Active ingredient of compound.

10. DISCUSSION.

a. The purpose of these studies was to obtain information concerning the potential health hazards associated with the use of the liquid propellant DANPE. The results from the acute oral studies show the ALD of DANPE (617 mg/kg) falls in the EPA Hazard Indicator toxicity category of three. Its container should have on the front panel the signal word "Caution."

b. A review of the results from the acute studies show that DANPE is fairly toxic by ingestion and by dermal absorption. The compound has no potential for causing skin sensitization or eye irritation. The DANPE did exhibit increases in chromosomal aberrations in CHO cells and a positive mutagenic response in cell culture.

c. The toxic responses in animals caused by administration of the DANPE compound can be placed in perspective by comparison with responses from other well known compounds. The compounds used for comparison were Han, Malathion, Benzene, and Deet. The data on these four compounds were obtained from the RTECS file in the National Library of Medicine except for Han in Table 2. The comparisons demonstrate that DANPE falls in severity between Han and Deet.

e. Additional studies involving DANPE are to be conducted at this Agency. These studies include a preliminary 14-day feeding study with male and female rats and a 90-day dermal application study with male and female rabbits.

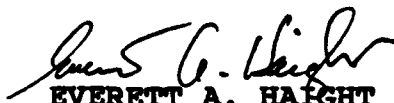
11. RECOMMENDATIONS. The following paragraphs are based on professional scientific judgment:

a. Continue chronic and subchronic toxicity studies listed in paragraph 10e in support of the tasking authorization.

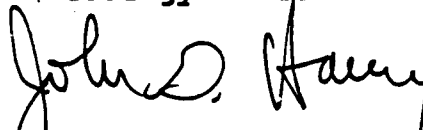
b. Extreme caution should be taken to prevent DANPE from coming into contact with the skin since studies indicate that this material is an effective skin penetrant. In the event of skin contamination, flush immediately with large volumes of water. Abrasive soap may increase absorption through the skin.

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c. Protective clothing should be worn by workers when contact is possible and splash guards should prevent splashing onto people or onto equipment that people handle. Work clothing should be changed if it becomes contaminated with DANPE.



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MAURICE H. WEEKS  
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APPENDIX A

REFERENCES

1. Title 40, Code of Federal Regulations (CFR), 1990 rev., Part 160, Good Laboratory Practice Standards.
2. Report, In Vitro Mutagenicity Test on DANPE Employing the Ames/Salmonella Plate Assay Test System, Integrated Laboratory Systems, P.O. Box 13501, Research Triangle Park, North Carolina 27709.
3. Report, Cytogenetic Testing on DANPE Employing the Rodent Bone Marrow Micronucleus Assay in Male B6C3F1 Mice, Integrated Laboratory Systems, P.O. Box 13501, Research Triangle Park, North Carolina 27709.
4. Report, Mouse Lymphoma Mutagenesis Assay on DANPE, Integrated Laboratory Systems, P.O. Box 13501, Research Triangle Park, North Carolina 27709.
5. Report, In Vitro Cytogenetic Testing on DANPE Employing the Chromosome Aberration Assay in Chinese Hamster Ovary Cells, Integrated Laboratory Systems, P.O. Box 13501, Research Triangle Park, North Carolina 27709.
6. Report, Determination of the Acute Oral LD<sub>50</sub> and Dominant Lethal Effects of DANPE in Mice, Omni Research Inc., 1501 Sulgrave Ave., Suite 200, Baltimore, Maryland 21209.
7. Report, In Vitro Mutagenicity Test of Ethyl Acetate Employing the Ames/Salmonella Plate Assay Test System, Integrated Laboratory Systems, P.O. Box 13501, Research Triangle Park, North Carolina 27709.
8. Report, Determination of the Acute Oral Approximate Lethal Dose and Dominant Lethal Effects of Ethyl Acetate in Mice, Omni Research Inc., 1501 Sulgrave Ave., Suite 200, Baltimore, Maryland 21209.
9. Report, DANPE: 8-Day Acute Dietary LC<sub>50</sub> Study in Bobwhite Quail, Bio-Life Associates LTD., Route 3, Box 156, Neillsville, Wisconsin 54456.

