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E. I. DU PONT DE NEMOURS AND COMPANY
Haskell Laboratory for Toxicology
and Industrial Medicine
P.O. Box 50, Elkton Road
Newark, Delaware 19714-0050

57-PP

May 26, 1992

DU PONT CENTRAL RESEARCH AND DEVELOPMENT

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Dear Coordinator:

8EHQ-0791-1303

In February of this year we informed you of the results of an acute 4-hour inhalation LC50 study in rats with the above referenced material.

Enclosed please find a copy of the final report on this study.

Sincerely,

Charles F. Reinhardt

Charles F. Reinhardt, M.D.
Director

CFR/ASP:dj
Phone: (302)366-5285

Enclosure (1): Final Report, Du Pont HLR 83-92, "Acute Inhalation Toxicity Study with Cymoxanil in Rats".

0 0 0 2

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Study Title

Acute Inhalation Toxicity Study with
DPX-T3217-115 (cymoxanil) in Rats

Data Requirements

U. S. EPA Pesticide Assessment Guidelines
Subdivision F, 81-3

OECD Guideline for Testing of Chemicals
403. Acute Inhalation Toxicity

MAFF Japan Testing Guideline For Acute Inhalation
Toxicity Study (59 NohSan No. 4200)

Author

Anthony S. Panepinto

Study Completed

May 12, 1992
(Revised On May 15, 1992)

Performing Laboratory

E. I. du Pont de Nemours and Company
Haskell Laboratory for Toxicology and Industrial Medicine
Elkton Road, P. O. Box 50
Newark, Delaware 19714

Laboratory Project ID

Haskell Laboratory Report No. 83-92

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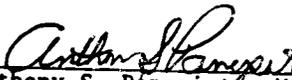
GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

This study was conducted according to EPA FIFRA Good Laboratory Practice Standards (40 CFR 160), OECD Principles of Good Laboratory Practice (C(81)30(Final), Annex 2), and MAFF Japan Good Laboratory Practice Standards (59 NohSan No. 3850). Any areas of noncompliance are documented in the study records. No deviations existed that affected the validity of the study.

Submitter: E. I. du Pont de Nemours and Company

Sponsor: E. I. du Pont de Nemours and Company
Wilmington, Delaware

Study Director:

 02/20/1992
Anthony S. Panepinto, M.S. Hygiene
Toxicologist
Acute Toxicology

Company Representative:

_____/_____
Registration Specialist

0005

REVISED

GENERAL INFORMATION

Haskell No.: H-19171

Purity: 98.2% by analysis

CAS Registry No.: 57966-95-7

Sponsor:

E. I. du Pont de Nemours and Company
Wilmington, DE 19898

Study Initiated: 11-08-91

Study Completed: 05-12-92 (Revised May 15, 1992)

In-Life Study Initiated: 11-18-91

In-Life Study Completed: 12-24-91

TABLE OF CONTENTS

	<u>Page</u>
Specific Country Requirements Page	2
Good Laboratory Practice Compliance Statement.	3
General Information.	4
Table of Contents.	5
Summary.	6
Signature Page	8
Quality Assurance Documentation.	9
Introduction	10
Materials and Methods.	10
Results and Discussion	14
Conclusion	16
References	17
Tables	
1. Atmospheric Concentration and Particle Size Distribution. . .	18
2. Chamber Environment	18
3. Summary of Clinical Observations in Male Rats	19
4. Summary of Clinical Observations in Female Rats	20
Figure	
1. Schematic of Exposure System	21
Appendices	
A. Generation Method Development	23
B. Exposure Chamber Conditions	25
1. Chamber Distribution of Particulate	26
2. Chamber Concentrations of DPX-T3217-115 (cymoxanil) and Active Ingredient	27
3. Chamber Environmental Conditions.	30
C. Individual Clinical Observations in Male Rats	32
D. Individual Clinical Observations in Female Rats	38
E. Individual Body Weights in Male Rats.	43
F. Individual Body Weights in Female Rats.	47
G. Pathology Report No. 1-92	51

Acute Inhalation Toxicity Study with
DPX-T3217-115 (cymoxanil) in Rats

SUMMARY

Three groups of 5 male and 5 female CRL:CD®BR rats was exposed to an atmosphere of DPX-T3217-115 (cymoxanil) for a single, 4-hour exposure period. The test atmosphere was generated by the suspension of the test material in air. During the exposure, the concentration of the test aerosol was determined by gravimetric analysis. A subsequent liquid chromatographic analysis of the eluent from the desorption of the gravimetric filters was carried out in order to verify the amount of DPX-T3217-115 (cymoxanil) collected. In the pursuant 14-day recovery period, rats were weighed and observed for clinical signs of toxicity. All rats underwent gross pathological examination at the end of the recovery period.

Rats were exposed to 3.21, 4.98, and 5.06 mg/L DPX-T3217-115 (cymoxanil). Total particulate was determined to be homogeneously distributed in the exposure chamber. The test aerosol during the exposure was characterized by measurement of a mass median aerodynamic diameter (MMAD). The MMAD of the aerosol generated during the exposures was 2.6 µm at 3.21 mg/L, 2.8 µm at 4.98 mg/L, and 3.1 µm at 5.06 mg/L DPX-T3217-115 (cymoxanil). Particles less than 1 µm ranged from 3.0% to 4.0%, particles less than 3 µm ranged from 48% to 62%, and particles less than 10 µm ranged from 98% to 100%.

All rats exposed to DPX-T3217-115 (cymoxanil) survived the exposures and the subsequent 14-day recovery period with the exception of one rat exposed to 4.98 mg/L which died during exposure. Clinical signs noted immediately following the exposure included oral, ocular, and nasal discharge, lethargy, low carriage, vocalizations, diarrhea, irregular respiration, and wet fur. Test material on the face was noted in all rats immediately following the exposure. Other clinical signs observed during the recovery period included ocular and nasal discharges, diarrhea, hunched posture, lethargy, alopecia, and stained fur. Three male rats, one from each exposure level experienced abnormal gait or mobility from day 2 through day 9 or day 2 through day 15. One male rat exposed to 4.98 mg/L DPX-T3217-115 (cymoxanil) exhibited a sore on his back day 8 through day 15 of the recovery period. One male rat exposed to 5.06 mg/L DPX-T3217-115 (cymoxanil) exhibited tremors day 7 through day 15 of the recovery period.

Rats from all exposure levels experienced slight to severe body-weight loss 1 day following exposure. Losses ranged from 4% to 18% original body weight for male rats, and 1% to 11% of original body weight for female rats. One female rat exposed to 3.21 mg/L DPX-T3217-115 (cymoxanil) experienced a body-weight gain of 3% one day following exposure. All rats showed an overall weight gain during the recovery period, although some transient weight losses did occur. Gross pathological examination revealed no evidence of organ-specific toxicity in any rats.

Under the conditions of this test, the LC_{50} for DPX-T3217-115 (cymoxanil) is greater than 5.06 mg/L. On an acute inhalation basis, DPX-T3217-115 (cymoxanil) is considered to have very low toxicity (LC_{50} greater than 2.0 mg/L).

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SIGNATURE PAGE

Technical Work by:

G. L. Poindexter
Gregory L. Poindexter
Technician

Technical Work by:

Maryanne M. Wilford
Maryanne M. Wilford, B.A.
Technician

Report Preparation by:

Karen L. Heaps
Karen L. Heaps, B.S.
Technician

Reviewed and
Approved for Issue:

Anthony S. Paupinto 5/15/92
Anthony S. Paupinto, M.S. Hygiene
Toxicologist

REVISED

QUALITY ASSURANCE DOCUMENTATION

(H-19171)

Dates of Inspection:

Conduct - 11/19/91

Records, Report(s) - 3/14, 22, 24, 25/92

Revisions 5/15/92

Date Findings Reported to:

Study Director - 3/25/92

Management - 4/30/92

Reported by:

James Mackay II
James Mackay II
Quality Assurance Auditor

5/15/92
Date

INTRODUCTION

The purpose of this study was to determine a 4-hour inhalation LC₅₀ for DPX-T3217-115 (cymoxanil) in male and female rats. The LC₅₀ is defined as the calculated atmospheric concentration of test material expected to cause the death of 50% of exposed animals either on the day of exposure or within at least 14 days postexposure. In the event that no deaths occur among rats exposed to a concentration of 5.0 mg/L or greater, the LC₅₀ is considered equal to or greater than that given concentration, and no further testing for the information is pursued.

