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E. I. DU PONT DE NEMOURS & COMPANY

INCORPORATED

WILMINGTON, DELAWARE 19898

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LEGAL DEPARTMENT

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September 11, 1992

Document Processing Center (TS-790)
Office of Pollution Prevention and Toxics
Environmental Protection Agency
401 M Street., S.W.
Washington, D.C. 20460
Attn: Section 8(e) Coordinator (CAP Agreement)

88920010979

Dear Coordinator:

8ECAP-0025

On behalf of the Regulatee and pursuant to Unit II B.1.b. and Unit II C of the 6/28/91CAP Agreement, E.I. Du Pont de Nemours and Co. hereby submits (*in triplicate*) the attached studies. Submission of this information is voluntary and is occasioned by unilateral changes in EPA's standard as to what EPA now considers as reportable information. Regulatee's submission of information is made solely in response to the new EPA §8(e) reporting standards and is not an admission: (1) of TSCA violation or liability; (2) that Regulatee's activities with the study compounds reasonably support a conclusion of substantial health or environmental risk or (3) that the studies themselves reasonably support a conclusion of substantial health or environmental risk.

The "Reporting Guide" creates new TSCA 8(e) reporting criteria which were not previously announced by EPA in its 1978 Statement of Interpretation and Enforcement Policy, 43 Fed Reg 11110 (March 16, 1978). The "Reporting Guide states criteria which expands upon and conflicts with the 1978 Statement of Interpretation. Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" raises significant due processes issues and clouds the appropriate reporting standard by which regulated persons can assure TSCA Section 8(e) compliance.

For Regulatee,

ORIGINAL


Mark H. Christman
Counsel
Legal D-7158
1007 Market Street
Wilmington, DE 19898
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GE CAP

3/27/95

## ATTACHMENT 1

Submission of information is made under the 6/28/91 CAP Agreement, Unit II. This submission is made voluntarily and is occasioned by recent changes in EPA's TSCA §8(e) reporting standard; such changes made, for the first time in 1991 and 1992 without prior notice and in violation of Regulatee's constitutional due process rights. Regulatee's submission of information under this changed standard is not a waiver of its due process rights; an admission of TSCA violation or liability, or an admission that Regulatee's activities with the study compounds reasonably support a conclusion of substantial risk to health or to the environment. Regulatee has historically relied in good faith upon the 1978 Statement of Interpretation and Enforcement Policy criteria for determining whether study information is reportable under TSCA §8(e), 43 Fed Reg 11110 (March 16, 1978). EPA has not, to date, amended this Statement of Interpretation.

After CAP registration, EPA provided the Regulatee the June 1, 1991 "TSCA Section 8(e) Reporting Guide". This "Guide" has been further amended by EPA, EPA letter, April 10, 1992. EPA has not indicated that the "Reporting Guide" or the April 1992 amendment supersedes the 1978 Statement of Interpretation. The "Reporting Guide" and April 1992 amendment substantively lowers the Statement of Interpretation 's TSCA §8(e) reporting standard[2]. This is particularly troublesome as the "Reporting Guide" states criteria, applied retroactively, which expands upon and conflicts with the Statement of Interpretation.[3] Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" and the April 1992 amendment clouds the appropriate standard by which regulated persons must assess information for purposes of TSCA §8(e).

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[2]In sharp contrast to the Agency's 1977 and 1978 actions to soliciting public comment on the proposed and final §8(e) Policy, EPA has unilaterally pronounced §8(e) substantive reporting criteria in the 1991 Section 8(e) Guide without public notice and comment, See 42 Fed Reg 45362 (9/9/77), "Notification of Substantial Risk under Section 8(e): Proposed Guidance".

[3]A comparison of the 1978 Statement of Interpretation and the 1992 "Reporting Guide" is a appended.

Throughout the CAP, EPA has mischaracterized the 1991 guidance as reflecting "longstanding" EPA policy concerning the standards by which toxicity information should be reviewed for purposes of §8(e) compliance. Regulatee recognizes that experience with the 1978 Statement of Interpretation may cause a review of its criteri. Regulatee supports and has no objection to the Agency's amending reporting criteria *provided that* such amendment is not applied to the regulated community in an unfair way. However, with the unilateral announcement of the CAP under the auspices of an OCM enforcement proceeding, EPA has wrought a terrific unfairness since much of the criteria EPA has espoused in the June 1991 Reporting Guide and in the Agency's April 2, 1992 amendment is new criteria which does not.exist in the 1978 Statement of Interpretation and Enforcement Policy.

The following examples of new criteria contained in the "Reporting Guide" that is not contained in the Statement of Interpretation follow:

o even though EPA expressly disclaims each "status report" as being preliminary evaluations that should not be regarded as final EPA policy or intent[4], the "Reporting Guide" gives the "status reports" great weight as "sound and adequate basis" from which to determine mandatory reporting obligations. ("Guide" at page 20).

o the "Reporting Guide" contains a matrix that establishes new numerical reporting "cutoff" concentrations for acute lethality information ("Guide" at p. 31). Neither this matrix nor the cutoff values therein are contained in the Statement of Interpretation. The regulated community was not made aware of these cutoff values prior to issuance of the "Reporting Guide" in June, 1991.

othe "Reporting Guide" states new specific definitional criteria with which the Agency, for the first time, defines as 'distinguishable neurotoxicological effects'; such criteria/guidance not expressed in the 1978 Statement of Interpretation.[5];

othe "Reporting Guide" provides new review/ reporting criteria for irritation and sensitization studies; such criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy.

othe "Reporting Guide" publicizes certain EPA Q/A criteria issued to the Monsanto Co. in 1989 which are not in the Statement of Interpretation; have never been published in the Federal Register or distributed by the EPA to the Regulatee. Such Q/A establishes new reporting criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy .

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[4]The 'status reports' address the significance, if any, of particular information reported to the Agency, rather than stating EPA's interpretation of §8(e) reporting criteria. In the infrequent instances in which the status reports contain discussion of reportability, the analysis is invariably quite limited, without substantial supporting scientific or legal rationale.

[5] *See, e.g,* 10/2/91 letter from Du Pont to EPA regarding the definition of 'serious and prolonged effects' as this term may relate to transient anesthetic effects observed at lethal levels; 10/1/91 letter from the American Petroleum Institute to EPA regarding clarification of the Reporting Guide criteria.

In discharging its responsibilities, an administrative agency must give the regulated community fair and adequate warning to as what constitutes noncompliance for which penalties may be assessed.

> Among the myriad applications of the due process clause is the fundamental principle that statutes and regulations which purport to govern conduct must give an adequate warning of what they command or forbid.... Even a regulation which governs purely economic or commercial activities, if its violation can engender penalties, must be so framed as to provide a constitutionally adequate warning to those whose activities are governed.

Diebold, Inc. v. Marshall, 585 F.2d 1327, 1335-36 (D.C. Cir. 1978). *See also*, Rollins Environemntal Services (NJ) Inc. v. U.S. Environmental Protection Agency, 937 F. 2d 649 (D.C. Cir. 1991).

While neither the are rules, This principle has been applied to hold that agency 'clarification', such as the Statement of Interpretation, the "Reporting Guide" nor the April 1992 amendments will not applied retroactively.

> ...a federal court will not retroactively apply an unforeseeable interpretation of an administrative regulation to the detriment of a regulated party on the theory that the post hoc interpretation asserted by the Agency is generally consistent with the policies underlying the Agency's regulatory program, when the semantic meaning of the regulations, as previously drafted and construed by the appropriate agency, does not support the interpretation which that agency urges upon the court.

Standard Oil Co. v. Federal Energy Administration, 453 F. Supp. 203, 240 (N.D. Ohio 1978), aff'd sub nom. Standard Oil Co. v. Department of Energy, 596 F.2d 1029 (Em. App. 1978):

The 1978 Statement of Interpretation does not provide adequate notice of, and indeed conflicts with, the Agency's current position at §8(e) requires reporting of all 'positive' toxicological findings without regard to an assessment of their relevance to human health. In accordance with the statute, EPA's 1978 Statement of Interpretation requires the regulated community to use scientific judgment to evaluate the significance of toxicological findings and to determining whether they reasonably support a conclusion of a substantial risk. Part V of the Statement of Interpretation urges persons to consider "the fact or probability" of an effect's occurrence. Similarly, the 1978 Statement of Interpretation stresses that an animal study is reportable only when "it contains reliable evidence ascribing the effect to the chemical." 43 Fed Reg. at 11112. Moreover, EPA's Statement of Interpretation defines the substantiality of risk as a function of both the seriousness of the effect and the probability of its occurrence. 43 Fed Reg 11110 (1978). Earlier Agency interpretation also emphasized the "substantial" nature of a §8(e) determination. See 42 Fed Reg 45362, 45363

(1977). [Section 8(e) findings require "extraordinary exposure to a chemical substance...which critically imperil human health or the environment"].

The recently issued "Reporting Guide" and April 1992 Amendment guidance requires reporting beyond and inconsistent with that required by the Statement of Interpretation. Given the statute and the Statement of Interpretation's explicit focus on substantial human or environmental risk, whether a substance poses a "substantial risk" of injury requires the application of scientific judgment to the available data on a case-by-case basis.

If an overall weight-of-evidence analysis indicates that this classification is unwarranted, reporting should be unnecessary under §8(e) because the available data will not "reasonably support the conclusion" that the chemical presents a substantial risk of serious adverse consequences to human health.

Neither the legislative history of §8(e) nor the plain meaning of the statute support EPA's recent lowering of the reporting threshold that TSCA §8(e) was intended to be a sweeping information gathering mechanism. In introducing the new version of the toxic substances legislation, Representative Eckhart included for the record discussion of the specific changes from the version of H. R. 10318 reported by the Consumer Protection and Finance Subcommittee in December 1975. One of these changes was to modify the standard for reporting under §8(e). The standard in the House version was changed from "causes or contributes to an unreasonable risk" to "causes or significantly contributes to a substantial risk". This particular change was one of several made in TSCA §8 to avoid placing an undue burden on the regulated community. The final changes to focus the scope of Section 8(e) were made in the version reported by the Conference Committee.

The word "substantial" means "considerable in importance, value, degree, amount or extent". Therefore, as generally understood, a "substantial risk" is one which will affect a considerable number of people or portion of the environment, will cause serious injury and is based on reasonably sound scientific analysis or data. Support for the interpretation can be found in a similar provision in the Consumer Product Safety Act. Section 15 of the CPSA defines a "substantial product hazard" to be:

> "a product defect which because of the pattern of defect, the number of defective products distributed in commerce, the severity of the risk, or otherwise, creates a substantial risk of injury to the public."

Similarly, EPA has interpreted the word 'substantial' as a quantitative measurement. Thus, a 'substantial risk' is a risk that can be quantified, *See,* 56 Fed Reg 32292, 32297 (7/15/91). Finally, since information pertinent to the exposure of humans or the environment to chemical substances or mixtures may be obtained by EPA through Sections 8(a) and 8(d) regardless of the degree of potential risk, §8(e) has specialized function. Consequently, information subject to §8(e) reporting should be of a type which would lead a reasonable man to conclude that some type action was required immediately to prevent injury to health or the environment.

## Attachment

***Comparison:***

Reporting triggers found in the 1978 "Statement of Interpretation/ Enforcement Policy",43 Fed Reg 11110 (3/16/78) and the June 1991 *Section 8(e) Guide.*

| TEST TYPE | 1978 POLICY CRITERIA EXIST? | New 1991 GUIDE CRITERIA EXIST? |
|---|---|---|
| **ACUTE LETHALITY** | | |
| Oral | N} | Y} |
| Dermal | N} | Y} |
| Inhalation (Vapors) | }[6] | }[7] |
| aerosol | N} | Y} |
| dusts/ particles | N} | Y} |
| **SKIN IRRITATION** | N | Y[8] |
| **SKIN SENSITIZATION (ANIMALS)** | N | Y[9] |
| **EYE IRRITATION** | N | Y[10] |
| **SUBCHRONIC (ORAL/DERMAL/INHALATION)** | N | Y[11] |
| **REPRODUCTION STUDY** | N | Y[12] |
| **DEVELOPMENTAL TOX** | Y[13] | Y[14] |

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[6]43 Fed Reg at 11114, comment 14:

"This policy statements directs the reporitng of specifiec effects when unknown to the Administrator. Many routine tests are based on a knowledge of toxicity associated with a chemicalL unknown effects occurring during such a range test may have to be reported if they are those of concern tot he Agency and if the information meets the criteria set forth in Parts V and VII."