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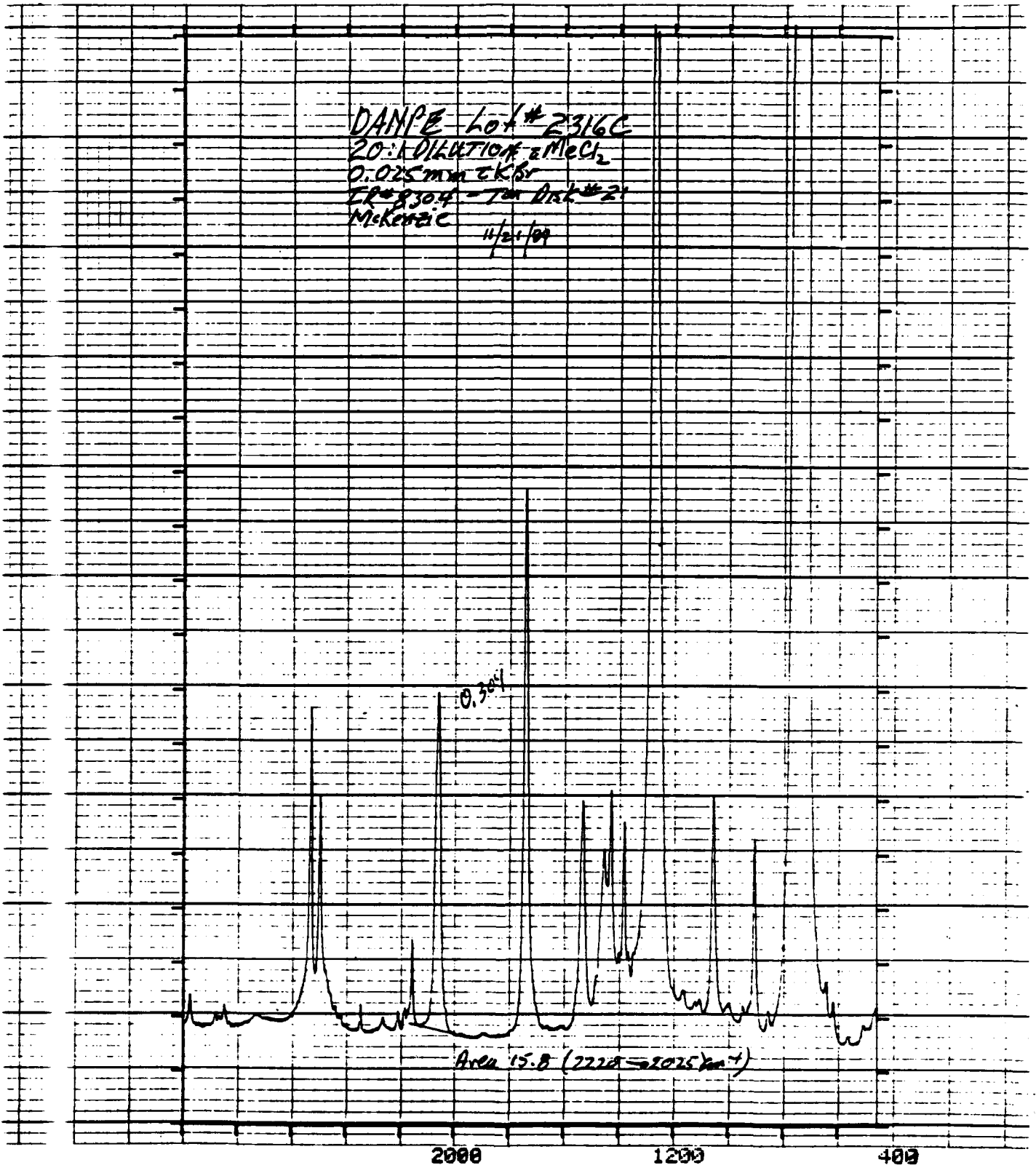
10. Report, DANPE: 9-Day Acute Dietary LC<sub>50</sub> Study in Mallard Ducklings, Bio-Life Associates LTD., Route 3, Box 156, Neillsville, Wisconsin 54456.
11. Report, DANPE: 21-Day Acute Oral LD<sub>50</sub> Study in Bobwhite Quail, Bio-Life Associates LTD., Route 3, Box 156, Neillsville, Wisconsin 54456.
12. Report, DANPE - Acute Toxicity to Bluegill Sunfish (*Lepomis Macrochirus*) Under Static Conditions, Springborn Laboratories, Inc., Environmental Sciences Division, 790 Main Street, Wareham, Massachusetts 02571.
13. Report, DANPE - "In Vitro Skin Bioassay (Sencar Mouse)", Pathology Associates Inc., 6217 Centre Park Drive, West Chester, Ohio 45069-3866.