In this study, the test atmosphere was generated by suspension of DPX-T3217-115 (cymoxanil) in air to mimic the expected physical state of the material in potential human exposure situations. A nose-only exposure mode was used to minimize the effects associated with the ingestion of test material from the fur.

The study was conducted according to the U. S. EPA Pesticide Assessment Guidelines, Subdivision F, Series 81-3, 1982,⁽¹⁾ the OECD Test Guideline No. 403, Acute Inhalation Toxicity, 1981,⁽²⁾ and the MAFF Japan Testing Guideline for Acute Inhalation Toxicity Study (59 NohSan No. 4200), 1985.⁽³⁾

MATERIALS AND METHODS

A. Test Material

The test material, DPX-T3217-115 (cymoxanil), was supplied by the sponsor as a milled solid formulation with a purity of 98.2% as reported by the sponsor.

The DPX-T3217-115 (cymoxanil) was milled in order to obtain a finer material for the generation of test atmospheres. The coarse test material was hammermilled and then air-milled, which resulted in the test sample having a volume median diameter of 1.8 μ m.

B. Animals

Young adult male and female Crl:CD®BR rats were received from Charles River Breeding Laboratories, Kingston, New York. The rats were approximately 7 weeks of age upon arrival.

Rats have historically been used in safety evaluation studies and their use is specified in the EPA, OECD, and MAFF Japan Guidelines for acute inhalation toxicity testing. The Crl:CD®BR rat has been chosen based on the consistently acceptable health status and the extensive experience with the strain at this laboratory.

C. Animal Husbandry

Quarantine and Animal Selection. Rats were quarantined after arrival for 6 days prior to testing. They were housed individually in 5" x 11" x 7" suspended, stainless steel, wire-mesh cages and weighed and observed 3 times during the quarantine period. Rats used on this study were obtained from the general population of stock rats released from quarantine.

Housing. During the test period, rats were housed either singly or in pairs (sexes separate) in 8" x 14" x 8" suspended, stainless steel, wire-mesh cages.

Animal Room Environment. During both the quarantine period and the testing period, the animal rooms were maintained on a timer-controlled, 12-hour light/12-hour dark cycle. Environmental conditions of the rooms were targeted for a temperature of $23 \pm 2^\circ\text{C}$ and a relative humidity of $50 \pm 10\%$. Excursions outside these ranges were judged to have been of insufficient magnitude and/or duration to have adversely affected the validity of the study.

Identification. Each rat was assigned a unique 6-digit identification number which corresponded to a numbered card affixed to the cage. The rat assigned the lower number in each cage was identified by a slash in the right ear. Prior to exposure, tails of the rats and cage cards were color-coded with water-insoluble markers so that individual rats could be identified after exposure.

Feed and Water. Except during exposure, Purina Certified Rodent Chow® #5002 and tap water from the Wilmington Suburban Water Corporation were available ad libitum.

D. Study Design

Three groups of 5 male and 5 female rats each were exposed nose-only for a 4-hour period to an atmosphere of DPX-T3217-115 (cymoxanil) in air. Rats were approximately 8 weeks of age at the time of exposure. The male rats ranged in weight from 225 to 259 grams; female rats weighed from 171 to 193 grams on the day of exposure.

Rats were observed for mortality during the exposure and observed for mortality and clinical signs of toxicity immediately after they were removed from the restrainers following exposure. During a 14-day postexposure period, rats were observed each day for mortality. Rats were weighed and observed for clinical signs of toxicity daily, excluding test days 6, 7, 11, 12, 13, and 14 for the 3.21 mg/L group and test days 5, 6, 10, 11, 12, and 13 for the 4.98 mg/L group. At the end of the recovery period, all rats were sacrificed by sodium pentobarbital anesthesia and exsanguination and subjected to gross pathological examination.

B. Inhalation Exposure Conditions

During exposure, rats were restrained in perforated stainless steel cylinders with conical nose pieces. The restrainers were inserted into the face plate of a 29-L cylindrical glass exposure chamber so that only the nose of each rat protruded into the chamber.

Chamber airflow was set and recorded at the beginning of the 4 hour exposure period. Airflow was monitored continuously using a calibrated Fluid Energy Jet-O-Mizer Model 00 jetmill and recorded approximately every 30 minutes. Chamber temperature was targeted at $23 \pm 2^\circ\text{C}$. Temperature was monitored continually with a Mercury Thermometer and recorded approximately every 30 minutes during the exposure. Relative humidity was targeted at $50 \pm 10\%$. Humidity in the exposure chamber was measured three times during the exposure with a Reuter-Stokes model RSS-230 Micropsychrometer. Chamber oxygen concentration was targeted to at least 19% and measured with a Biosystems Model 3100R oxygen monitor three times during the exposure.

F. Generation Method Development

Prior to any testing with animals, trial atmospheres of DPX-T3217-115 (cymoxanil) were generated. Two separate trials for the generation of test atmospheres were completed in order to obtain the best possible suspension of test material for conditions of a limit test. No animals were exposed, and trials were generally less than 4 hours in duration. Gravimetric air samples and cascade impactor samples were taken to evaluate the efficacy of changes made to the exposure system.

In these pre-test trials, the Fluid Energy Jet-O-Mizer jetmill was used to generate the test material. The chamber airflow, the test material feed rate, and the use of cyclonic separators were varied in order to eliminate particles of larger sizes while providing appropriate concentrations for this study.

Chamber distribution of the aerosol was characterized during these trials by taking gravimetric samples from several different locations on the chamber face plate and comparing the total dust concentrations with similar samples taken from the sampling port. No animals were in the chamber so that air samples could be readily drawn from the location of rat breathing zones.

G. Atmosphere Generation

An atmosphere of DPX-T3217-115 (cymoxanil) was generated by suspension of the previously milled test material in air using a Fluid Energy Jet-O-Mizer jetmill. The test material was metered into the jetmill using a K-Tron twin screw volumetric feeder which was controlled by a K-Tron Model PCM23401A digital speed controller. Filtered, high-pressure air introduced into the jetmill swept the resulting aerosol through 2-L and 0.5-L cyclones in tandem, and into the 29-L glass exposure chamber. A baffle consisting of a single perforated polycarbonate plate positioned 5 - 6" inside the exposure chamber was used to promote uniform distribution of test material.

The chamber concentration of DPX-T3217-115 (cymoxanil) was controlled by varying either the feed rate of test material to the jetmill or the rate at which air flows through the jetmill. Refer to Figure 1.

The chamber atmosphere was exhausted through a high-capacity dust filter and an MSA particulate filter prior to being discharged into the fume hood.

H. Characterization of Chamber Atmospheres

The atmospheric concentration of DPX-T3217-115 (cymoxanil) was determined at approximately 10-minute intervals during the exposure using gravimetric analysis. Approximately 2-4 samples of chamber atmosphere were drawn from the breathing zone of the rats through a 25 mm filter cassette that contained a preweighed Gelman glass fiber (Type A/E) filter. The filters were weighed on a Oahn Model C-31 Microbalance. The atmospheric concentration of DPX-T3217-115 (cymoxanil) was calculated from the difference in the pre- and post-sampling filter weights.

Gravimetric filters were desorbed in 20 mL of acetonitrile in order to verify the concentration of the active ingredient. The resulting solution obtained from the desorption of these gravimetric samples was analyzed by high performance liquid chromatography using diode array as the method of detection. The liquid chromatograph used for the analysis was the Hewlett Packard Model 1090 equipped with a 200 mm x 2.1 mm ODS-Hypersil column. The atmospheric concentration of active ingredient in these samples was determined by comparison with liquid standards prepared in acetonitrile.

A sample to determine particle size distribution (mass median aerodynamic diameter and percent particles less than 1, 3, and 10 μ m diameter) was determined with a Sierra® Series 210 cyclone preseparator/cascade impactor and Sierra® Series 110 Constant Flow Air Sampler (4).

I. Pathology

All rats from this study underwent gross pathological examination. Rats were sacrificed by sodium pentobarbital anesthesia and exsanguination on the 14th day of the recovery period.