[7]Guide at pp.22, 29-31.

[8]Guide at pp-34-36.

[9]Guide at pp-34-36.

[10]Guide at pp-34-36.

[11]Guide at pp-22; 36-37.

[12]Guide at pp-22

[13]43 Fed Reg at 11112

"Birth Defects" listed.

[14]Guide at pp-22

| | | |
|---|---|---|
| **NEUROTOXICITY** | N | Y[15] |
| **CARCINOGENICITY** | Y[16] | Y[17] |
| **MUTAGENICITY** | | |
| *In Vitro* | Y}[18] | Y} [19] |
| *In Vivo* | Y} | Y} |
| **ENVIRONMENTAL** | | |
| Bioaccumulation | Y} | N |
| Bioconcentration | Y}[20] | N |
| Oct/water Part. Coeff. | Y} | N |
| Acute Fish | N | N |
| Acute Daphnia | N | N |
| Subchronic Fish | N | N |
| Subchronic Daphnia | N | N |
| Chronic Fish | N | N |
| **AVIAN** | | |
| Acute | N | N |
| Reproductive | N | N |
| Reprodcutive | N | N |

---

[15] Guide at pp-23; 33-34.
[16] 43 Fed Reg at 11112
"Cancer" listed
[17] Guide at pp-21.
[18] 43 Fed Reg at 11112; 11115 at Comment 15
"Mutagenicity" listed/ *in vivo* vs *invitro* discussed; discussion of "Ames test".
[19] Guide at pp-23.
[20] 43 Fed Reg at 11112; 11115 at Comment 16.

(1)

CAS #75-12-7
Chem: Formamide
Title: Subchronic Inhalation Toxicity Study with Formamide In Rats
Date: April 5, 1988
Summary of Effects: Persistent lymphopenia and pathologic changes in the kidney.

Study Title

# Subchronic Inhalation Toxicity Study with Formamide in Rats

Author

David B. Warheit

Study Completed On

April 5, 1988

Performing Laboratory

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

Medical Research No.

5602-001

Laboratory Project ID

Haskell Laboratory Report No. 139-88

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## GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

This study was conducted according to EPA Good Laboratory Practice Regulations (40 CFR 792). Any areas of noncompliance are documented in the study records. No deviations existed that significantly affected the validity of the study.

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

Sponsor: Central Research and Development Department
E. I. du Pont de Nemours and Company, Inc.

Study Director: David B Warheit 3/17/88
David B. Warheit, Ph.D.
Research Toxicologist
Acute and Developmental Toxicology Division

# QUALITY ASSURANCE DOCUMENTATION

STUDY: MR 5602-001 Subchronic Inhalation Toxicity Study
H# 16,728 with Formamide in Rats

Because short-term studies are numerous and routine in nature, representative studies from this test type are audited quarterly to ensure the studies are designed and conducted in compliance with the Good Laboratory Practice Standards.

Reported by: Melissa R. Moore 4/4/88
Melissa R. Moore Date
Quality Assurance Auditor

## GENERAL INFORMATION

| | |
|---|---|
| Material Tested: | Formamide |
| Medical Research No.: | 5602-001 |
| Haskell No.: | 16,728 |
| Physical Form: | Colorless liquid |
| Purity: | Greater than 99% |
| Other Code: | Aldrich Chemical Co., Cat. No. 29,587-6 |
| CAS Registry Number: | 75-12-7 |
| Stability: | The test material is known to decompose in air at temperatures greater than approximately 180°C (Merck Index, 9th Ed.) forming carbon monoxide and ammonia. Although sample decomposition may have occurred under the conditions of atmosphere generation, no attempt was made to identify or quantitate the decomposition products. |
| In Life Phase Initiated - Completed: | 8/24/87 - 9/18/87 |
| Notebooks: | E-51347, pp. 2-152<br>E-54662, pp. 1-17<br>E-51347-AA |
| Sponsor: | Central Research and Development Department<br>E. I. du Pont de Nemours and Company, Inc.<br>Wilmington, Delaware |
| Material Submitted By: | David B. Warheit<br>Central Research and Development Department<br>E. I. du Pont de Nemours and Company, Inc.<br>Wilmington, Delaware |

There are 144 pages in this report.

| | |
|---|---|
| Distribution: | G. L. Kennedy Jr. (1)<br>N. C. Chromey/D. B. Warheit (1)<br>J. B. Rhodes (1) |

# Subchronic Inhalation Toxicity Study with Formamide in Rats

## SUMMARY

A study was carried out to determine the toxic effects of repeated inhalation of sublethal concentrations of formamide. Three groups of 10 male Crl:CD®BR rats were exposed 6 hours/day, 5 days/week for 2 weeks to design concentrations of 100, 500 or 1500 ppm of formamide vapor in air. A control group of 10 male rats was exposed simultaneously to air only. At the end of the exposure period, blood and urine samples were collected for clinical analyses, and 5 rats per group were sacrificed for pathologic examination. The remaining 5 rats per group were retained for a 14-day postexposure observation period and then subjected to the same clinical and pathologic examinations.

Male rats exposed to 1500 ppm had significantly depressed body weights and body weight gains during the exposure and recovery periods compared to controls. In addition, 3 rats from this group either were found dead or sacrificed in extremis prior to completion of the study. No biologically significant body weight changes were observed in male rats exposed to 100 or 500 ppm. In addition, rats exposed to 1500 ppm had increased incidences of clinical signs of toxicity, manifested by diarrhea, weakness and hunched postures.

Clinical pathologic examinations revealed that rats exposed to 500 and 1500 ppm of formamide were thrombocytopenic after 10 days of exposure and following 14 days of recovery. The biological significance of this mild thrombocytopenia was considered to be equivocal. A lymphopenia and minimal hypercholesterolemia were also observed in rats in the 1500 ppm group after 10 days of exposure. The biologically and statistically significant lymphopenia persisted after 14 days of recovery.

Pathologic examinations revealed compound-related microscopic changes in the kidneys of rats exposed to 1500 ppm formamide. Nephrosis was characterized by necrosis and regeneration of the renal tubular cells in the deep cortical nephrons. These alterations were prominent after the 10th exposure, however, only regeneration of the tubular cells was evident following the 14-day recovery period. In addition, statistically and biologically significant lower mean final body weights and elevated kidney-to-body weight ratios were observed in rats exposed to 1500 ppm formamide. Mean absolute kidney weights of this group at 0 day recovery were elevated, significant biologically but not statistically. After 14 days of recovery, the same group had statistically and biologically significant lower mean final body weights and elevated mean absolute and relative (i.e., kidney-to-body weight ratios) kidney weights.

Based upon the hematologic and clinical chemical parameters measured, the no-effect exposure concentration for repeated inhalation of formamide was considered to be 100 ppm, under the conditions of this study. The findings of treatment-related microscopic lesions in the kidneys concomitant with increases in kidney-to-body weight ratios reflect the target organ toxicity.

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Acknowledgements: Laura A. Kinney and Thomas A. Kegelman also participated in the conduct of this study.

DBW:smk:HLR87.3

## REFERENCES

1. Kennedy GL, Jr. Biological effects of acetamide, formamide, and their monomethyl and dimethyl derivatives.

2. Scailteur V and Lauwerys RR. Dimethylformamide (DMF) hepatotoxicity. Toxicology 43: 231-238, 1987.

3. BASF Corp., unpublished data.

4. The Du Pont Co. unpublished data, HLR 727-87.

5. The Du Pont Co. unpublished data, MR-125-26.

## INTRODUCTION

Formamide is widely used as a solvent in the manufacture and processing of plastics (1). The current TLV® for formamide is based primarily on the toxicity information of an analog, i.e., dimethylformamide (DMF). The target organ for DMF following most routes of exposure is the liver (1,2). A recently completed 3-month dermal study with formamide produced a number of organ weight changes and polycythemia but did not show the liver to be particularly sensitive to the compound (3). Since inhalation is the exposure route of industrial importance, it was necessary to investigate the inhalation toxicity of formamide following single and repeated exposures.

Formamide is slightly toxic in male rats on an acute inhalation basis (4-hour ALC of 21 mg/l (11,403 ppm)(4). The purpose of this study was to determine the toxic effects of repeated inhalation of sublethal concentrations of formamide.

## MATERIALS AND METHODS

### A. General Experimental Design

Four groups of 10 male rats were used to assess the toxic effects of repeated formamide inhalation on body weights, clinical signs, clinical pathology and pathology parameters. Three test groups were exposed to design concentrations of 100, 500 or 1500 ppm of formamide vapor in air. A control group of age-, sex- and weight-matched rats was exposed simultaneously to air only. Rats were exposed 6 hours/day, 5 days/week for 2 weeks, and were retained for a 14-day postexposure recovery period. All rats were monitored for body weight changes and clinical signs of toxicity throughout the study.

At the end of the exposure period, blood and urine samples were collected from all surviving rats per group for clinical analyses, and 5 rats per group were sacrificed for pathologic examination (In the 1500 ppm group, 2 rats were found dead on test days 3 and 9; additionally, 1 rat was sacrificed *in extremis* on test day 11). After 14 days of recovery, the remaining 5 male rats per group were given similar clinical and pathologic examinations (4 rats in the 1500 ppm group).

The complete protocol and protocol amendments for this study are attached as Appendix A.

B. Animal Husbandry

Seven-week-old Crl:CD®BR rats (born 6/29/87) were received from Charles River Breeding Laboratories, Kingston, New York on 8/18/87. Rats were housed 1 per cage in 5" x 11" x 7" suspended, stainless steel, wire mesh cages. Each rat was assigned a 6-digit identification number which was recorded on a card affixed to the cage. Rats were quarantined for 1 week prior to testing, and were weighed and observed 3 times during the quarantine period. During this time, rats were assigned to 4 treatment groups of 10 male rats each. The rats were grouped using a computer randomization program such that the groups' mean body weights 3 days prior to the start of the exposures were similar. After grouping, each rat was assigned a 1-2 digit identification number that was tattooed on the rat's tail and recorded on a card affixed to the cage. Upon grouping, rats were housed in pairs in 8" x 14" x 8" cages. Rats were approximately 8 weeks old and weighed between 215 and 247 grams at the start of exposures. Except during exposures, Purina Certified Rodent Chow® #5002 and water were available ad libitum.

C. Inhalation Procedures

1. Exposure Protocol

Four groups of 10 male rats were individually restrained in perforated, stainless steel cylinders with conical nose pieces. Each restrainer was inserted into a face plate on the exposure chambers such that only the nose of each rat protruded into the chamber. The exposures were conducted 6 hours/day, 5 days/week for 2 weeks, and were followed by a 14-day recovery period. Three test groups were exposed nose-only to design concentrations of 100, 500 or 1500 ppm of formamide vapor in air (groups III, V and VII, respectively). A control group was exposed to air only (group I).

2. Atmosphere Generation

For the low-level chamber, the test atmosphere was generated by metering formamide into a 1000 ml Instatherm® flask using a Harvard® model 975, compact infusion pump. The flask was heated to 182°C which vaporized the formamide. For the intermediate level and high level exposure chambers, a 1000 ml, three-neck, round-bottom flask was heated to up to 240°C inside a heating mantle. Nitrogen introduced into the system at the flask swept the vapor into the chamber. Dilution air was introduced between the flask and chamber (approximately 42 l/min). For all exposure chambers, the vapor/air mixtures were dispersed with a dispersion funnel as they entered the 38-liter glass exposure chambers. The chambers were exhausted through scrubbers containing water, dry ice cold traps and MSA cartridge filters prior to being vented into the hoods. The control rats were exposed in the same type of exposure chamber to approximately 40 l/min of air only.

3. Analysis of the Test Atmospheres

The atmospheric concentration of formamide in each exposure chamber was determined at approximately 45-minute intervals during each exposure. Samples of the chamber atmospheres were collected in duplicate from the rats' breathing zones with tandem midget impingers containing methanol as a trapping solvent. Each sample was injected into a Hewlett Packard 5880 gas chromatograph equipped with a flame ionization detector. Samples were chromatographed isothermally at 70°C on a 30 m x 0.53 mm ID polydimethylsiloxane capillary column. The atmospheric concentration of formamide was calculated by comparing peak areas with standard curves prepared daily. Standards were prepared weekly or when deemed necessary by study personnel by diluting a known amount of liquid formamide in a volumetric flask containing methanol.