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APPENDIX B

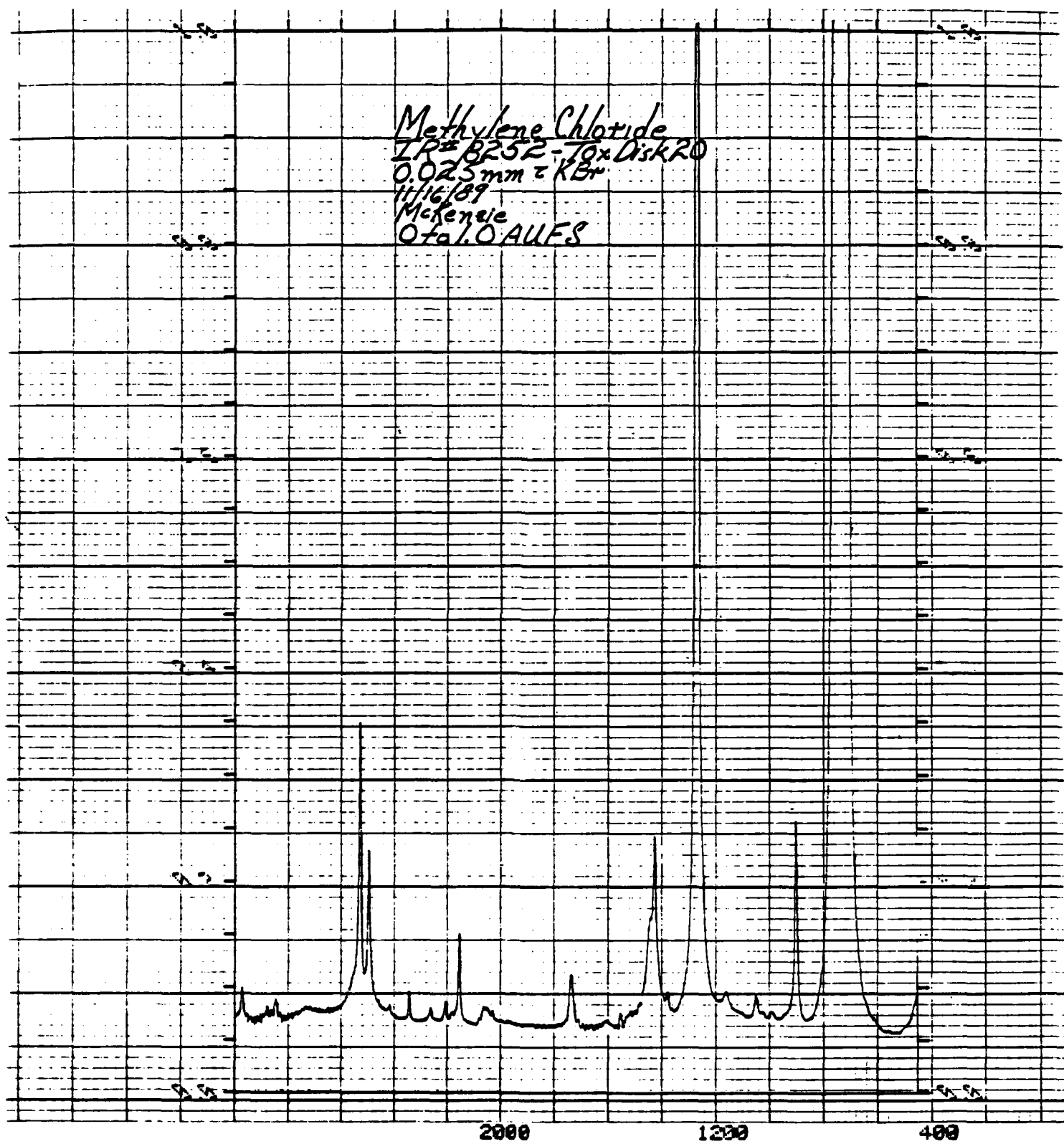
SPECTRA DIAGRAM OF DANPE LOT NO. 2316C

DANPE Lot # 2316C  
20:1 DILUTION in MeCl<sub>2</sub>  
0.025 mm EK5r  
IR # 8304 - 7th Disk # 21  
McKENZIE  
11/21/09



rintout of DANPE Lot No. 2316C

Methylene Chloride  
IR# B252-70x Disk 20  
0.025mm KBr  
11/16/89  
McKenzie  
Ota, OAUFS



Reference Material Spectra

APPENDIX C

EVALUATION OF SKIN REACTIONS\*

Erythema and Eschar Formation

No erythma	0
Very slight erythema (barely perceptible)	1
Well defined erythema	2
Moderate-to-severe erythema	3
Severe erythema (beet redness to slight eschar formation)	4

Edema Formation

No edema	0
Very slight (barely perceptible)	1
Slight edema (edges or area well defined by definite raising)	2
Moderate edema (edges raised approximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond area of exposure)	4

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\* An individual irritation score is equal to the sum of the scores for edema formation and erythema and eschar formation.