J. Records Retention

All raw data and the final report will be stored in the archives of Haskell Laboratory for Toxicology and Industrial Medicine, Newark, Delaware, or in the Du Pont Records Management Center, E. I. du Pont de Nemours and Company, Wilmington, Delaware.

RESULTS AND DISCUSSION

A. Generation Method Development

Prior to the initiation of the test exposure, pre-test trials were conducted to determine the most suitable method of generating test atmospheres of DPX-T3217-115 (cymoxanil). The two goals of this preliminary testing were 1) to achieve a reasonably stable atmospheric concentration at or above 5 mg/L and 2) to attain a particle size distribution in which the majority of the particulate present was within the ranges of respirability for the rat. Changes to the exposure system and the results of gravimetric sampling and particle size analyses for evaluating these changes are tabulated in Appendix A.

The preliminary generation trials involved the use of a single jetmill. Initially, generation air introduced into the jetmill further ground the previously milled test material and swept the resulting aerosol through a 2-L cyclone, through a curved glass delivery tube and into the exposure chamber (Appendix A, Trial 1). This method provided a stable concentration of approximately 6.05 mg/L; however, the mass median diameter was 4.0 μm . In an attempt to achieve a smaller MMAD, a 500 ml cyclone was placed in tandem with the 2-L cyclone (Appendix A, Trial 2). These changes resulted in a stable chamber concentration of 5.02 mg/L and an MMAD of 3.0 μm was achieved.

During the trials for generation methods, a study of chamber distribution of particulate concentration was performed. No statistical differences were observed using the Student's t-test at $p \leq 0.05$ when samples taken at 3 locations in the face plate were compared to 4 samples taken at different time intervals from the sampling port. The material was considered to be homogeneously distributed at a design concentration of 5.0 mg/L DPX-T3217-115 (cymoxanil). Chamber distribution of particulate data is recorded in Appendix B.1.

B. Animal Exposure

A total of 3 test exposures were conducted. Characterization of the chamber atmospheres during the exposure showed the mean total particulate concentrations to be 3.21, 4.98, and 5.06 mg/L DPX-T3217-115 (cymoxanil). A summary of exposure concentration data is presented in Table 1. The exposure concentration data is recorded in Appendix B.2.

Chromatographic analyses of the gravimetric filters from the 3.21, 4.98, and 5.06 mg/L exposures showed that the total analytical concentrations of DPX-T3217-115 were 3.03, 4.37, and 4.14 mg/L, respectively. The active ingredient concentration data is presented in Appendix B.2

A single particle size sample of the test material was taken during each exposure. The MMAD of the aerosol generated during the exposures was 2.6 μ m at 3.21 mg/L, 2.8 μ m at 4.98 mg/L, and 3.1 μ m at 5.06 mg/L DPX-T3217-115 (cymoxanil). Particles less than 1 μ m ranged from 3.0% to 4.0%, particles less than 3 μ m ranged from 48% to 62%, and particles less than 10 μ m ranged from 98% to 100%. Particle size distribution data is summarized in Table 1.

During the exposures, chamber airflow was set at 20 L/min. Chamber temperatures ranged from 22 to 26°C, relative humidity ranged from 29% to 35%, and the oxygen concentration was 21%. The environmental conditions are tabulated in Appendix B.3 and summarized in Table 2.

C. Mortality and LC₅₀ Determination

One rat exposed to 4.98 mg/L DPX-T3217-115 (cymoxanil) died during exposure. All other rats survived the exposures to DPX-T3217-115 (cymoxanil) and the subsequent 14 day recovery period. The median lethal concentration for 4 hours of inhalation exposure to DPX-T3217-115 (cymoxanil) was considered to be greater than 5.06 mg/L.

D. Clinical Signs and Body Weights

Clinical signs of toxicity could not be assessed during the exposure because the density of the atmosphere prevented clear visual observation of the rats. Upon removal of the rats from the restrainers immediately following exposure, several clinical signs were observed. These included: ocular, nasal and oral discharges, lethargy, low carriage, vocalizations, irregular respiration, diarrhea, and wet underbody. Compound on face was noted on all animals immediately following exposure and is expected during nose-only exposures involving a solid particulate. One male rat from each exposure level exhibited abnormal gait or mobility on day 2. Rats exposed to 4.98 and 5.06 mg/L DPX-T3217-115 (cymoxanil) recovered from this clinical sign by test day 9, but the rat exposed to 3.21 mg/L DPX-T3217-115 (cymoxanil) did not recover. Alopecia was present in three rats; 1 male rat exposed to 4.98 mg/L showed alopecia on his back days 14 and 15, and one male rat exposed to 5.06 mg/L showed alopecia on his shoulder days 7 through 15, and a female rat exposed to 5.06 mg/L showed alopecia on her neck days 4 and 5 and days 7 through 15.

Hunched posture was seen in rats from all groups and seen transiently throughout the recovery period. Stained fur was seen intermittently during recovery in rats exposed to all levels of DPX-T3217-115 (cymoxanil). One male rat exposed to 5.06 mg/L exhibited tremors beginning on day 7 and continuing through day 15. A sore was present on a male rat exposed to 4.98 mg/L DPX-T3217-115 (cymoxanil) on days 8 through 15. The incidences of clinical signs are summarized in Table 3 and 4. Individual clinical signs for males and females are reported in Appendices C and D.

The first day following exposure, male rats exhibited weight losses ranging from 4% to 18% of original body weight and female rats exhibited weight losses ranging from 1% to 11% of original body weight. One female rat exposed to 3.21 mg/L DPX-T3217-115 (cymoxanil) exhibited a body-weight gain of 3%. The second day following exposure one male rat from each group experienced moderate weight loss (6% to 7% body-weight loss from the previous day). Rats exposed to 3.21 and 5.06 mg/L DPX-T3217-115 (cymoxanil) showed slight to moderate weight losses test days 4 through 6. By the end of the recovery period, with the exception of some transient weight loss, rats exhibited patterns of normal weight gain. Individual body weights for male and female rats are presented in Appendices E and F.

E. Pathology

All exposed rats were sacrificed and subjected to a gross pathologic examination 14 days after exposure. Gross observations included alopecia and an ulcerated back in one male rat, and stained skin in another male rat exposed to 4.98 mg/L DPX-T3217-115 (cymoxanil). Two rats, a male and female, exposed to 5.06 mg/L DPX-T3217-115 (cymoxanil) had liver discoloration localized to one lobe, and another male rat had an enlarged bilateral lymph node. These observations were considered to be incidental. No target organ was identified in these rats. Pathology Report No. 1-92 is attached as Appendix G.

CONCLUSION

The purpose of this study was to determine the inhalation median lethal concentration of DPX-T3217-115.

Under the conditions of this test, the LC_{50} for DPX-T3217-115 is greater than 5.06 mg/L. On an acute inhalation basis, DPX-T3217-115 is considered to have very low toxicity.

REFERENCES

1. Pesticide Assessment Guidelines Subdivision F, Hazard Evaluation: Human and Domestic Animals. (1982) U.S. Environmental Protection Agency (EPA), Office of Pesticide and Toxic Substances.
2. Guideline for Testing of Chemicals, Section 403, Acute Inhalation Toxicity. (1981) Organisation for Economic Co-Operation and Development (OECD).
3. Testing Guidelines for Toxicology Studies; 59 NohSan No. 4200, Acute Inhalation Toxicity Study. (1985) Ministry of Agriculture, Forestry, and Fisheries (MAFF Japan).
4. Calculation described in Sierra Instruments, Inc., Bulletin 7-79-219IM, Instruction Manual: Series 210 Ambient Cascade Impactors and Cyclone Preseparators.

Acute Inhalation Toxicity Study with DPX-T3217-115 (cyboxanil)

TABLE 1

Atmospheric Concentration and Particle Size Distribution

Mean	Atmospheric ^a Concentration (mg/L)		Mass Median Aerodynamic ^b Diameter(μm)	Geometric Standard ^c Deviation	% Particles by mass ^d		
	S.D.	Range			<1% μm	<3% μm	<10 μm
3.21	0.48	2.48 - 4.11	2.6	1.7	4.0	62	100
4.98	1.10	3.32 - 6.91	2.8	1.8	4.0	54	78
5.06	0.40	4.42 - 5.60	3.1	1.8	3.0	48	98

- ^a Represents the mean, standard deviation (S.D.), and range for the exposure. Eight samples were taken during the exposure. Values are expressed as 2 or 3 significant figures.
- ^b One sample taken during the exposure. Values are expressed as 2 significant figures.
- ^c One sample taken during the exposure. Values expressed as 2 significant figures.
- ^d One sample taken during the exposure. Values expressed as 2 or 3 significant figures.