During each exposure, chamber temperatures were measured with mercury thermometers, relative humidities were measured with a Vaisala® HMI 31F Temperature and Humidity Indicator or Bendix Model 566 psychrometer, and chamber oxygen contents were measured with a Biosystems Model 3100R oxygen monitor.

D. Body Weights and Clinical Observations

During the exposure period, all rats were weighed and observed for clinical signs of toxicity before each exposure. Rats could not be observed during exposure due to the physical design of the chambers. However, group observations for clinical signs were taken immediately following each exposure. During the recovery period, all rats were weighed and observed daily, weekends excluded except when warranted by the rats' condition.

E. Clinical Measurements

Urine samples were collected overnight from all surviving rats after the 9th exposure, and from the remaining rats on the 13th day of recovery. Samples were analyzed for volume, osmolality, urobilinogen, pH, hemoglobin or occult blood, glucose, protein, bilirubin and ketone by personnel from the Clinical Pathology Section of Haskell Laboratory. The color and transparency of each sample was noted, and the sediment from each sample was examined microscopically.

Blood samples were taken from the orbital sinus of all surviving rats after the 10th exposure, and from the remaining rats on the 14th day of recovery. Blood samples were analyzed for erythrocyte count, hemoglobin concentration, hematocrit, platelet count, leukocyte count, and relative numbers of neutrophils, band neutrophils, lymphocytes, atypical lymphocytes, eosinophils, monocytes and basophils by personnel from the

Clinical Pathology Section of Haskell Laboratory. Mean corpuscular volume, mean corpuscular hemoglobin and mean corpuscular hemoglobin concentration were calculated from the erythrocyte data. Serum activities of alkaline phosphatase, alanine aminotransferase and aspartate aminotransferase, and serum concentrations of urea nitrogen, creatinine, total protein and cholesterol were also measured.

## F. Pathology

The 10 male rats per group were each subdivided into groups of 5 based on computer-generated random number tables. The first 5 rats per group were killed after the 10th exposure by sodium pentobarbital anesthesia and exsanguination (3 from group VII), and the remaining rats were killed on the 14th day of recovery for gross and histopathologic examinations (4 from group VII). The lungs, liver, kidneys, spleen and testes were weighed at necropsy, and representative samples of the following tissues were obtained for microscopic examination: heart, lungs, mesenteric lymph nodes, nasal cavities (nose), trachea, liver, pancreas, esophagus, stomach, duodenum, jejunum, ileum, cecum, colon, rectum, kidneys, urinary bladder, bone marrow (sternal), spleen, thymus, thyroid gland, adrenal glands, brain, eyes, testes, epididymides, and any other organs or tissues with gross lesions.

## G. Statistical Analyses

Mean body weights and body weight gains for test rats were compared to controls during the exposure and recovery periods. Data were statistically analyzed by one-way analysis of variance. Exposure group values were compared to controls by the least significant difference test when the ratio of variance (F) indicated a significant among-to-within group variation. Significant differences were declared at the 0.05 probability level. The statistical analyses used to evaluate the clinical pathology data, mean organ weights ("absolute" weights) and mean organ-to-body weight ratios ("relative" weights) are described in the respective supplementary reports (Appendices E and F).

## H. Records Retention

All raw data (including slides and paraffin-blocked tissues) and final reports 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, Inc., Wilmington, Delaware.

## RESULTS AND DISCUSSION

### A. Exposure Conditions

In the test chambers, chamber temperatures ranged between 23-32°C, relative humidities ranged from 31-51%, and chamber oxygen contents ranged from 20-21%. In the control chamber, chamber temperature ranged between 23-32°C, relative humidity ranged from 31-51%, and chamber oxygen content was 21%. Overall mean atmospheric concentrations are presented in the following table. Daily atmospheric characterization data are presented in Appendix B.

Mean Atmospheric Concentrations of Formamide[a]

| Group No. | Design Concentration | Analyzed Concentration (ppm) Mean | S.D. | Range |
|---|---|---|---|---|
| I | 0 ppm | - | - | - |
| III | 100 ppm | 113 | 33.8 | 56.2 - 280 |
| V | 500 ppm | 500 | 97.4 | 148 - 841 |
| VII | 1500 ppm | 1504 | 284 | 449 - 2215 |

[a] Represents the mean, standard deviation and range of all samples from all exposures (approximately 100 samples per exposure chamber).
- Refers to values which were not measured.

### B. Body Weight Analyses

No biologically significant differences in mean body weights were observed in rats exposed to 100 or 500 ppm of formamide. A few instances of statistically significant reductions in body weight gains were observed in rats exposed during the first week of exposure to 100 and 500 ppm of formamide. All of these and other sporadic differences were considered incidental and unrelated to the test material.

Rats exposed to 1500 ppm had significantly depressed mean body weights which were evident following the 4th exposure and lasted until the 6th day of the postexposure recovery period. Similarly, mean body weight gains were significantly reduced during the 1st week of exposure in rats exposed to 1500 ppm formamide. Growth curves for rats are attached as Figure 1. Daily mean body weights and mean body weight gains are presented in Tables 1 and 2. Individual body weights are presented in Appendix C.

## C. Clinical Observations

Immediately following exposures, rats in all groups (including controls) frequently had red nasal and ocular discharges and/or diarhhea, effects common in rats under restraint. No other clinical signs of toxicity were observed following exposure.

During the test period, 2 rats (Nos. 425524 and 425526) exposed to 1500 ppm formamide were found dead on days 3 and 9, respectively. Another rat from this group (No. 425523) was sacrificed in extremis on test day 11. The rat found dead on test day 3 had no gross or microscopic lesions which would suggest the cause of death. The other 2 rats had moderate and severe nephrosis, as revealed by microscopic examination of the kidneys.

During the exposure period, low incidences of diarrhea were observed in all groups. In addition, a low incidence of weakness and hunched posture was observed in rats exposed to 1500 ppm formamide. Following termination of the exposure period, colored discharges of the eyes and/or nose were observed in 2 rats from the control group and in 2 rats exposed to 1500 ppm formamide. Five rats exhibited diarrhea in the 1500 ppm group during the recovery period. Summaries of clinical observations for male rats are presented in Table 3. Individual clinical observations are presented in Appendix D. Group observations of clinical signs taken immediately following exposures are not presented.

## D. Clinical Pathology

A statistically significant thrombocytopenia was present in male rats exposed to 500 and 1500 ppm of formamide. There was no evidence of platelet regeneration observed in blood smears from rats in the affected groups. The biological significance of this mild thrombocytopenia was considered to be equivocal. In addition, a statistically and biologically significant lymphopenia was observed in rats exposed to 1500 ppm formamide. Following 14 days of recovery, the thrombocytopenia persisted in both groups, and the lymphocyte count remained depressed in animals exposed to 1500 ppm formamide.

Statistically significant increases in serum cholesterol were observed in rats exposed to 1500 ppm formamide after 10 exposures, but this result was considered to be of minimal biological significance. All other observed differences were considered incidental and unrelated to the test material. Clinical Pathology Report No. 2-88 is attached as Appendix E. Under the conditions of this study, the no-observable-effect level was considered to be 100 ppm for the hematologic and clinical chemical parameters measured.

E. Pathology

Compound-related lesions were observed in the kidneys of male rats exposed to 1500 ppm of formamide. These alterations, diagnosed as nephrosis, were zonal in the inner cortex and outer medulla and were characterized by degeneration and necrosis of the tubulular epithelium. All tubular segments in the deep cortical nephrons were affected. After the 10th exposure, the minimal to severe renal lesions consisted of necrosis and regeneration of the tubulular epithelium. Tubules were lined by basophilic regenerative cells, some of which were in mitosis, and desquamated necrotic cells filled the lumens. Some tubules were dilated and lined by flattened epithelium. Occasionally, mineralized necrotic debris was surrounded by granulomatous inflammation. After 14 days of recovery, the mild renal lesion consisted of regeneration of the tubulular epithelium with no necrosis present.

A number of changes diagnosed microscopically were not considered to be compound-related. These alterations included depletion of lymphocytes in the spleen, thymus, and lymph nodes, gastric erosion, degeneration of seminiferous epithelium in the testes, and atrophy of bone marrow. Such changes are not uncommon or unexpected in stressed rats with weight gain reductions.

Statistically and biologically significant reduced mean final body weights and increased kidney-to-body weight ratios were observed after the 10th exposure in rats exposed to 1500 ppm of formamide. Following the 14-day recovery period, rats had statistically and biologically significant reduced mean final body weights and elevated mean absolute weights and kidney-to-body weight ratios. Although not statistically significant, the mean absolute and relative spleen weights in the 1500 ppm formamide group were elevated, as were the mean relative testis weights.

The alterations in kidney weights reflect target organ toxicity, while the differences in spleen and testis weights are most probably indicative of weight gain inhibition and stress. Based on the renal lesion produced by formamide exposure under the conditions of this study, the no-effect exposure concentration for histopathology was considered to be 500 ppm. Pathology Report No. 2-88 is attached as Appendix F.

## CONCLUSION

Male rats exposed to 1500 ppm formamide had compound-related renal lesions. Following termination of exposure, formamide-induced nephrosis was characterized by necrosis and regeneration of the renal tubular cells in the deep cortical nephrons. After a 14-day recovery period, regeneration of the tubulular cells was the the only feature of the lesion. Rats exposed to 1500 ppm formamide had statistically and biologically significant decreased mean body weights and higher relative kidney weights following termination of exposure. Mean absolute kidney weights were also elevated but were not statistically significant. Following the 14-day recovery period, the alterations in these parameters were unchanged when compared to controls.

A statistically significant thrombocytopenia was present in male rats exposed to 500 and 1500 ppm of formamide. There was no evidence of platelet regeneration observed in blood smears from rats in the affected groups. In addition, a statistically and biologically significant lymphopenia was observed in rats exposed to 1500 ppm formamide. Following 14 days of recovery, the thrombocytopenia persisted in both groups, and the lymphocyte count remained depressed in animals exposed to 1500 ppm formamide.

Although a thrombocytopenia was observed in rats exposed to 500 and 1500 ppm of formamide, the biological significance of this finding was considered to be equivocal. Furthermore, histopathologic examination of rats exposed to 100, 500, or 1500 ppm of formamide failed to demonstrate any alterations in bone marrow megakaryocytopoiesis which might confirm the effects of formamide exposure on platelet production.

In retrospect, the statistically significant increase in urea nitrogen in the 1500 ppm group was probably due to the renal lesions observed in histopathologic studies. However, urea nitrogen and creatinine are relatively insensitive indicators of renal filtration function and present little or no information about tubular function. The fact that urea nitrogen, creatinine, and urine osmolality are not biologically significant indicates that at least one-third or more of the nephrons were functional.

Rats exposed to 1500 ppm had significantly depressed body weights and body weight gains during the exposure and recovery phases of the study. In addition, increased incidences of clinical signs of toxicity were evident in the 1500 ppm group, manifested by diarrhea, weakness and hunched postures.