APPENDIX D

TOPICAL HAZARD EVALUATION PROGRAM  
DEFINITIONS OF CATEGORIES OF COMPOUNDS BEING  
CONSIDERED FOR ACUTE SKIN APPLICATION

CATEGORY I - Compounds producing no primary irritation of the intact skin or no greater than mild primary irritation of the skin surrounding an abrasion.

CATEGORY II - Compounds producing mild primary irritation of the intact skin and the skin surrounding an abrasion.

CATEGORY III - Compounds producing moderate primary irritation of the intact skin and the skin surrounding an abrasion.

CATEGORY IV - Compounds producing moderate to severe primary irritation of the intact skin and of the skin surrounding an abrasion and, in addition, producing necrosis, vesiculation and/or eschars.

CATEGORY V - Compounds impossible to classify because of straining of the skin or other masking effects owing to physical properties of the compound.

EYE CATEGORIES:

- A. Compounds noninjurious to the eye.
- B. Compounds producing mild injury to the cornea.
- C. Compounds producing mild injury to the cornea, and in addition some injury to the conjunctiva.
- D. Compounds producing moderate injury to the cornea.
- E. Compounds producing moderate injury to the cornea, and in addition producing some injury to the conjunctiva.
- F. Compounds producing severe injury to the cornea and to the conjunctiva.

APPENDIX E

SCALE FOR SCORING OCULAR LESIONS

1. Cornea

a. Opacity-degree of density (most dense area taken for reading)

No opacity.....	0
Scattered or diffuse area, details of iris clearly visible.....	1
Easily discernible translucent areas, details of iris slightly obscured.....	2
Opalescent areas, no details of iris visible, size of pupil barely discernible.....	3
Opaque, iris invisible.....	4

b. Area of cornea involved

One quarter (or less) but not zero.....	1
Greater than one quarter but less than one half.....	2
Greater than one half but less than three quarters.....	3
Greater than three quarters up to whole area.....	4

Score = (a) x (b) x (5) = Total max score = 80

2. Iris

Values

Normal.....	0
Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof) iris still reacting to light (sluggish reaction is positive).....	1
No reaction to light, hemorrhage, gross destruction (any or all of these).....	2

Score = (a) x (5) = Total max score = 10

3. Conjunctivae

a. Redness (refers to palpebral and bulbar conjunctivae excluding cornea and iris)

Vessels normal.....	0
Vessels definitely injected above normal.....	1
More diffuse, deeper crimson red, individual vessels not easily discernible.....	2
Diffuse beefyred.....	3

b. Chemosis

No swelling.....	0
Any swelling above normal (included nictitating membrane).....	1
Obvious swelling with partial eversion of lids.....	2
Swelling with lids about half closed.....	3
Swelling with lids about half closed to completely closed.....	4

c. Discharge

No discharge.....	0
Any amount different from normal (does not include small amounts observed with moistening of the lids and hairs just adjacent to lids.....	2
Discharge with moistening of the lids and hairs, and considerable area around the eye.....	3

Score (a + b + c ) x (2) = Total max score = 20

The individual numerical scores for each eye to which a given compound has been applied are added together and then divided by the number of eyes used to obtain the score.

APPENDIX F

TABLE. EPA HAZARD INDICATORS

Hazard Indicators	Toxicity Categories			
	I	II	III	IV
Oral LD <sub>50</sub>	Up to and including 50 mg/kg	From 50 thru 500 mg/kg	From 500 thru 5,000 mg/kg	Greater than 5,000 mg/kg
Dermal LD <sub>50</sub>	Up to and including 200 mg/kg	From 200 thru 2,000 mg/kg	From 2000 thru 20,000 mg/kg	Greater than 20,000 mg/kg
Eye effects	Corrosive, (Irreversible destruc of ocular tiss) or corneal involv or irrit persist 21 days	Corneal involv or irrit clrng in 8-21 days	Corneal involv or irrit clrng in 7 days or less	Min effects clrng in less than 24 hrs
Skin effects	Corrosive (Tiss destruc into dermis and/or	Sev irrit at 72 hrs (sev erythema or edema)	Mod irrit at 72 hrs (mod erythema)	Mild or slt irrit (no irrit or slt erythema)

References.

40 CFR 156.10 Labeling Requirements. Revised 1 July 1991.

Eye Effects: [EPA] PR Notice 81-3; Label Improvement Program: Change in Test Methods for and Categorization of Eye Irritation. September 29, 1981.