TABLE 2

Chamber Environment^a

Mean Aerosol Concentration (mg/L)	Chamber Airflow Range (L/min)	Temperature Range (°C)	Relative Humidity Range (%)	Oxygen (%)
3.21	20	23 - 25	33 - 35	21
4.98	20	23 - 25	29 - 31	21
5.06	20	22 - 26	30 - 32	21

- ^a Values are expressed as 2 or 3 significant figures.

Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Table 3

Summary of Clinical Observations in Male Rats^a

Group: Concentration (mg/L):	<u>EXP-1</u> 3.21	<u>EXP-2</u> 4.98	<u>EXP-3</u> 5.06
<u>Observation</u>	<u>Number of Rats Exhibiting Sign^b</u>		
ABNORMAL GAIT OR MOBILITY	1 (2) ^c	1 (2)	1 (2)
ALOPECIA	0	1 (14)	1 (7)
COLORED DISCHARGE EYE(S)	3 (1)	5 (1)	5 (1)
COLORED DISCHARGE MOUTH	4 (1)	3 (1)	0
COLORED DISCHARGE NOSE	5 (1)	5 (1)	5 (1)
DIARRHEA	1 (2)	0	1 (2)
HUNCHED OVER	4 (2)	1 (3)	3 (2)
IRREGULAR RESPIRATION	0	2 (1)	0
LETHARGY	5 (1)	4 (1)	3 (1)
SORE	0	1 (8)	0
STAINED FUR	0	0	5 (2)
TREMORS	0	0	1 (7)
VOCALIZATION	1 (1)	0	0

^a Excluding clinical signs observed during exposure.

^b 5 male and 5 female rats per group at study start.

^c The number in parentheses is the median day on the test that the sign was first observed.

Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Table 4

Summary of Clinical Observations in Female Rats^a

Group: Concentration (mg/L):	<u>EXP-1</u> <u>3.21</u>	<u>EXP-2</u> <u>4.98</u>	<u>EXP-3</u> <u>5.06</u>
<u>Observation</u>	<u>Number of Rats Exhibiting Sign^b</u>		
ABNORMAL GAIT OR MOBILITY	0	0	0
ALOPECIA	0	0	1 (4) ^c
COLORED DISCHARGE EYE(S)	0	2 (1)	5 (1)
COLORED DISCHARGE MOUTH	4 (1)	3 (1)	0
COLORED DISCHARGE NOSE	3 (1)	4 (1)	5 (1)
DIARRHEA	0	1 (1)	0
HUNCHED OVER	0	0	5 (2)
IRREGULAR RESPIRATION	0	0	1 (1)
LETHARGY	5 (1)	1 (1)	5 (1)
SORE	0	0	0
STAINED FUR	3 (2)	3 (2)	5 (2)
TREMORS	0	0	0
VOCALIZATION	2 (1)	0	0
WET UNDERBODY	0	0	1 (1)

^a Excluding clinical signs observed during exposure.

^b 5 male and 5 female rats per group at study start.

^c The number in parentheses is the median day on the test that the sign was first observed.

0022

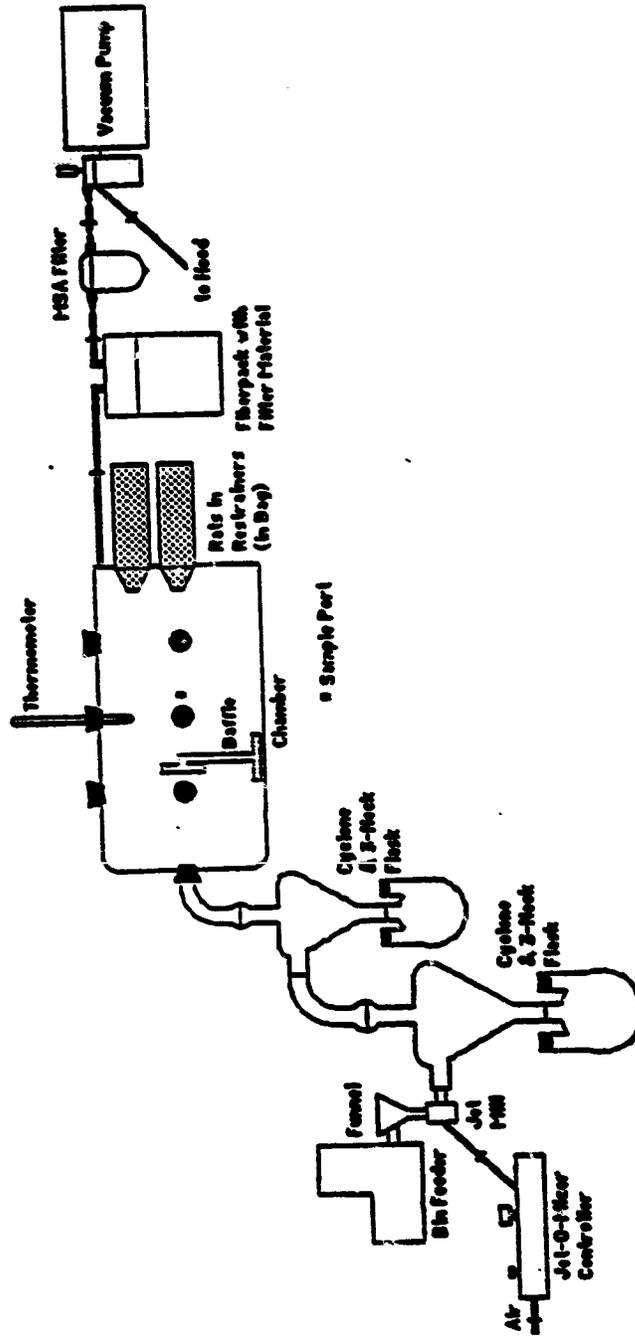
Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Figure 1
Schematic of Exposure System

Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Figure 1

Schematic of Exposure System



Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Appendix A

Generation Method Development

Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Appendix A

Generation Method Development

<u>Exposure System Conditions</u>				<u>Results</u>		
<u>Trial</u>	<u>Generation Method</u>	<u>Cyclone Size(s) (L)</u>	<u>Total Airflow (L/min)</u>	<u>Total* DPX-T3217-115 (cymoxanil) (mg/L)</u>	<u>MMAD (um)</u>	<u><1 um (%)</u>
1	1 Jetmill	2.0	20	2.4 - 10.2	4.0	0.5
2	1 Jetmill	2.0/0.5	20	4.6 - 5.5	2.6	9.0

* Range of total DPX-T3217-115 (cymoxanil) is based on gravimetric analysis.

0026

Acute Inhalation Toxicity Study with DFX-T3217-115 (cymoxanil)

Appendix B

Exposure Chamber Conditions

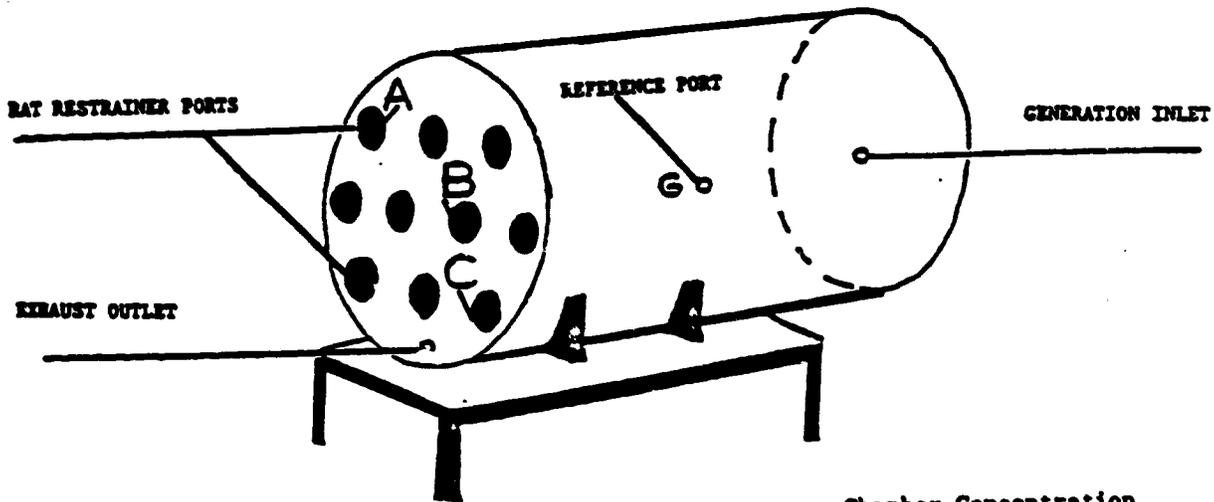
0027

REVISED

Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Appendix B.1

Chamber Distribution of Particulate



<u>Chamber Port</u>	<u>Sample Number</u>	<u>Chamber Concentration of DPX-T3217-115 (cymoxanil) (mg/L)^a</u>
A	1	4.62
B	1	5.13
C	1	5.49
		Mean <u>5.08^b</u>
G ^c	1	4.81
	2	4.90
	3	5.30
	4	4.61
		Mean <u>4.91^b</u>