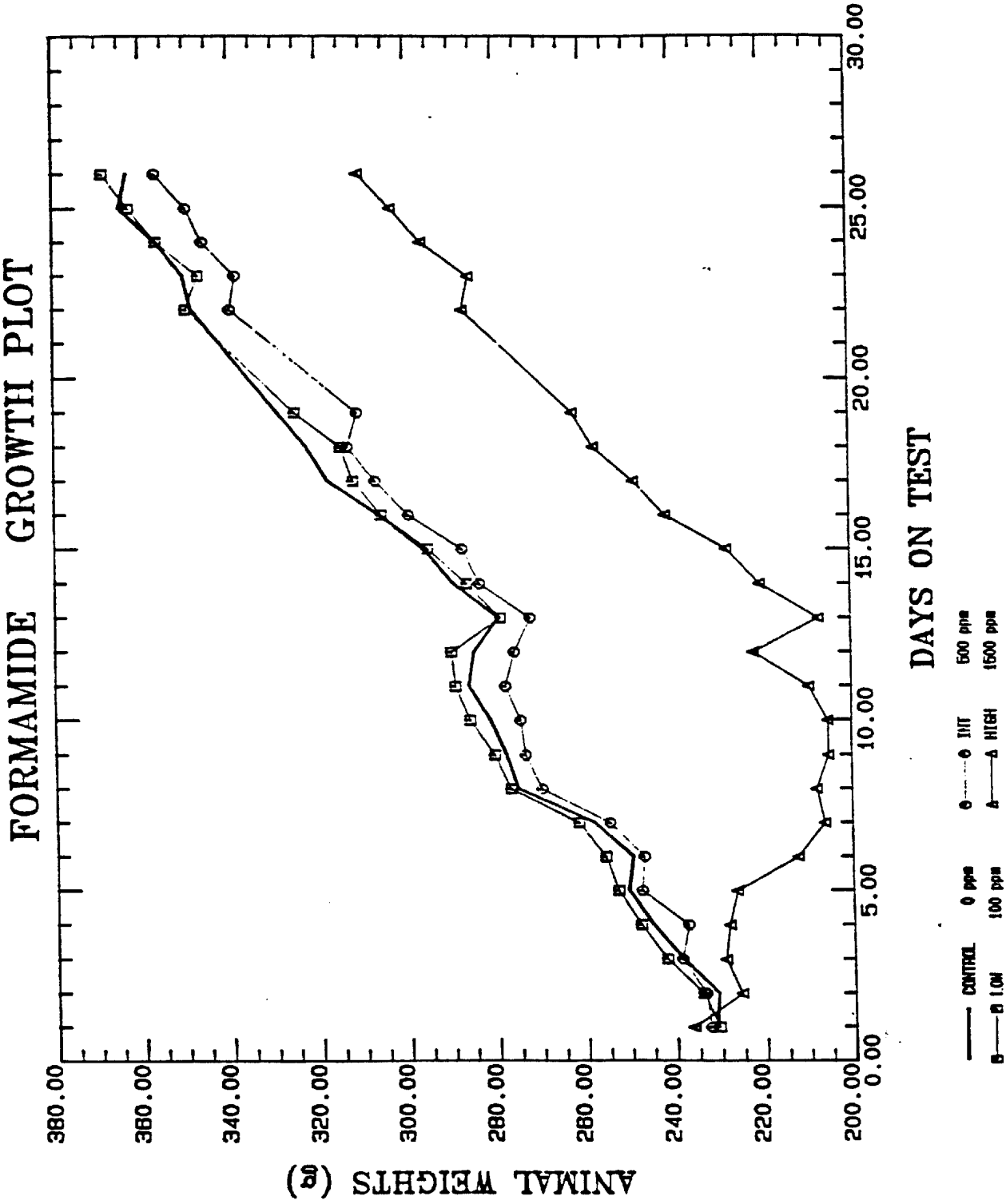
There is a paucity of data regarding the inhalation toxicity of formamide. Previous reports have suggested that toxicity by inhalation exposure was low. In these studies, no signs of toxicity were detected in rats given a single exposure of formamide for 6 hours at 3900 ppm or in 2 rats exposed for 10 days duration at concentrations approximating 1500 ppm vapor (5). In the latter study, no indications of organ damage were observed

following pathologic evaluation. The studies presented here indicate that 10 repeated exposures to formamide at concentrations of 1500 ppm produce nephrotoxicity, characterized by necrosis and regeneration of renal tubular cells. Moreover, formamide exposure resulted in a thrombocytopenia and lymphopenia.

The current TLV® for formamide is based essentially on information regarding the toxicity of an analog, i.e, dimethyl formamide (DMF). The target organ for DMF is the liver. We have demonstrated here that the liver does not appear to be affected by repeated formamide exposures. In contrast to DMF, we have shown that formamide-induced lesions were observed in the kidneys of male rats exposed to 1500 ppm of formamide.

Under the conditions of this study, the no-effect exposure level for male rats is considered to be 100 ppm, based on the hematologic and clinical chemical parameters measured in the rats exposed to 500 ppm formamide. Clinical pathologic examinations revealed that rats exposed to 500 and 1500 ppm of formamide were thrombocytopenic after 10 days of exposure and following 14 days of recovery. The biological significance of this mild thrombocytopenia was considered to be equivocal. Based upon the histopathologic finding of renal lesions at 1500 ppm, as well as a biologically significant lymphopenia at 1500 ppm, 500 ppm appears to be the exposure concentration at which adverse effects begin to occur in male rats.

FIGURE 1


FORMAMIDE GROWTH PLOT
ANIMAL WEIGHTS (g)
380.00
360.00
340.00
320.00
300.00
280.00
260.00
240.00
220.00
200.00
0.00
5.00
10.00
15.00
20.00
25.00
30.00
DAYS ON TEST
CONTROL
LOW
0 ppm
100 ppm
INT
500 ppm
HIGH
1500 ppm

Subchronic Inhalation Toxicity Study with Formamaide

Table 1

Mean Body Weights (grams) of Male Rats

| Group: | I | III | V | VII |
|---|---|---|---|---|
| Conc.: | 0 ppm | 100 ppm | 500 ppm | 1500 ppm |
| **Days on Test** | | | | |
| **Exposure Period** | | | | |
| 1 | 230.9 (8.06) | 230.7 (6.96) | 232.4 (9.16) | 236.3 (8.45) |
| 2 | 230.5 (9.74) | 234.1 (7.12) | 233.5 (9.08) | 225.5 (14.0) |
| 3 | 238.3 (9.17) | 242.1 (9.06) | 238.8 (11.6) | 229.0 (16.9) |
| 4 | 244.9 (12.6) | 247.9 (9.71) | 237.2 (10.6) | 228.1 (12.9)* |
| 5 | 250.3 (11.3) | 252.9 (10.3) | 247.5 (13.3) | 226.3 (18.9)* |
| 6 | 249.2 (11.5) | 255.6 (9.89) | 246.9 (14.6) | 212.5 (17.7)* |
| 7 | 258.0 (12.9) | 261.7 (10.3) | 254.7 (15.7) | 206.4 (18.9)* |
| 8 | 275.1 (13.4) | 277.2 (10.8) | 270.0 (17.0) | 208.1 (14.4)* |
| 9 | 277.7 (12.8) | 280.6 (12.3) | 273.7 (18.0) | 205.3 (18.0)* |
| 10 | 281.3 (15.9) | 286.1 (13.5) | 274.7 (17.8) | 205.5 (21.3)* |
| 11 | 286.1 (16.4) | 289.3 (12.6) | 278.2 (18.8) | 209.7 (29.2)* |
| 12 | 284.9 (20.0) | 290.2 (19.7) | 276.1 (26.0) | 222.2 (15.8)* |
| **Recovery Period** | | | | |
| 13 | 279.2 (11.6) | 279.1 (9.28) | 272.4 (14.5) | 207.4 (6.48)* |
| 14 | 289.5 (11.9) | 286.7 (9.48) | 283.8 (16.6) | 220.6 (5.41)* |
| 15 | 296.2 (10.7) | 295.4 (8.91) | 287.5 (21.5) | 227.9 (5.49)* |
| 16 | 306.3 (12.2) | 305.8 (9.21) | 299.7 (19.3) | 241.5 (6.37)* |
| 17 | 317.7 (12.1) | 312.2 (11.0) | 307.2 (20.4) | 248.5 (7.89)* |
| 18 | 322.5 (11.3) | 315.1 (8.45) | 313.4 (20.0) | 257.6 (8.04)* |
| 19 | 329.1 (13.0) | 325.4 (9.62) | 311.1 (30.1) | 262.3 (5.59) |
| 22 | 348.3 (15.0) | 349.8 (10.2) | 339.7 (26.4) | 287.1 (11.2) |
| 23 | 350.1 (15.0) | 347.0 (9.98) | 338.5 (26.9) | 285.6 (15.1) |
| 24 | 356.4 (14.7) | 356.6 (9.73) | 346.0 (27.8) | 296.2 (13.4) |
| 25 | 364.6 (16.5) | 362.7 (9.08) | 349.5 (27.5) | 303.2 (16.0) |
| 26 | 362.8 (17.9) | 368.6 (6.22) | 356.7 (32.7) | 310.6 (12.0) |

Values in parentheses are standard deviations.
* Significantly different from controls by least significant difference test ($p<0.05$).

Subchronic Inhalation Toxicity Study with Formamide

Table 2

Mean Body Weight Gains (grams) of Male Rats

| Group: Conc.: | I 0 ppm | III 100 ppm | V 500 ppm | VII 1500 ppm |
|---|---|---|---|---|
| Days on Test | | | | |
| 1- 2 | -0.4 (3.97) | 3.4 (3.85) | 1.1 (4.87) | -10.8 (11.2)* |
| 2- 3 | 7.8 (2.59) | 8.0 (3.21) | 5.2 (4.13) | 3.4 (8.18) |
| 3- 4 | 6.6 (5.33) | 5.8 (2.55) | -1.6 (4.74)* | -4.4 (9.05)* |
| 4- 5 | 5.3 (4.96) | 5.0 (2.50) | 10.4 (5.61)* | -1.8 (7.78)* |
| 5- 6 | -1.0 (3.27) | 2.7 (2.34)* | -0.6 (3.48) | -13.8 (5.51)* |
| 6- 7 | 8.8 (2.98) | 6.0 (2.14) | 7.7 (2.51) | -6.1 (9.18)* |
| 7- 8 | 17.1 (3.82) | 15.5 (2.90) | 15.3 (4.77) | 1.7 (11.0)* |
| 8- 9 | 2.6 (1.71) | 3.4 (8.24) | 3.8 (4.38) | -2.8 (7.99) |
| 9-10 | 3.6 (4.40) | 5.5 (8.58) | 1.0 (2.99) | 0.8 (5.79) |
| 10-11 | 4.8 (1.68) | 3.2 (3.88) | 3.4 (2.72) | 4.2 (14.3) |
| 11-12 | -1.2 (7.98) | 1.0 (11.5) | -2.1 (12.0) | 2.8 (15.1) |
| 12-13 | -8.6 (6.48) | -0.8 (16.4) | -8.5 (14.5) | -10.4 (7.36) |
| 13-14 | 10.2 (5.46) | 7.6 (2.80) | 11.4 (3.63) | 13.3 (3.42) |
| 14-15 | 6.7 (1.82) | 8.7 (1.76) | 3.7 (8.81) | 7.3 (3.46) |
| 15-16 | 10.1 (2.29) | 10.5 (2.43) | 12.2 (7.24) | 13.6 (1.05) |
| 16-17 | 11.5 (2.27) | 6.3 (1.89) | 7.6 (1.70) | 7.0 (3.09) |
| 17-18 | 4.8 (3.64) | 2.9 (3.32) | 6.1 (3.72) | 9.1 (4.32) |
| 18-19 | 6.6 (4.81) | 10.4 (2.45) | -2.2 (15.9) | 4.7 (3.55) |
| 19-22 | 19.2 (5.30) | 24.4 (2.67) | 28.5 (12.1) | 24.8 (5.89) |
| 22-23 | 1.8 (3.59) | -2.8 (1.87) | -1.2 (2.56) | -1.5 (6.10) |
| 23-24 | 6.3 (2.81) | 9.6 (4.08) | 7.5 (3.18) | 10.6 (1.96) |
| 24-25 | 8.1 (3.27) | 6.1 (5.09) | 3.6 (2.34) | 7.0 (2.99) |
| 25-26 | -1.7 (8.67) | 5.9 (5.12) | 7.2 (6.45) | 7.3 (8.35) |
| 1-5[a] | 19.4 (5.48) | 22.2 (6.36) | 15.1 (6.61) | -9.2 (19.0)* |
| 8-12[b] | 9.8 (10.1) | 13.1 (12.5) | 6.2 (14.0) | 13.0 (23.5) |
| 1-12[c] | 54.0 (15.6) | 59.5 (16.1) | 43.7 (20.5) | -12.2 (19.4)* |
| 13-26[d] | 83.6 (11.4) | 89.5 (7.92) | 84.3 (19.6) | 103.2 (17.0) |

Values in parentheses are standard deviations.
* Significantly different from controls by least significant difference test ($p<0.05$).
[a] First week of exposures
[b] Second week of exposures
[c] Exposure period
[d] Recovery period

Subchronic Inhalation Toxicity Study with Formamide

Table 3

Summary of Clinical Observations in Male Rats[a]

| Exposure Group: | I | III | V | VII |
|---|---|---|---|---|
| Concentration: | 0 ppm | 100 ppm | 500 ppm | 1500 ppm |
| Observation | Number of Rats Exhibiting Sign[b] | | | |
| Colored Discharge Eye(s) Left | 1 (15) | 0 | 0 | 1 (16) |
| Colored Discharge Eye(s) Right | 1 (15) | 0 | 0 | 0 |
| Colored Discharge Nose | 1 (16) | 0 | 0 | 2 (11) |
| Hunched Over | 0 | 0 | 0 | 3 ( 3) |
| Diarrhea | 3 ( 4) | 2 ( 9) | 1 ( 3) | 5 ( 7) |
| Weak | 0 | 0 | 0 | 2 ( 3) |
| Total Group Incidence: | 6 | 2 | 1 | 13 |

[a] Excluding clinical signs observed during or immediately following exposure.
[b] 10 rats per group.
[c] The number in parentheses is the median day on test that the sign was first observed.