- Chamber distribution was determined at a design concentration of 5.0 mg/L. Concentrations listed are based on gravimetric analysis of filter samples.
- No significant difference based on Student's t-test at p < 0.05.
- Reference sampling port.

0028

Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Appendix B.2

Chamber Concentrations of DPX-T3217-115 (cymoxanil)
and Active Ingredient^a at 3.21 mg/L

<u>Sample Number</u>	<u>Gravimetric Concentration (mg/L)</u>	<u>Concentration of Active Ingredient^b (mg/L)</u>
1	4.11	3.87
2	3.33	2.93
3	3.23	3.01
4	3.27	3.21
5	2.77	2.69
6	3.43	3.21

7	3.06	3.02
8	2.48	2.32
Mean	= 3.21	Mean = 3.03
S.D.	= 0.48	S.D. = 0.47
Min.	= 2.48	Min. = 2.32
Max.	= 4.11	Max. = 3.87

-
- a Values are expressed as 2 or 3 significant figures.
 - b Filters desorbed in 20 mL of acetonitrile. Active ingredient concentration is determined from filter eluent and expressed as concentration in air.
 - c *** denotes that the particle size was taken between samples 6 and 7.

Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Appendix B.2 (continued)

Chamber Concentrations of DPX-T3217-115 (cymoxanil)
and Active Ingredient^a at 4.98 mg/L

<u>Sample Number</u>	<u>Gravimetric Concentration (mg/L)</u>	<u>Concentration of Active Ingredient^b (mg/L)</u>
1	3.54	3.24
2	3.32	2.95
3	4.95	4.56
**** 4	5.02	4.64
5	5.02	4.09
6	5.55	5.01
7	6.91	6.52
8	5.50	3.98
Mean =	4.98	Mean = 4.37
S.D. =	1.14	S.D. = 1.09
Min. =	3.32	Min. = 2.95
Max. =	6.91	Max. = 6.52

-
- a Values are expressed as 2 or 3 significant figures.
 - b Filters desorbed in 20 mL of acetonitrile. Active ingredient concentration is determined from filter eluent and expressed as concentration in air.
 - c *** denotes that the particle size was taken between samples 3 and 4.

Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Appendix B.2 (continued)

Chamber Concentrations of DPX-T3217-115 (cymoxanil)
and Active Ingredient^a at 5.06 mg/L

<u>Sample Number^b</u>	<u>Gravimetric Concentration (mg/L)</u>	<u>Concentration of Active Ingredient^c (mg/L)</u>
1	4.57	4.05
2	4.42	3.95
3	5.43	4.75
4	5.26	4.53
5	5.60	2.76
6 **** ^d	5.00	4.57
7	5.10	4.34

Mean = 5.06
S.D. = 0.40
Min. = 4.42
Max. = 5.60

Mean = 4.14
S.D. = 0.65
Min. = 2.76
Max. = 4.75

-
- ^a Values are expressed as 2 or 3 significant figures.
 - ^b Initially there were 8 samples for this exposure, but due to analytical problems one sample is not included.
 - ^c Filters desorbed in 20 mL of acetonitrile. Active ingredient concentration is determined from filter eluent and expressed as concentration in air.
 - ^d *** denotes that the particle size was taken between samples 6 and 7

Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Appendix B.3

Chamber Environmental Conditions at 3.21 mg/L

<u>Reading #</u>	<u>Temperature (°C)</u>	<u>Relative Humidity (Percent)</u>	<u>Oxygen (Percent)</u>	<u>Air Flow (L/min)</u>
Initial	23	--	--	20
1	24	33	21	20
2	25	--	--	20
3	25	--	--	20
4	25	35	21	20
5	25	--	--	20
6	25	--	--	20
7	25	--	--	20
8	25	33	21	20
9	25	--	--	20

Chamber Environmental Conditions at 4.98 mg/L

<u>Reading #</u>	<u>Temperature (°C)</u>	<u>Relative Humidity (Percent)</u>	<u>Oxygen (Percent)</u>	<u>Air Flow (L/min)</u>
Initial	23	--	--	20
1	25	31	21	20
2	25	--	--	20
3	25	--	--	20
4	25	--	--	20
5	25	31	21	20
6	25	--	--	20
7	25	--	--	20
8	25	29	21	20

Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Appendix B.3 (continued)

Chamber Environmental Conditions at 5.06 mg/L

<u>Reading #</u>	<u>Temperature (°C)</u>	<u>Relative Humidity (Percent)</u>	<u>Oxygen (Percent)</u>	<u>Air Flow (L/min)</u>
Initial	22	--	--	20
1	25	32	21	20
2	26	--	--	20
3	26	--	--	20
4	25	--	--	20
5	25	30	21	20
6	25	--	--	20
7	25	--	--	20
8	25	30	21	20

Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Appendix C

Individual Clinical Observations in Male Rats

NR (not recovered) - the given sign was observed on the date that the animal died.

Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Appendix C

Individual Clinical Observations in Male Rats
Exposed to 3.21 mg/L

<u>Animal #</u>	<u>Observation</u>	<u>Day First Observed</u>	<u>Day Last Observed</u>
511466	COLORED DISCHARGE EYE(S) CLEAR SLIGHT	1	1
	COLORED DISCHARGE NOSE CLEAR SLIGHT	1	1
	LETHARGY	1	1
	LOW CARRIAGE	1	1
	VOCALIZATION	1	1
	COMPOUND ON FACE	1	1
	COLORED DISCHARGE EYE(S) RED SLIGHT	2	4
	COLORED DISCHARGE NOSE RED SLIGHT	2	3
	DIARRHEA	2	4
	HUNCHED OVER SLIGHT	2	3
	ABNORMAL GAIT OR MOBILITY	2	15 NR
	HUNCHED OVER MODERATE	4	10
	HUNCHED OVER SLIGHT	15	15 NR
	511467	COLORED DISCHARGE NOSE CLEAR SLIGHT	1
COLORED DISCHARGE MOUTH CLEAR SLIGHT		1	1
LETHARGY		1	1
HUNCHED OVER SLIGHT		1	1
COMPOUND ON FACE		1	2
COLORED DISCHARGE EYE(S) RED SLIGHT		1	1
COLORED DISCHARGE NOSE RED SLIGHT		2	2
511468	COLORED DISCHARGE MOUTH CLEAR SLIGHT	1	1
	COLORED DISCHARGE EYE(S) CLEAR SLIGHT	1	1
	LETHARGY	1	3
	LOW CARRIAGE	1	3
	COMPOUND ON FACE	1	1
	COLORED DISCHARGE NOSE RED SLIGHT	1	1
		2	3

Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Appendix C (continued)

Individual Clinical Observations in Male Rats
Exposed to 3.21 mg/L

<u>Animal #</u>	<u>Observation</u>	<u>Day First Observed</u>	<u>Day Last Observed</u>
511469	COLORED DISCHARGE MOUTH CLEAR SLIGHT	1	1
	COLORED DISCHARGE NOSE CLEAR SLIGHT	1	1
	LETHARGY	1	1
	LOW CARRIAGE	1	1
	COMPOUND ON FACE	1	1
	HUNCHED OVER SLIGHT	2	2
511470	COLORED DISCHARGE MOUTH CLEAR SLIGHT	1	1
	COLORED DISCHARGE NOSE CLEAR SLIGHT	1	1
	LETHARGY	1	1
	HUNCHED OVER SLIGHT	1	2
	COMPOUND ON FACE	1	1

Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Appendix C (continued)

Individual Clinical Observations in Male Rats
Exposed to 4.98 mg/L

<u>Animal #</u>	<u>Observation</u>	<u>Day First Observed</u>	<u>Day Last Observed</u>
511459	COLORED DISCHARGE EYE(S) CLEAR SLIGHT	1	
	COLORED DISCHARGE NOSE CLEAR SLIGHT	1	1
	COLORED DISCHARGE MOUTH CLEAR SLIGHT	1	1
	IRREGULAR RESPIRATION	1	1
	LETHARGY	1	9
	COMPOUND ON FACE	1	1
	COLORED DISCHARGE EYE(S) RED SLIGHT	2	4
	COLORED DISCHARGE NOSE RED SLIGHT	2	4
	ABNORMAL GAIT OR MOBILITY	2	9
	HUNCHED OVER MODERATE	3	9
511460	COLORED DISCHARGE EYE(S) CLEAR SLIGHT	1	1
	COLORED DISCHARGE NOSE CLEAR SLIGHT	1	1
	LETHARGY	1	1
	LOW CARRIAGE	1	1
	COMPOUND ON FACE	1	1
	COLORED DISCHARGE NOSE RED SLIGHT	2	3
511461	COLORED DISCHARGE EYE(S) CLEAR SLIGHT	1	1
	COLORED DISCHARGE NOSE CLEAR SLIGHT	1	1
	LETHARGY	1	1
	LOW CARRIAGE	1	1
	COMPOUND ON FACE	1	1
	SORE BACK SLIGHT	8	9
	SORE BACK SEVERE	14	15 NR
	ALOPECIA BACK SEVERE	14	15 NR
511462	COLORED DISCHARGE NOSE CLEAR SLIGHT	1	1 NR
	COLORED DISCHARGE EYE(S) CLEAR SLIGHT	1	1 NR
	COLORED DISCHARGE MOUTH CLEAR SLIGHT	1	1 NR
	LOW CARRIAGE	1	1 NR
	IRREGULAR RESPIRATION	1	1 NR
	LETHARGY	1	1 NR
	COMPOUND ON FACE	1	1 NR
	511463	COLORED DISCHARGE NOSE CLEAR SLIGHT	1
COLORED DISCHARGE MOUTH CLEAR SLIGHT		1	1
COLORED DISCHARGE EYE(S) CLEAR SLIGHT		1	1
COMPOUND ON FACE		1	1
COLORED DISCHARGE NOSE RED SLIGHT		2	2

Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Appendix C (continued)

Individual Clinical Observations in Male Rats
Exposed to 5.06 mg/L

<u>Animal #</u>	<u>Observation</u>	<u>Day First Observed</u>	<u>Day Last Observed</u>
512168	COLORED DISCHARGE NOSE CLEAR SLIGHT	1	1
	COLORED DISCHARGE EYE(S) CLEAR SLIGHT	1	1
	LETHARGY	1	1
	LOW CARRIAGE	1	1
	COMPOUND ON FACE	1	1
	ABNORMAL GAIT OR MOBILITY SEVERE	1	1
	DIARRHEA	2	6
	STAINED PERINEUM YELLOW SLIGHT	2	11
	COLORED DISCHARGE NOSE RED SLIGHT	2	6
	COLORED DISCHARGE EYE(S) RED SLIGHT	2	6
	HUNCHED OVER SLIGHT	2	2
	COLORED DISCHARGE EYE(S) RED MODERATE	2	2
	HUNCHED OVER SEVERE	3	6
	ABNORMAL GAIT OR MOBILITY MODERATE	3	9
	TREMORS MODERATE	7	9
	COLORED DISCHARGE EYE(S) RED SLIGHT	7	10
	HUNCHED OVER MODERATE	7	9
	TREMORS SLIGHT	10	10
	HUNCHED OVER SLIGHT	11	15 NR
11		11	
512169	COLORED DISCHARGE NOSE CLEAR SLIGHT	1	1
	COLORED DISCHARGE EYE(S) CLEAR SLIGHT	1	1
	LETHARGY	1	1
	LOW CARRIAGE	1	1
	COMPOUND ON FACE	1	1
	STAINED UNDERBODY YELLOW MODERATE	1	1
	COLORED DISCHARGE NOSE RED SEVERE	2	2
	COLORED DISCHARGE EYE(S) RED MODERATE	2	2
	STAINED UNDERBODY YELLOW SLIGHT	2	2
COLORED DISCHARGE NOSE RED MODERATE	3	3	
3		3	
512170	COLORED DISCHARGE NOSE CLEAR SLIGHT	1	1
	COLORED DISCHARGE EYE(S) CLEAR SLIGHT	1	1
	LETHARGY	1	1
	LOW CARRIAGE	1	1
	COMPOUND ON FACE	1	1
	STAINED UNDERBODY YELLOW SLIGHT	1	1
2		3	

Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Appendix C (continued)

Individual Clinical Observations in Male Rats
Exposed to 5.06 mg/L

<u>Animal #</u>	<u>Observation</u>	<u>Day First Observed</u>	<u>Day Last Observed</u>
512171	COLORED DISCHARGE NOSE CLEAR SLIGHT	1	1
	COLORED DISCHARGE EYE(S) CLEAR SLIGHT	1	1
	COMPOUND ON FACE	1	1
	STAINED UNDERBODY YELLOW MODERATE	2	3
	COLORED DISCHARGE NOSE RED SLIGHT	2	2
	HUNCHED OVER SLIGHT	2	3
	ALOPECIA LEFT FRONT SHOULDER(S) SLIGHT	7	15 NR
512172	COLORED DISCHARGE NOSE CLEAR SLIGHT	1	1
	COLORED DISCHARGE EYE(S) CLEAR SLIGHT	1	1
	COMPOUND ON FACE	1	1
	STAINED UNDERBODY YELLOW MODERATE	2	3
	COLORED DISCHARGE NOSE RED SLIGHT	2	2
	COLORED DISCHARGE EYE(S) RED SLIGHT	2	2
	HUNCHED OVER SLIGHT	2	3

Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Appendix D

Individual Clinical Observations in Female Rats

NR (not recovered) - the given sign was observed on the date that the animal died

0 0 4 0

Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Appendix D

Individual Clinical Observations in Female Rats
Exposed to 3.21 mg/L

<u>Animal #</u>	<u>Observation</u>	<u>Day First Observed</u>	<u>Day Last Observed</u>
511497	COLORED DISCHARGE MOUTH CLEAR SLIGHT	1	1
	COLORED DISCHARGE NOSE CLEAR SLIGHT	1	1
	LETHARGY	1	1
	LOW CARRIAGE	1	1
	COMPOUND ON FACE	1	1
	STAINED PERINEUM YELLOW SLIGHT	2	3
511498	COLORED DISCHARGE NOSE CLEAR SLIGHT	1	1
	LETHARGY	1	1
	LOW CARRIAGE	1	1
	COMPOUND ON FACE	1	1
511499	COLORED DISCHARGE MOUTH CLEAR SLIGHT	1	1
	LETHARGY	1	1
	LOW CARRIAGE	1	1
	COMPOUND ON FACE	1	1
	STAINED PERINEUM YELLOW SLIGHT	2	2
511500	COLORED DISCHARGE MOUTH CLEAR SLIGHT	1	1
	COLORED DISCHARGE NOSE CLEAR SLIGHT	1	1
	LETHARGY	1	1
	VOCALIZATION	1	1
	LOW CARRIAGE	1	1
	COMPOUND ON FACE	1	1
	STAINED PERINEUM YELLOW MODERATE	2	2
511501	COLORED DISCHARGE MOUTH CLEAR SLIGHT	1	1
	LETHARGY	1	1
	VOCALIZATION	1	1
	LOW CARRIAGE	1	1
	COMPOUND ON FACE	1	1

0 0 4 1

Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Appendix D (continued)