Subchronic Inhalation Toxicity Study with Formamide

## Appendix A

## Protocol and Amendments

# PROTOCOL

## SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE
(MR 5602-001, H# 16,728, Test Code 17)

## PURPOSE

Formamide has very low toxicity on an acute inhalation basis with a 4-hour ALC in rats of approximately 7000 ppm (Haskell Laboratory, report in progress). The purpose of this study is to determine the toxic effects in rats of repeated inhalation of sublethal concentrations of formamide.

## SPONSOR AND TEST DATES

The sponsor of this study is the Central Research and Development Department, E. I. du Pont de Nemours and Company, Inc., Wilmington, Delaware. The sponsor approved of this project on 1/15/87 as indicated by the departmental representative's signature on the MR proposal. The exposure period of this study will begin on 8/24/87. The recovery period will end on 9/18/87.

## STUDY CONDUCT

This protocol and the Acute and Developmental Toxicology Section SOP's constitute the protocol for this study. Except as documented in the SOP's or in the study records, this study will be conducted according to the Environmental Protection Agency, 40 CFR Part 792, Toxic Substances Control Act Good Laboratory Practice Standards.

## TEST MATERIAL

The test material is formamide, greater than 99% pure. The sample was purchased from Aldrich Chemical Company, Lot No. 11021JP and was supplied by D. B. Warheit, Central Research and Development Department, Haskell Laboratory for Toxicology and Industrial Medicine, Newark, Delaware. The test material is assumed to be stable throughout the exposure phase of the test.

## TEST SYSTEM AND HUSBANDRY

| | |
|---|---|
| Sex/Species/Strain | Male Crl:CD®BR rats |
| Source | Charles River Breeding Laboratories, Kingston, New York |
| Age | 8 weeks old at the initiation of the test |
| Weight Range | Approximately 200-260 grams |

### Identification

Each rat will be assigned a unique, 6-digit identification number which will be recorded on a card affixed to the cage. Upon grouping, rats will be assigned 1-2 digit identification numbers that will be tattooed on the rats' tails and recorded on cage cards. Tattoo numbers and corresponding 6-digit numbers will be recorded in the study records. Prior to exposure, rats' tails and cage cards may be color-coded with water-insoluble markers to help identify the exposure group to which each rat belongs.

### Quarantine

Rats will be quarantined for 6 days prior to testing, and will be weighed and observed at least three times during the quarantine period. Rats will be grouped and tattooed during the quarantine period.

### Housing Environment

Animal rooms will be maintained at approximately 50 ± 10% relative humidity and 23 ± 2°C on a 12 hour/12 hour light/dark cycle. Excursions outside of these ranges will not be reported unless they are judged to have significantly affected the study. Before grouping, rats will be housed individually in 5" x 11" x 7" suspended, stainless steel, wire-mesh cages. For the remainder of the test, rats will be housed either in pairs (exposure period) or individually (recovery period) in 8" x 14" x 8" cages except during exposures. Except during exposures, Purina Certified Rodent Chow® #5002 and water will be available *ad libitum*.

# STUDY DESIGN

## General Study Design

Four groups of 10 male rats will be used to assess the toxic effects of repeated formamide inhalation on body weights, clinical signs, clinical pathology and pathology parameters.

Prior to each exposure, each rat will be individually restrained in a perforated, stainless steel cylinder with a conical nose piece. Each restrainer will be inserted into the exposure chamber such that only the nose of each rat protrudes into the chamber. Each group of 10 rats will be exposed nose-only, 6 hours/day, 5 days/week for 2 weeks, followed by a 14-day recovery period. Three test groups will be exposed to design concentrations of 100, 500 or 1500 ppm of formamide vapor in air (Groups III, V and VII, respectively). A control group (Group I) will be exposed simultaneously to air only. Rats will be weighed and observed daily throughout the exposure and recovery periods, weekends excluded unless warranted by the rats' condition.

At the end of the exposure period, blood and urine samples will be collected from 10 rats per group (control and test) for clinical analyses, and 5 rats per group will be killed for pathologic examination. At the end of the recovery period, the remaining 5 rats per group will be given similar clinical pathology and pathology examinations.

## Allocating Rats to Treatment Groups

To control bias, rats will be randomly assigned to control and treatment groups. Four groups of 10 male rats will be selected by computer randomization such that the pretest mean body weights of all groups are similar. Rats will be selected for clinical sampling and sacrifice based on random number tables.

## Rangefinding

Prior to study initiation, rangefinding exposures at all planned exposure concentrations will be conducted to establish the generation parameters needed to produce the desired atmospheric concentrations. In addition, rangefinding exposures in which rats are present in the chamber will be conducted at the high level design concentration to help determine if the chosen concentration will cause detrimental effects without causing mortality. Based on the results of rangefinding exposures, the design concentrations may be adjusted accordingly.

Viability Checks

Each rat will be weighed and observed daily prior to exposure. Observations of group clinical signs will be taken during each exposure and before rats are returned to their cages after exposure. During the recovery period, remaining rats will be weighed and observed daily. Rats will not be weighed on weekends unless warranted by the rats' condition.

Clinical Pathology Examinations

Overnight urine samples will be collected from 10 rats per group after the 9th exposure, and from the remaining 5 rats per group on the 13th day of recovery. Each urine sample will be analyzed by the Clinical Pathology staff of Haskell Laboratory for volume, osmolality, pH, urobilinogen, blood, glucose, protein, bilirubin and ketone. Each specimen will be noted for color and transparency, and the sediment from each sample will be examined microscopically.

Orbital sinus blood samples will be collected from 10 rats per group after the 10th exposure, and from the remaining 5 rats per group on the 14th day of recovery. Blood samples will be analyzed by the Clinical Pathology staff for erythrocyte count, hemoglobin concentration, hematocrit, platelet count, leukocyte count, and relative numbers of neutrophils, band neutrophils, lymphocytes, atypical lymphocytes, eosinophils, monocytes and basophils. Mean corpuscular volume, mean corpuscular hemoglobin and mean corpuscular hemoglobin concentration will be calculated from the erythrocyte data. In addition, serum activities of alkaline phosphatase, alanine aminotransferase and aspartate aminotransferase, and serum concentrations of urea nitrogen, creatinine, total protein and cholesterol will be measured. Additional parameters may be measured at the discretion of the Clinical Pathologist and will be documented in the study records.

Pathology Examinations

Five rats per group will be sacrificed after the 10th exposure, and 5 rats per group will be sacrificed on the 14th day of recovery for gross and histopathologic examination. Rats will be killed by sodium pentobarbital anesthesia and exsanguination by the Pathology staff of Haskell Laboratory. Organs and tissues to be examined include the heart, lungs, mesenteric lymph nodes, nasal cavities, trachea, liver, pancreas, esophagus, stomach, duodenum, jejunum, ileum, cecum, colon, rectum, kidneys, urinary bladder, bone marrow, sternum, spleen, thymus, thyroid gland, adrenal glands, brain, eyes, testes and epididymides. The lungs, liver, kidneys, spleen and testes will be weighed at necropsy. Additional organs or tissues may be examined at the discretion of the Pathologist and will be documented in the study records.

## Statistical Methods

Mean body weights for test rats will be compared to the air controls during the exposure and recovery periods. At each sacrifice, mean organ weights and organ-to-body weight ratios for the lungs, liver, spleen, kidneys and testes will be compared to the air controls. Data will be statistically analyzed by a one-way analysis of variance. Test rats will be compared to the controls by least significant difference (body weights) or by LSD and Dunnett's tests (organ weights) when the ratio of variance (F) indicates a significant among-to-within group variation. Significance will be judged at the 0.05 probability level. Statistical analyses used for clinical pathology and pathology data will be documented in the respective supplementary reports. Additional statistical analyses may be conducted at the discretion of the Study Director and will be documented in the study records.

# ADMINISTRATION OF THE TEST MATERIAL

## Atmosphere Generation

Vapor atmospheres of formamide will be generated by pumping the liquid test material into heated glass round bottom flasks. Nitrogen introduced at the flasks will sweep the resulting vapors through glass connecting tubing and into 38-liter cylindrical glass exposure chambers. Dilution air will be added to the vapor/nitrogen mixtures, and the mixtures will be dispersed with baffles as they enter the chambers. If needed, oxygen gas will be added to the atmospheres to maintain a minimium oxygen level of 19%. The chamber exhausts will be drawn through scrubbers containing an appropriate solvent, dry-ice cold traps and MSA cartridge filters prior to being vented into the hoods. The actual generation equipment and conditions used will be documented in the study records.

## Analysis of the Test Atmospheres

The atmospheric concentration of formamide vapor in each exposure chamber will be measured daily at approximately 30-minute intervals. Known volumes of the chamber atmospheres will be drawn from the rats' breathing zones through midgit impingers containing a suitable trapping solvent. Each sample will be analyzed in duplicate with a Hewlett Packard gas chromatograph equipped with a flame ionization detector. The atmospheric concentrations of formamide will be calculated by comparing the detector response with standard curves prepared daily. Standards will be prepared as needed by diluting known amounts of liquid formamide in the appropriate solvent. Chamber temperatures, relative humidities and oxygen contents in each exposure chamber will be measured daily. Actual analytical equipment and conditions used will be documented in the study records.

## DISPOSAL OF WASTE MATERIALS

Waste materials will be packed in absorbant material and incinerated on site. Unused test material will be returned to the sponsor or discarded.

## FINAL REPORT

A final report will be written which includes, but is not limited to, the items cited in CFR 40, Part 792, Subpart J, Section 792.185.

## PROTOCOL CHANGES

Changes in this protocol will be documented in amendments to this protocol signed by the Study Director.

Study Director: Laura A. Kinney 8/20/87
Laura A. Kinney
Chemist

Approved by: A. Michael Kaplan for NCC 8/21/87
Nancy C. Chromey, Ph.D.
Section Supervisor
Acute and Developmental Toxicology Section

LAK:smk:LAK6.37

CENTRAL RESEARCH AND DEVELOPMENT DEPARTMENT
HASKELL LABORATORY FOR TOXICOLOGY
AND INDUSTRIAL MEDICINE

cc: Q.A. Group

February 21, 1988

TO: MEDICAL RESEARCH PROJECT NO. 5602-001

PROTOCOL AMENDMENT #1

SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

Effective 10/1/87, DB Warheit assumed responsibility from LA Kinney as study director of this project.

Prepared by: David B Warheit

David B. Warheit, Ph.D.
Research Toxicologist
Acute and Developmental Toxicology Division

CENTRAL RESEARCH AND DEVELOPMENT DEPARTMENT
HASKELL LABORATORY FOR TOXICOLOGY
AND INDUSTRIAL MEDICINE

cc: Q.A. Group

March 15, 1988

TO: MEDICAL RESEARCH PROJECT NO. 5602-001

PROTOCOL AMENDMENT #2

SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

The protocol indicated that 5 rats per group would be sacrificed for pathologic analyses both after the exposure and recovery periods. Due to 3 premature deaths in the 200 mg/m³ group, only 3 and 4 rats from this group, respectively, were sacrificed following the end of exposure and recovery periods.

Prepared by: David B Warheit

David B. Warheit, Ph.D.
Research Toxicologist
Acute and Developmental Toxicology Division

Subchronic Inhalation Toxicity Study with Formamide

## Appendix B

## Daily Atmospheric Analyses

# Subchronic Inhalation Toxicity Study with Formamide

## Appendix B

## Daily Atmospheric Analyses

Controls - 0 ppm

| Exposure No. | Formamide[a] Concentration (ppm) Mean | S.D. | Range | Chamber[b] Temp. (°C) | Relative[c] Humidity (%) | Oxygen[d] Content (%) |
|---|---|---|---|---|---|---|
| 1 | - | - | - | 25-26 | 34 | - |
| 2 | - | - | - | 24 | 37 | - |
| 3 | - | - | - | 25-26 | 39 | 21 |
| 4 | - | - | - | 24 | 41 | 21 |
| 5 | - | - | - | 23-25 | 46 | - |
| 6 | - | - | - | 23 | 47 | 20.6 |
| 7 | - | - | - | 24-25 | 44 | 20.9 |
| 8 | - | - | - | 23-25 | 51 | 21 |
| 9 | - | - | - | 24 | 43 | 20.9 |
| 10 | - | - | - | 23-24 | 48 | - |

Design Concentration of 100 ppm

| Exposure No. | Formamide[a] Concentration (ppm) Mean | S.D. | Range | Chamber[b] Temp. (°C) | Relative[c] Humidity (%) | Oxygen[d] Content (%) |
|---|---|---|---|---|---|---|
| 1 | 84.5 | 19.1 | 56.2 - 112 | 26 | 34 | 21.1 |
| 2 | 131 | 22.1 | 95.3 - 167 | 27-30 | 37 | - |
| 3 | 159 | 46.0 | 77.6 - 222 | 28-29 | 37 | 21.2 |
| 4 | 132 | 53.1 | 89.5 - 280 | 29 | 51 | 21.5 |
| 5 | 117 | 20.1 | 79.1 - 149 | 28-31 | 47 | - |
| 6 | 94.3 | 10.5 | 77.6 - 115 | 28-30 | 46 | 20.3 |
| 7 | 91.1 | 13.2 | 75.2 - 118 | 28-30 | 41 | 20.8 |
| 8 | 115 | 18.1 | 85.7 - 150 | 28-31 | 46 | 20.8 |
| 9 | 101 | 14.7 | 81.7 - 129 | 28-31 | 40 | 20.9 |
| 10 | 108 | 10.4 | 91.5 - 121 | 27-28 | 46 | - |

[a] Mean of 9-11 samples per exposure
[b] One to 3 measures per exposure
[c] One measure per exposure
[d] One measure per exposure
- Refers to values which were not measured

# Subchronic Inhalation Toxicity Study with Formamide

## Appendix B

## Daily Atmospheric Analyses

Design Concentration of 500 ppm

| Exposure No. | Formamide[a] Concentration (ppm) Mean | S.D. | Range | Chamber[b] Temp. (°C) | Relative[c] Humidity (%) | Oxygen[d] Content (%) |
|---|---|---|---|---|---|---|
| 1 | 457 | 30.2 | 409 - 496 | 27-30 | 34 | 21.1 |
| 2 | 485 | 161 | 148 - 657 | 28-30 | 36 | - |
| 3 | 536 | 70.0 | 443 - 673 | 26-30 | 37 | 21.1 |
| 4 | 516 | 153 | 311 - 841 | 27-30 | 51 | 21.0 |
| 5 | 522 | 66.3 | 359 - 619 | 27-30 | 42 | - |
| 6 | 457 | 93.4 | 355 - 617 | 27-30 | 43 | 20.5 |
| 7 | 512 | 107 | 341 - 670 | 27-28 | 42 | 20.9 |
| 8 | 501 | 49.6 | 427 - 562 | 26-30 | 44 | 20.8 |
| 9 | 504 | 69.6 | 324 - 577 | 27-30 | 41 | 20.9 |
| 10 | 509 | 94.5 | 437 - 731 | 27-28 | 45 | - |

Design Concentration of 1500 ppm

| Exposure No. | Formamidea Concentration (ppm) Mean | S.D. | Range | Chamber[b] Temp. (°C) | Relative[c] Humidity (%) | Oxygen[d] Content (%) |
|---|---|---|---|---|---|---|
| 1 | 1576 | 200 | 1264 - 1780 | 29-32 | 31 | 20.8 |
| 2 | 1384 | 116 | 1245 - 1585 | 29-31 | 37 | - |
| 3 | 1815 | 331 | 1304 - 2055 | 27-32 | 35 | 20.9 |
| 4 | 1519 | 407 | 1058 - 2215 | 28-30 | 42 | 21.1 |
| 5 | 1496 | 176 | 1267 - 1699 | 26-30 | 44 | - |
| 6 | 1360 | 341 | 449 - 1686 | 27-31 | 40 | 20.6 |
| 7 | 1449 | 189 | 1239 - 1805 | 27-30 | 37 | 20.9 |
| 8 | 1418 | 280 | 1074 - 1799 | 27-30 | 43 | 20.8 |
| 9 | 1481 | 249 | 1005 - 1916 | 27-31 | 37 | 20.9 |
| 10 | 1569 | 204 | 1174 - 1837 | 26-29 | 37 | - |

[a] Mean of 9-11 samples per exposure
[b] One to 3 measures per exposure
[c] One measure per exposure
[d] One measure per exposure

Subchronic Inhalation Toxicity Study with Formamide

## Appendix C

## Individual Body Weights (grams) of Male Rats

Subchronic Inhalation Toxicity Study with Formamide

Appendix C
Individual Body Weights (grams) of Male Rats
Group: I Concentration: 0 ppm

| Rat No. | Days on Test 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
|---|---|---|---|---|---|---|---|---|---|
| 425489 | 221.6 | 221.5 | 227.8 | 231.8 | 236.6 | 238.8 | 244.0 | 262.5 | 267.0 |
| 425490 | 234.7 | 231.0 | 241.8 | 244.2 | 250.2 | 248.6 | 262.1 | 270.9 | 271.0 |
| 425491 | 221.4 | 221.6 | 227.6 | 238.4 | 248.0 | 248.4 | 256.4 | 275.4 | 279.0 |
| 425492 | 234.2 | 233.8 | 245.1 | 250.7 | 257.1 | 255.9 | 262.1 | 280.4 | 284.0 |
| 425493 | 223.2 | 225.2 | 234.2 | 240.1 | 242.0 | 242.4 | 248.0 | 269.0 | 273.0 |
| 425494 | 221.0 | 214.2 | 224.1 | 222.3 | 229.2 | 226.0 | 232.9 | 247.8 | 252.0 |
| 425495 | 239.8 | 235.5 | 243.9 | 250.7 | 257.7 | 251.3 | 263.6 | 284.8 | 285.0 |
| 425496 | 238.7 | 238.1 | 246.1 | 250.1 | 263.3 | 259.2 | 267.5 | 284.8 | 286.0 |
| 425497 | 235.4 | 238.0 | 242.0 | 253.3 | 256.3 | 254.4 | 266.5 | 279.7 | 281.0 |
| 425498 | 239.0 | 246.3 | 250.5 | 267.7 | 262.2 | 267.3 | 276.7 | 295.7 | 299.0 |

| Rat No. | Days on Test 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 |
|---|---|---|---|---|---|---|---|---|---|
| 425489 | 270.2 | 275.8 | 279.1 | 263.3 | 274.6 | 284.5 | 290.6 | 304.5 | 312.1 |
| 425490 | 275.2 | 278.2 | 275.4 | 270.8 | 284.0 | 289.6 | 300.1 | 310.3 | 310.8 |
| 425491 | 286.9 | 293.2 | 294.9 | SD | 09/04/87 | | | | |
| 425492 | 285.6 | 293.5 | 289.6 | 287.8 | 293.5 | 299.9 | 311.2 | 324.1 | 327.8 |
| 425493 | 273.6 | 277.5 | 255.1 | SD | 09/04/87 | | | | |
| 425494 | 247.1 | 250.1 | 250.0 | SD | 09/04/87 | | | | |
| 425495 | 285.7 | 289.9 | 295.2 | 289.6 | 306.7 | 312.3 | 323.1 | 335.2 | 337.9 |
| 425496 | 290.9 | 297.3 | 300.0 | 284.7 | 288.5 | 294.5 | 306.3 | 314.5 | 323.9 |
| 425497 | 291.6 | 296.4 | 296.9 | SD | 09/04/87 | | | | |
| 425498 | 305.9 | 309.1 | 312.7 | SD | 09/04/87 | | | | |

| Rat No. | Days on Test 19 | 22 | 23 | 24 | 25 | 26 |
|---|---|---|---|---|---|---|
| 425489 | 310.9 | 331.3 | 329.0 | 339.2 | 343.8 | 352.1 |
| 425490 | 322.9 | 340.7 | 347.9 | 351.8 | 357.5 | 342.2 |
| 425491 | SD | 09/04/87 | | | | |
| 425492 | 335.3 | 346.9 | 349.8 | 354.0 | 362.5 | 363.0 |
| 425493 | SD | 09/04/87 | | | | |
| 425494 | SD | 09/04/87 | | | | |
| 425495 | 345.3 | 371.6 | 371.3 | 379.7 | 388.5 | 389.7 |
| 425496 | 330.9 | 350.9 | 352.5 | 357.5 | 370.5 | 367.2 |
| 425497 | SD | 09/04/87 | | | | |
| 425498 | SD | 09/04/87 | | | | |

Subchronic Inhalation Toxicity Study with Formamide

Appendix C

Individual Body Weights (grams) of Male Rats
Group: III Concentration: 100 ppm

| Rat No. | Days on Test 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
|---|---|---|---|---|---|---|---|---|---|
| 425499 | 230.8 | 232.1 | 239.9 | 248.2 | 251.2 | 255.6 | 261.8 | 274.6 | 281.0 |
| 425500 | 218.3 | 224.7 | 228.0 | 234.6 | 242.7 | 242.2 | 249.4 | 264.3 | 266.0 |
| 425501 | 224.1 | 224.2 | 233.0 | 236.9 | 239.9 | 246.7 | 251.9 | 268.9 | 269.0 |
| 425502 | 229.7 | 240.5 | 246.2 | 254.2 | 259.7 | 264.7 | 271.6 | 282.1 | 282.0 |
| 425503 | 235.4 | 235.2 | 243.2 | 249.0 | 251.3 | 254.0 | 259.9 | 277.3 | 277.0 |
| 425504 | 230.7 | 234.8 | 238.5 | 238.1 | 242.2 | 246.2 | 247.4 | 264.1 | 284.0 |
| 425505 | 243.2 | 247.5 | 259.6 | 265.8 | 274.3 | 275.5 | 280.2 | 301.2 | 307.0 |
| 425506 | 235.5 | 239.5 | 252.4 | 257.4 | 259.4 | 262.1 | 268.1 | 281.8 | 292.0 |
| 425507 | 233.8 | 231.4 | 241.7 | 248.5 | 256.5 | 256.6 | 265.6 | 280.0 | 268.0 |
| 425508 | 225.5 | 231.3 | 239.0 | 246.5 | 251.9 | 252.8 | 260.9 | 277.3 | 280.0 |

| Rat No. | Days on Test 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 |
|---|---|---|---|---|---|---|---|---|---|
| 425499 | 285.1 | 291.4 | 293.5 | 288.1 | 293.0 | 302.4 | 315.5 | 323.1 | 325.5 |
| 425500 | 268.4 | 277.3 | 285.2 | 272.9 | 281.7 | 292.2 | 302.5 | 309.3 | 314.0 |
| 425501 | 281.0 | 280.3 | 249.6 | 277.8 | 282.2 | 288.7 | 301.5 | 306.3 | 310.8 |
| 425502 | 297.9 | 294.6 | 298.8 | SD | 09/04/87 | | | | |
| 425503 | 280.9 | 283.6 | 283.2 | SD | 09/04/87 | | | | |
| 425504 | 273.0 | 272.6 | 276.1 | 267.9 | 276.7 | 286.5 | 294.5 | 298.5 | 304.0 |
| 425505 | 315.7 | 317.1 | 326.5 | SD | 09/04/87 | | | | |
| 425506 | 292.7 | 298.2 | 301.4 | SD | 09/04/87 | | | | |
| 425507 | 286.3 | 290.9 | 295.1 | 289.0 | 299.9 | 307.0 | 315.2 | 323.7 | 321.0 |
| 425508 | 280.1 | 286.8 | 292.9 | SD | 09/04/87 | | | | |

| Rat No. | Days on Test 19 | 22 | 23 | 24 | 25 | 26 |
|---|---|---|---|---|---|---|
| 425499 | 334.7 | 357.7 | 356.9 | 369.7 | 369.1 | 374.5 |
| 425500 | 323.0 | 351.9 | 346.3 | 355.3 | 366.0 | 374.2 |
| 425501 | 322.9 | 346.5 | 343.8 | 356.9 | 360.3 | 362.9 |
| 425502 | SD | 09/04/87 | | | | |
| 425503 | SD | 09/04/87 | | | | |
| 425504 | 311.8 | 333.8 | 332.3 | 342.4 | 348.0 | 361.3 |
| 425505 | SD | 09/04/87 | | | | |
| 425506 | SD | 09/04/87 | | | | |
| 425507 | 334.7 | 359.1 | 355.6 | 358.6 | 370.2 | 370.3 |
| 425508 | SD | 09/04/87 | | | | |