Individual Clinical Observations in Female Rats
Exposed to 4.98 mg/L

<u>Animal #</u>	<u>Observation</u>	<u>Day First Observed</u>	<u>Day Last Observed</u>
511481	COLORED DISCHARGE NOSE CLEAR SLIGHT	1	1
	COLORED DISCHARGE EYE(S) CLEAR SLIGHT	1	1
	COMPOUND ON FACE	1	1
	STAINED FUR BACK YELLOW MODERATE	2	3
	STAINED PERINEUM YELLOW SLIGHT	2	2
	STAINED FUR BACK YELLOW SLIGHT	4	4
511482	COLORED DISCHARGE NOSE CLEAR SLIGHT	1	1
	LETHARGY	1	1
	COMPOUND ON FACE	1	1
	STAINED BACK YELLOW MODERATE	2	3
	STAINED PERINEUM YELLOW SLIGHT	2	2
511483	COLORED DISCHARGE NOSE CLEAR SLIGHT	1	1
	COLORED DISCHARGE EYE(S) CLEAR SLIGHT	1	1
	COLORED DISCHARGE MOUTH CLEAR SLIGHT	1	1
	COMPOUND ON FACE	1	1
	COLORED DISCHARGE NOSE RED SLIGHT	2	2
	COLORED DISCHARGE EYE(S) RED SLIGHT	2	2
	STAINED PERINEUM YELLOW MODERATE	2	4
511484	COLORED DISCHARGE NOSE CLEAR SLIGHT	1	1
	COLORED DISCHARGE MOUTH CLEAR SLIGHT	1	1
	COMPOUND ON FACE	1	1
511485	COLORED DISCHARGE MOUTH CLEAR SLIGHT	1	1
	DIARRHEA	1	1
	COMPOUND ON FACE	1	1

0042

Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Appendix D (continued)

Individual Clinical Observations in Female Rats
Exposed to 5.06 mg/L

<u>Animal #</u>	<u>Observation</u>	<u>Day First Observed</u>	<u>Day Last Observed</u>
512190	COLORED DISCHARGE NOSE CLEAR SLIGHT	1	1
	COLORED DISCHARGE EYE(S) CLEAR SLIGHT	1	1
	LETHARGY	1	1
	COMPOUND ON FACE	1	1
	STAINED UNDERBODY YELLOW MODERATE	2	3
	COLORED DISCHARGE NOSE RED SLIGHT	2	3
	HUNCHED OVER SLIGHT	2	3
512191	COLORED DISCHARGE NOSE CLEAR SLIGHT	1	1
	COLORED DISCHARGE EYE(S) CLEAR SLIGHT	1	1
	LETHARGY	1	1
	COMPOUND ON FACE	1	1
	STAINED PERINEUM YELLOW SLIGHT	2	5
	COLORED DISCHARGE NOSE RED SLIGHT	2	5
	COLORED DISCHARGE EYE(S) RED SLIGHT	2	5
HUNCHED OVER SLIGHT	2	5	
512192	COLORED DISCHARGE NOSE CLEAR SLIGHT	1	1
	COLORED DISCHARGE EYE(S) CLEAR SLIGHT	1	1
	LETHARGY	1	1
	COMPOUND ON FACE	1	1
	STAINED UNDERBODY YELLOW SLIGHT	2	5
	COLORED DISCHARGE NOSE RED SLIGHT	2	3
	COLORED DISCHARGE EYE(S) RED SLIGHT	2	3
	HUNCHED OVER SLIGHT	2	3
	ALOPECIA NECK SLIGHT	4	5
ALOPECIA NECK SLIGHT	7	15 NR	
512193	COLORED DISCHARGE NOSE CLEAR SLIGHT	1	1
	COLORED DISCHARGE EYE(S) CLEAR SLIGHT	1	1
	LETHARGY	1	1
	COMPOUND ON FACE	1	1
	STAINED UNDERBODY YELLOW MODERATE	2	4
	COLORED DISCHARGE NOSE RED MODERATE	2	3
	COLORED DISCHARGE EYE(S) RED SLIGHT	2	3
	HUNCHED OVER SLIGHT	2	4

Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Appendix D (continued)

Individual Clinical Observations in Female Rats
Exposed to 5.06 mg/L

<u>Animal #</u>	<u>Observation</u>	<u>Day First Observed</u>	<u>Day Last Observed</u>
512194	COLORED DISCHARGE NOSE CLEAR SLIGHT	1	1
	COLORED DISCHARGE EYE(S) CLEAR SLIGHT	1	1
	LETHARGY	1	2
	COMPOUND ON FACE	1	1
	LOW CARRIAGE	1	1
	IRREGULAR RESPIRATION	1	1
	VET UNDERBODY	1	1
	STAINED UNDERBODY YELLOW SEVERE	2	4
	COLORED DISCHARGE NOSE RED MODERATE	2	3
	COLORED DISCHARGE EYE(S) RED MODERATE	2	3
	HUNCHED OVER SLIGHT	2	4

0 0 4 4

Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Appendix E

Individual Body Weights in Male Rats

NOTE:

SD - Sacrifice by Design. Rats sent to necropsy for pathological examination.

FD - Found Dead. Animal found dead following exposure or during the recovery period.

Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Appendix E

Individual Body Weights (g) of Male Rats
Exposed to 3.21 mg/L

<u>Animal #</u>	<u>Days on Test</u>							
	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>5</u>	<u>8</u>	<u>9</u>	<u>10</u>
511466	239.0	203.3	190.7	181.5	178.3	173.9	178.0	181.9
511467	227.0	204.0	215.8	227.4	235.6	256.6	260.3	272.5
511468	239.0	223.8	236.8	249.4	251.8	299.3	312.3	313.8
511469	225.0	213.6	228.7	235.0	247.4	269.2	275.0	280.0
511470	231.0	218.5	227.5	235.1	247.3	270.3	284.1	286.8

<u>Animal #</u>	<u>Days on Test</u>
	<u>15</u>
511466	199.3 (SD Day 15)
511467	302.8 (SD Day 15)
511468	375.8 (SD Day 15)
511469	324.1 (SD Day 15)
511470	332.0 (SD Day 15)

Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Appendix E (continued)

Individual Body Weights (g) of Male Rats
Exposed to 4.98 mg/L

<u>Animal #</u>	<u>Days on Test</u>							
	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>7</u>	<u>8</u>	<u>9</u>	<u>14</u>
511459	240.0	199.8	186.3	188.1	206.6	218.8	229.9	279.7
511460	240.0	215.1	228.2	245.1	270.1	277.7	284.0	314.4
511461	259.0	241.3	247.8	253.5	297.1	310.4	320.6	382.2
511462	252.0	FD (Day 1)						
511463	249.0	240.4	257.6	270.1	301.5	311.5	322.8	388.9

<u>Animal #</u>	<u>Days on Test</u>
	<u>15</u>
511459	286.7 (SD Day 15)
511460	315.9 (SD Day 15)
511461	381.6 (SD Day 15)
511462	
511463	393.8 (SD Day 15)

Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Appendix E (continued)

Individual Body Weights (g) of Male Rats
Exposed to 5.06 mg/L

<u>Animal #</u>	<u>Days on Test</u>							
	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>5</u>	<u>6</u>	<u>7</u>	<u>8</u>
512168	253.0	207.0	192.8	181.6	175.2	171.7	178.6	183.8
512169	240.0	213.3	219.9	238.1	245.9	251.2	273.4	282.7
512170	243.0	231.3	253.3	262.1	270.8	276.1	291.6	307.4
512171	259.0	243.7	251.5	269.3	276.4	286.3	309.4	319.8
512172	243.0	227.6	235.9	243.0	251.7	261.0	280.6	284.8

<u>Animal #</u>	<u>Days on Test</u>						
	<u>9</u>	<u>10</u>	<u>11</u>	<u>12</u>	<u>13</u>	<u>14</u>	<u>15</u>
512168	194.9	204.1	219.8	226.0	237.5	249.5	260.7 (SD Day 15)
512169	289.1	295.3	307.0	311.9	315.2	329.5	340.7 (SD Day 15)
512170	309.1	321.0	326.4	336.0	343.3	351.7	363.0 (SD Day 15)
512171	327.4	345.9	350.8	363.9	377.1	381.5	400.4 (SD Day 15)
512172	301.3	305.9	317.4	320.4	331.1	341.4	346.0 (SD Day 15)

Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Appendix F

Individual Body Weights in Female Rats

NOTE:

SD - Sacrifice by Design. Rats sent to necropsy for pathological examination.

Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Appendix F

Individual Body Weights (g) of Female Rats
Exposed to 3.21 mg/L

<u>Animal #</u>	<u>Days on Test</u>							
	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>5</u>	<u>8</u>	<u>9</u>	<u>10</u>
511497	193.0	198.6	204.9	212.1	220.3	241.6	242.4	246.1
511498	171.0	168.4	176.0	183.0	186.6	203.8	208.4	197.1
511499	185.0	180.6	187.4	195.0	199.0	211.5	219.3	220.3
511500	184.0	180.2	185.8	191.8	204.0	207.2	226.2	225.8
511501	182.0	180.1	186.2	195.1	205.0	218.0	223.0	220.6

<u>Animal #</u>	<u>Days on Test</u>
	<u>15</u>
511497	272.9 SD (Day 15)
511498	225.4 SD (Day 15)
511499	245.4 SD (Day 15)
511500	241.5 SD (Day 15)
511501	243.3 SD (Day 15)

Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Appendix F (continued)

Individual Body Weights (g) of Female Rats
Exposed to 4.98 mg/L

<u>Animal #</u>	<u>Days on Test</u>							
	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>7</u>	<u>8</u>	<u>9</u>	<u>14</u>
511481	179.0	174.1	174.5	190.6	205.5	209.4	203.5	241.7
511482	190.0	185.8	189.4	199.4	223.1	222.1	236.2	270.7
511483	185.0	178.9	186.3	193.5	206.6	210.3	219.1	223.5
511484	190.0	182.0	193.9	205.7	218.4	227.7	231.9	250.5
511485	190.0	186.8	191.8	200.4	219.1	227.4	225.3	258.9

<u>Animal #</u>	<u>Days on Test</u>
	<u>15</u>
511481	243.8 SD (Day 15)
511482	277.0 SD (Day 15)
511483	237.3 SD (Day 15)
511484	259.8 SD (Day 15)
511485	265.8 SD (Day 15)

Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Appendix F (continued)

Individual Body Weights (g) of Female Rats
Exposed to 5.06 mg/L

<u>Animal #</u>	<u>Days on Test</u>							
	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>5</u>	<u>6</u>	<u>7</u>	<u>8</u>
512190	183.0	170.2	181.4	188.5	186.6	191.2	208.7	210.2
512191	182.0	161.7	161.9	157.3	159.7	165.4	186.1	199.3
512192	182.0	172.9	176.7	185.5	190.1	194.3	206.8	216.7
512193	176.0	158.2	160.2	169.1	173.8	185.4	200.1	210.2
512194	186.0	168.7	168.7	184.3	190.0	194.3	208.1	209.1

<u>Animal #</u>	<u>Days on Test</u>						
	<u>9</u>	<u>10</u>	<u>11</u>	<u>12</u>	<u>13</u>	<u>14</u>	<u>15</u>
512190	216.2	207.3	217.3	220.1	227.1	222.5	228.7 SD (Day 15)
512191	202.6	205.2	207.5	218.1	224.0	224.7	226.9 SD (Day 15)
512192	220.0	215.0	224.0	225.4	230.8	226.6	236.3 SD (Day 15)
512193	213.6	208.6	219.6	222.7	226.1	215.5	230.2 SD (Day 15)
512194	212.0	216.4	225.2	226.0	235.4	238.4	243.1 SD (Day 15)

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Acute Inhalation Toxicity Study with DPX-T3217-115 (cymoxanil)

Appendix G

Pathology Report No. 1-92

DU PONT CENTRAL RESEARCH AND DEVELOPMENT
HASKELL LABORATORY FOR TOXICOLOGY
AND INDUSTRIAL MEDICINE

February 6, 1992

FROM: HANS H. C. CHEN *HC*

PATHOLOGY REPORT NO. 1-92

Attached is Pathology Report No. 1-92. This report is for the following study:

ACUTE INHALATION TOXICITY STUDY WITH DPX-T3217-115 IN RATS

GROSS PATHOLOGY

The following information pertains to the study:

ACUTE INHALATION TOXICITY STUDY WITH DPX-T3217-115 IN RATS

GROSS PATHOLOGY

PATHOLOGY REPORT NO. 1-92

0055

ACUTE INHALATION TOXICITY STUDY WITH DPX-T3217-115 IN RATS

GROSS PATHOLOGY

SUMMARY

Three groups of 5 male and 3 groups of 5 female Cri:CDØBR rats each were exposed to DPX-T3217-115 by inhalation for 4 hours followed by a 2-week post exposure observation period. Exposure concentrations for both male and female rats were 3.21, 4.98, and 5.06 mg/L. Rats were necropsied when found dead (FD) or sacrificed by design (SD) at the end of the 2-week observation period. Rats were euthanatized by intraperitoneal injection of sodium pentobarbital followed by exsanguination.

Tables 1 and 2 contain the individual animal gross observations for male and female rats, respectively.

One male rat in the 4.98 mg/L group died on the day of exposure. This rat had skin stain around the mouth which was considered to be associated with salivation prior to death. No other rats died during the study. Gross observations noted in rats which were sacrificed by design were considered to be incidental. No target organ was identified.

Report by:

Hans H. C. Chen

Hans H. C. Chen, D.V.M.
Senior Research Pathologist

Approved by:

James R. Gibson

James R. Gibson, Ph.D., D.A.B.T.
Assistant Director
Haskell Laboratory for Toxicology
and Industrial Medicine

Date issued:

May 7, 1992

Acknowledgment: Joan A. Wolfe, pathology supervisor

HHCC/JRG/wfd
WSPS-CHEN 743

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ACUTE INHALATION TOXICITY STUDY WITH DPX-T3217-115

TABLE 1
GROSS PATHOLOGY OBSERVATIONS FOR MALE RATS

<u>Animal Number</u>	<u>Test Days</u>	<u>Recovery Days</u>	<u>Mode of* Death</u>	<u>Observations</u>
<u>3.21 MG/L</u>				
511466	15	14	SD	No abnormalities detected
511467	15	14	SD	No abnormalities detected
511468	15	14	SD	No abnormalities detected
511469	15	14	SD	No abnormalities detected
511470	15	14	SD	No abnormalities detected
<u>4.98 MG/L</u>				
511459	15	14	SD	No abnormalities detected
511460	15	14	SD	No abnormalities detected
511461	15	14	SD	Skin - alopecia, back, severe, ulcerated, (2 cm in diameter)
511462	1	0	FD	Skin - stain, brown, minimal; mouth
511463	15	14	SD	No abnormalities detected
<u>5.06 MG/L</u>				
512168	15	14	SD	Mandibular Lymph Node - large, moderate, bilateral
512169	15	14	SD	Liver - discoloration, gray, left lobe, mottled, minimal
512170	15	14	SD	No abnormalities detected
512171	15	14	SD	No abnormalities detected
512172	15	14	SD	No abnormalities detected

* SD = Sacrificed by design; FD = Found dead

ACUTE INHALATION TOXICITY STUDY WITH DPX-T3217-115

TABLE 2
GROSS PATHOLOGY OBSERVATIONS FOR FEMALE RATS

<u>Animal Number</u>	<u>Test Days</u>	<u>Recovery Days</u>	<u>Mode of Death</u>	<u>Observations</u>
<u>3.21 MG/L</u>				
511497	15	14	SD	No abnormalities detected
511498	15	14	SD	No abnormalities detected
511499	15	14	SD	No abnormalities detected
511500	15	14	SD	No abnormalities detected
511501	15	14	SD	No abnormalities detected
<u>4.98 MG/L</u>				
511481	15	14	SD	No abnormalities detected
511482	15	14	SD	No abnormalities detected
511483	15	14	SD	No abnormalities detected
511484	15	14	SD	No abnormalities detected
511485	15	14	SD	No abnormalities detected
<u>5.06 MG/L</u>				
512190	15	14	SD	No abnormalities detected
512191	15	14	SD	No abnormalities detected
512192	15	14	SD	No abnormalities detected
512193	15	14	SD	Liver - discoloration, gray, left lobe, mottled, minimal
512194	15	14	SD	No abnormalities detected

* SD = Sacrificed by design

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