Subchronic Inhalation Toxicity Study with Formamide

Appendix C

Individual Body Weights (grams) of Male Rats
Group: V Concentration: 500 ppm

| Rat No. | Days on Test 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
|---|---|---|---|---|---|---|---|---|---|
| 425509 | 214.8 | 226.3 | 225.5 | 223.2 | 235.1 | 232.0 | 243.5 | 252.6 | 262.0 |
| 425510 | 229.8 | 226.9 | 233.6 | 231.2 | 242.8 | 238.8 | 247.5 | 271.6 | 271.0 |
| 425511 | 228.5 | 229.2 | 237.6 | 227.0 | 243.4 | 243.0 | 248.9 | 265.0 | 266.0 |
| 425512 | 246.9 | 252.2 | 260.0 | 254.3 | 271.2 | 275.3 | 284.9 | 305.8 | 311.0 |
| 425513 | 232.0 | 232.3 | 231.1 | 234.9 | 246.8 | 240.4 | 247.3 | 264.4 | 262.0 |
| 425514 | 238.0 | 236.4 | 240.2 | 238.6 | 249.0 | 245.5 | 254.5 | 266.4 | 273.0 |
| 425515 | 236.8 | 240.4 | 250.1 | 244.9 | 252.9 | 253.7 | 260.5 | 274.5 | 279.0 |
| 425516 | 242.8 | 240.3 | 251.0 | 252.8 | 267.3 | 268.5 | 278.9 | 290.5 | 298.0 |
| 425517 | 226.1 | 220.6 | 224.5 | 229.2 | 230.5 | 232.6 | 237.5 | 254.9 | 253.0 |
| 425518 | 228.7 | 230.7 | 234.1 | 235.6 | 236.3 | 239.5 | 243.2 | 253.8 | 262.0 |

| Rat No. | Days on Test 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 |
|---|---|---|---|---|---|---|---|---|---|
| 425509 | 259.5 | 261.5 | 269.5 | SD | 09/04/87 | | | | |
| 425510 | 275.9 | 276.4 | 271.9 | 260.4 | 275.1 | 263.2 | 287.8 | 294.3 | 305.9 |
| 425511 | 266.1 | 269.9 | 247.0 | 262.9 | 271.7 | 279.4 | 289.5 | 295.7 | 297.2 |
| 425512 | 311.6 | 313.5 | 316.3 | SD | 09/04/87 | | | | |
| 425513 | 267.9 | 271.6 | 276.9 | 266.1 | 273.5 | 280.6 | 286.7 | 295.6 | 301.1 |
| 425514 | 270.0 | 276.4 | 270.4 | SD | 09/04/87 | | | | |
| 425515 | 278.9 | 287.0 | 290.0 | 276.7 | 287.3 | 293.4 | 301.9 | 308.3 | 315.7 |
| 425516 | 299.4 | 305.8 | 318.5 | 295.7 | 311.4 | 320.9 | 332.4 | 342.3 | 347.0 |
| 425517 | 256.8 | 257.7 | 260.5 | SD | 09/04/87 | | | | |
| 425518 | 261.3 | 262.0 | 240.2 | SD | 09/04/87 | | | | |

| Rat No. | Days on Test 19 | 22 | 23 | 24 | 25 | 26 |
|---|---|---|---|---|---|---|
| 425509 | SD | 09/04/87 | | | | |
| 425510 | 275.8 | 324.8 | 325.4 | 328.9 | 335.8 | 345.9 |
| 425511 | 298.0 | 318.5 | 315.1 | 321.5 | 325.3 | 322.1 |
| 425512 | SD | 09/04/87 | | | | |
| 425513 | 304.0 | 330.1 | 326.2 | 338.2 | 338.5 | 344.7 |
| 425514 | SD | 09/04/87 | | | | |
| 425515 | 321.7 | 340.4 | 342.5 | 349.0 | 352.4 | 361.2 |
| 425516 | 356.2 | 384.6 | 383.3 | 392.2 | 395.6 | 409.6 |
| 425517 | SD | 09/04/87 | | | | |
| 425518 | SD | 09/04/87 | | | | |

Subchronic Inhalation Toxicity Study with Formamide

Appendix C

Individual Body Weights (grams) of Male Rats
Group: VII Concentration: 1500 ppm

| Rats No. | Days on Test 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
|---|---|---|---|---|---|---|---|---|---|
| 425519 | 228.9 | 224.4 | 229.8 | 234.5 | 235.4 | 216.6 | 204.7 | 205.1 | 204.0 |
| 425520 | 235.4 | 238.4 | 239.3 | 230.9 | 220.5 | 201.6 | 194.6 | 192.3 | 171.0 |
| 425521 | 239.7 | 244.3 | 252.4 | 246.6 | 254.9 | 241.5 | 219.8 | 210.1 | 204.0 |
| 425522 | 240.5 | 227.9 | 238.3 | 231.8 | 236.8 | 217.8 | 216.6 | 222.5 | 223.0 |
| 425523 | 228.1 | 204.8 | 214.5 | 215.2 | 217.9 | 209.2 | 218.8 | 229.8 | 231.0 |
| 425524 | 243.7 | 215.1 | 196.9 | FD | 08/26/87 | | | | |
| 425525 | 219.9 | 209.4 | 216.4 | 216.5 | 208.5 | 206.2 | 204.9 | 200.4 | 207.0 |
| 425526 | 243.4 | 241.2 | 245.1 | 245.2 | 248.3 | 233.1 | 232.0 | 216.2 | 210.0 |
| 425527 | 236.4 | 214.8 | 219.3 | 220.3 | 217.5 | 205.1 | 199.6 | 212.3 | 212.0 |
| 425528 | 247.1 | 235.1 | 237.6 | 211.9 | 197.0 | 181.5 | 166.6 | 184.1 | 186.0 |

| Rat No. | Days on Test 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 |
|---|---|---|---|---|---|---|---|---|---|
| 425519 | 213.6 | 218.5 | 233.5 | SD | 09/04/87 | | | | |
| 425520 | 164.7 | 141.9 | SE | 09/03/87 | | | | | |
| 425521 | 207.8 | 233.9 | 248.4 | SD | 09/04/87 | | | | |
| 425522 | 219.7 | 222.5 | 216.6 | 209.4 | 219.4 | 226.9 | 241.2 | 245.1 | 254.6 |
| 425523 | 228.3 | 228.9 | 202.4 | SD | 09/04/87 | | | | |
| 425524 | FD | 08/26/87 | | | | | | | |
| 425525 | 213.8 | 216.3 | 229.2 | 208.7 | 225.6 | 235.7 | 250.3 | 258.9 | 269.6 |
| 425526 | FD | 09/01/87 | | | | | | | |
| 425527 | 214.9 | 216.0 | 216.5 | 213.2 | 223.9 | 226.3 | 239.1 | 249.7 | 252.7 |
| 425528 | 181.5 | 199.8 | 208.6 | 198.1 | 213.5 | 222.8 | 235.3 | 240.4 | 253.5 |

| Rat No. | Days on Test 19 | 22 | 23 | 24 | 25 | 26 |
|---|---|---|---|---|---|---|
| 425519 | SD | 09/04/87 | | | | |
| 425520 | SE | 09/03/87 | | | | |
| 425521 | SD | 09/04/87 | | | | |
| 425522 | 262.2 | 283.2 | 286.5 | 296.5 | 302.2 | 315.7 |
| 425523 | SD | 09/04/87 | | | | |
| 425524 | FD | 08/26/87 | | | | |
| 425525 | 269.8 | 302.3 | 301.8 | 311.7 | 320.9 | 315.9 |
| 425526 | FD | 09/01/87 | | | | |
| 425527 | 256.3 | 275.8 | 265.4 | 278.9 | 282.3 | 292.6 |
| 425528 | 261.0 | 287.3 | 288.7 | 297.8 | 307.5 | 318.0 |

Subchronic Inhalation Toxicity Study with Formamide

## Appendix D

## Individual Clinical Observations of Male Rats

Subchronic Inhalation Toxicity Study with Formamide

Appendix D

Individual Clinical Observations of Male Rats

| Rat Number | Observation | Day First Observed | Day Not Observed |
|---|---|---|---|
| Controls | | | |
| 425494 | Diarrhea | 4 | 5 |
| 425496 | Diarrhea | 4 | 5 |
| 425493 | Diarrhea | 9 | 10 |
| 425489 | Colored Discharge Right Eye | 15 | 16 |
| 425496 | Colored Discharge Left Eye | 15 | 17 |
| 425496 | Colored Discharge Nose Black | 16 | 22 |
| 425496 | Colored Discharge Left Eye, Nose Black | 25 | NR |
| 100 ppm | | | |
| 425500 | Diarrhea | 9 | 10 |
| 425508 | Diarrhea | 9 | 10 |
| 425500 | Diarrhea | 16 | 17 |
| 500 ppm | | | |
| 425516 | Diarrhea | 3 | 4 |
| 425516 | Diarrhea | 9 | 10 |

Subchronic Inhalation Toxicity Study with Formamide

Appendix D

Individual Clinical Observations of Male Rats

| Rat Number | Observation | Day First Observed | Day Not Observed |
|---|---|---|---|
| 1500 ppm | | | |
| 425524 | Hunched Over, Weak | 3 | NR |
| 425528 | Diarrhea | 7 | 8 |
| 425528 | Hunched Over | 7 | 12 |
| 425520 | Hunched Over, Weak | 9 | NR |
| 425526 | Diarrhea | 9 | NR |
| 425528 | Diarrhea | 9 | 10 |
| 425519 | Diarrhea | 10 | 11 |
| 425523 | Diarrhea | 10 | 11 |
| 425520 | Colored Discharge Nose Brown | 11 | NR |
| 425525 | Colored Discharge Nose Brown | 16 | 18 |
| 425525 | Colored Discharge Left Eye | 16 | 18 |
| 425528 | Diarrhea | 16 | 17 |
| 425522 | Diarrhea | 17 | 19 |
| 425525 | Colored Discharge Left Eye | 23 | 25 |

Notes:

- Excluding signs observed during or immediately following exposures.
- Exposure period - Days 1-12; Recovery period - Days 13-26.
- Rats not listed had no adverse clinical signs.
- NR (not recovered) - the sign was observed at the last weighing prior to the animal's death.

Subchronic Inhalation Toxicity Study with Formamide

Appendix E

Clinical Pathology Report No. 10-87

ES-3662 REV. 12-85

DU PONT

ESTABLISHED 1802

E. I. DU PONT DE NEMOURS & COMPANY

INCORPORATED

HASKELL LABORATORY FOR TOXICOLOGY
AND INDUSTRIAL MEDICINE
P.O. BOX 50, ELKTON ROAD
NEWARK, DELAWARE 19714

CENTRAL RESEARCH AND DEVELOPMENT DEPARTMENT



# CLINICAL PATHOLOGY REPORT NO. 2-88

MEDICAL RESEARCH REPORT NO. 5602-001 HASKELL LABORATORY NO. 16728

## SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

CENTRAL RESEARCH AND DEVELOPMENT DEPARTMENT

DATE ISSUED: APRIL 5, 1988

# SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE


## Summary

Male Crl:CD®BR rats were exposed by inhalation to formamide at design concentrations of 0 (control), 100, 500, or 1500 ppm six hours per day for ten days.

A sub-clinical thrombocytopenia was observed in rats in the 500 and 1500 ppm groups after ten days of exposure and following 14 days of recovery. A lymphopenia and minimal hypercholesterolemia were also observed in rats in the 1500 ppm group after ten exposures. The lymphopenia persisted after 14 days of recovery.

Under the conditions of this study the no-observable-effect concentration was considered to be 100 ppm for the hematologic and clinical chemical parameters measured.



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## Procedure

Three groups of ten male Crl:CD®BR rats were exposed, by inhalation, for six hours per day for ten days to formamide at design concentrations of 0 (control), 100 (low), or 500 (intermediate) ppm. Another group of seven male Crl:CD®BR rats were exposed, by inhalation, for six hours per day for ten days to formamide at a concentration of 1500 (high) ppm.

After the tenth exposure (12 DAYS ON TEST) blood was taken from the orbital sinus of each rat for enumeration of erythrocytes (RBC), leukocytes (WBC), and platelets (PLAT); analysis of hemoglobin concentration (Hb) and hematocrit (Ht); and determination of relative numbers of neutrophils (Neut), band neutrophils (Band), lymphocytes (Lymph), atypical lymphocytes (Alym), monocytes (Mono), eosinophils (Eosin), and basophils (Baso). Absolute values for the various types of leukocytes were calculated from the leukocytic data. Mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) were calculated from the erythrocytic data.

Serum activities of alkaline phosphatase (ALP), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) and serum concentrations of urea nitrogen (BUN), creatinine (CREAT), total protein (TPROT), and cholesterol (CHOL) were also measured.

One day prior to the tenth exposure, an overnight (approximately 16-hour) urine specimen was collected from each rat to measure volume (VOL), osmolality (OSMOL), urobilinogen (UROBL), and pH; and to determine the presence of hemoglobin or occult blood (BLOOD), glucose, protein, bilirubin, and ketone (acetoacetic acid). The appearance (color and transparency) was recorded and the sediment from each specimen was microscopically examined.

After the 12-day sampling time, five rats from the 0, 100, and 500 ppm groups and three rats from the 1500 ppm group were killed for pathologic evaluation.

Following a 14-day recovery period (26 DAYS ON TEST), the hematologic and clinical chemical (serum and urine) measurements were repeated on the remaining five rats in the 0, 100, and 500 ppm groups and the four remaining rats in the 1500 ppm group.

## Statistical Analyses

A one-way analysis of variance (ANOVA) and Bartlett's test were calculated for each sampling time. When the F-test from ANOVA was significant, the Dunnett test was used to compare means from the control group and each of the groups exposed to formamide. When the results of the Bartlett test were significant ($p \leq 0.005$), the Kruskal-Wallis test was employed and the Mann-Whitney U test was used to compare means from the control group and each of the groups exposed to formamide. Significance was judged at the 5% probability level.

## Results

Statistically significant results are summarized in Table 1. Group means and standard deviations for hematologic (Table 2), clinical chemical (Table 3), and urinalysis (Table 4) data are presented after the Discussion and Conclusions. Data for individual animals are listed in Appendix A. Terms and criteria used for urinalyses are presented in Appendix A.

H-16728
MR-5602-001
HC-17

SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

TABLE 1

SUMMARY OF STATISTICALLY SIGNIFICANT HEMATOLOGIC AND CLINICAL CHEMICAL FINDINGS FOR MALE RATS

| Sampling Time | 12 DAYS ON TEST | 26 DAYS ON TEST |
|---|---|---|
| **Measurement** | | |
| **Hematology** | | |
| MCV | ↓ VII | – |
| MCHC | – | ↑ V,VII |
| PLAT | ↓ V,VII | ↓ V,VII |
| Lymph | ↓ VII | – |
| Alym | – | ↑ III |
| **Clinical Chemistry (Serum)** | | |
| ALT | ↓ V+ | – |
| BUN | ↑ VII | – |
| CREAT | – | ↓ VII |
| TPROT | – | ↓ VII |
| CHOL | ↑ VII | – |
| **Clinical Chemistry (Urine)** | | |
| OSMOL | – | ↑ V |
| pH | ↓ V,VII | – |

↑ = Significantly higher than controls by Dunnett or Mann-Whitney U (+) criteria

↓ = Significntly lower than controls by Dunnett or Mann-Whitney U (+) criteria

– = Not statistically significant

Group Designation and Concentration (ppm)
III - Low (100)
V - Intermediate (500)
VII - High (1500)

## Discussion and Conclusions

A statistically significant sub-clinical thrombocytopenia was present in both the 500 and 1500 ppm groups. There was no evidence of platelet regeneration observed on blood smears from rats in the affected groups. The biological significance of this mild thrombocytopenia was considered equivocal. A statistically and biologically significant lymphopenia was also observed in the 1500 ppm group. Following 14 days of recovery, the thrombocytopenia persisted in both affected groups, and the lymphocyte count remained decreased in the 1500 ppm group.

The statistically significant increase in cholesterol observed in the 1500 ppm group after 10 exposures was considered of minimal biologic significance. The remaining statistically significant findings listed in Table 1 were considered biologically insignificant.

Under the conditions of this study the no-observable-effect concentration was considered to be 100 ppm for the hematologic and clinical chemical parameters measured.

DRH:bl
CP 11.23

SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

H-16728
MR-5602-001
HC-17

TABLE 2

SUMMARY OF HEMATOLOGIC FINDINGS FOR MALE RATS

| TESTS | CONCENTRATION (ppm) | SAMPLING TIME 12 DAYS ON TEST | 26 DAYS ON TEST |
|---|---|---|---|
| RBC $x10^6$/ul | 0 | 7.29( 0.56)[a] | 7.36( 0.31) |
| | 100 | 7.17( 0.25) | 7.23( 0.14) |
| | 500 | 7.41( 0.37) | 7.50( 0.34) |
| | 1500 | 7.69( 0.63) | 7.24( 0.34) |
| Hb g/dl | 0 | 14.5( 0.8) | 14.8( 0.6) |
| | 100 | 14.3( 0.4) | 14.6( 0.4) |
| | 500 | 15.2( 0.4) | 15.6( 0.5) |
| | 1500 | 15.2( 1.2) | 15.3( 0.9) |
| Ht % | 0 | 52.( 3.) | 52.( 2.) |
| | 100 | 51.( 2.) | 51.( 1.) |
| | 500 | 53.( 2.) | 54.( 2.) |
| | 1500 | 54.( 4.) | 52.( 3.) |
| MCV fl | 0 | 71.( 1.) | 71.( 1.) |
| | 100 | 71.( 1.) | 71.( 1.) |
| | 500 | 71.( 1.) | 72.( 1.) |
| | 1500 | 70.( 1.)* | 72.( 1.) |
| MCH pg | 0 | 20.( 1.) | 20.( 1.) |
| | 100 | 20.( 1.) | 20.( 0.) |
| | 500 | 21.( 1.) | 21.( 1.) |
| | 1500 | 20.( 0.) | 21.( 0.) |
| MCHC g/dl | 0 | 28.( 1.) | 28.( 1.) |
| | 100 | 28.( 1.) | 28.( 0.) |
| | 500 | 29.( 1.) | 29.( 0.)* |
| | 1500 | 28.( 0.) | 29.( 0.)* |
| PLAT $x10^3$/ul | 0 | 1142.( 273.) | 1180.( 268.) |
| | 100 | 1080.( 184.) | 1105.( 124.) |
| | 500 | 882.( 119.)* | 831.( 69.)* |
| | 1500 | 847.( 90.)* | 747.( 294.)* |

[a] Group means and standard deviations(SD)
* Significantly different from control at 5% level by Dunnett criteria

SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

H-16728
MR-5602-001
HC-17

TABLE 2 (continued)

SUMMARY OF HEMATOLOGIC FINDINGS FOR MALE RATS

| TESTS | CONCENTRATION (ppm) | SAMPLING TIME 12 DAYS ON TEST | SAMPLING TIME 26 DAYS ON TEST |
|---|---|---|---|
| WBC $x10^3/ul$ | 0 | 14.9( 3.3)[a] | 16.8( 3.0) |
| | 100 | 14.1( 4.4) | 14.6( 2.2) |
| | 500 | 13.6( 3.7) | 16.0( 3.2) |
| | 1500 | 10.1( 1.2) | 11.3( 3.6) |
| Neut WBCx% | 0 | 3167.( 1639.) | 3675.( 1178.) |
| | 100 | 3272.( 1556.) | 2751.( 1360.) |
| | 500 | 3183.( 1671.) | 4047.( 764.) |
| | 1500 | 2519.( 1088.) | 2792.( 1720.) |
| Band WBCx% | 0 | 0.( 0.) | 0.( 0.) |
| | 100 | 0.( 0.) | 0.( 0.) |
| | 500 | 0.( 0.) | 0.( 0.) |
| | 1500 | 0.( 0.) | 0.( 0.) |
| Lymph WBCx% | 0 | 11088.( 2144.) | 12137.( 2368.) |
| | 100 | 10067.( 3164.) | 11015.( 1279.) |
| | 500 | 9883.( 2537.) | 11227.( 2799.) |
| | 1500 | 6956.( 596.)* | 7868.( 2022.) |

[a] Group means and standard deviations(SD)
* Significantly different from control at 5% level by Dunnett criteria

SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

H-16728
MR-5602-001
HC-17

TABLE 2 (continued)

SUMMARY OF HEMATOLOGIC FINDINGS FOR MALE RATS

| TESTS | CONCENTRATION (ppm) | SAMPLING TIME 12 DAYS ON TEST | 26 DAYS ON TEST |
|---|---|---|---|
| Alym WBCx% | 0 | 82.( 166.)[a] | 0.( 0.) |
| | 100 | 87.( 175.) | 210.( 172.)* |
| | 500 | 90.( 225.) | 109.( 100.) |
| | 1500 | 68.( 104.) | 61.( 70.) |
| Mono WBCx% | 0 | 539.( 436.) | 893.( 240.) |
| | 100 | 618.( 504.) | 635.( 343.) |
| | 500 | 369.( 171.) | 562.( 395.) |
| | 1500 | 464.( 189.) | 539.( 273.) |
| Eosin WBCx% | 0 | 45.( 73.) | 76.( 105.) |
| | 100 | 46.( 101.) | 29.( 64.) |
| | 500 | 95.( 128.) | 34.( 76.) |
| | 1500 | 51.( 69.) | 65.( 75.) |
| Baso WBCx% | 0 | 0.( 0.) | 0.( 0.) |
| | 100 | 0.( 0.) | 0.( 0.) |
| | 500 | 0.( 0.) | 0.( 0.) |
| | 1500 | 0.( 0.) | 0.( 0.) |

[a] Group means and standard deviations(SD)
* Significantly different from control at 5% level by Dunnett criteria

SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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TABLE 3

SUMMARY OF CLINICAL CHEMICAL FINDINGS FOR MALE RATS

| TESTS | CONCENTRATION (ppm) | SAMPLING TIME 12 DAYS ON TEST | 26 DAYS ON TEST |
|---|---|---|---|
| ALP U/L | 0 | 357.( 107.)[a] | 387.( 119.) |
| | 100 | 351.( 116.) | 330.( 85.) |
| | 500 | 411.( 157.) | 403.( 174.) |
| | 1500 | 389.( 122.) | 427.( 67.) |
| ALT U/L | 0 | 40.( 7.) | 43.( 5.) |
| | 100 | 40.( 20.) | 39.( 4.) |
| | 500 | 32.( 4.)# | 46.( 12.) |
| | 1500 | 39.( 12.) | 39.( 11.) |
| AST U/L | 0 | 80.( 11.) | 73.( 8.) |
| | 100 | 74.( 21.) | 61.( 5.) |
| | 500 | 71.( 8.) | 69.( 10.) |
| | 1500 | 87.( 8.) | 66.( 11.) |
| BUN mg/dl | 0 | 17.( 3.) | 19.( 5.) |
| | 100 | 14.( 2.) | 17.( 2.) |
| | 500 | 15.( 2.) | 16.( 1.) |
| | 1500 | 21.( 4.)* | 16.( 1.) |
| CREAT mg/dl | 0 | 0.64( 0.05) | 0.72( 0.11) |
| | 100 | 0.62( 0.04) | 0.62( 0.04) |
| | 500 | 0.62( 0.04) | 0.62( 0.04) |
| | 1500 | 0.61( 0.04) | 0.60( 0.00)* |
| TPROT g/dl | 0 | 6.5( 0.4) | 6.7( 0.4) |
| | 100 | 6.4( 0.3) | 6.3( 0.3) |
| | 500 | 6.5( 0.3) | 6.3( 0.3) |
| | 1500 | 6.4( 0.5) | 5.9( 0.2)* |
| CHOL mg/dl | 0 | 31.( 9.) | 64.( 17.) |
| | 100 | 28.( 6.) | 55.( 6.) |
| | 500 | 37.( 14.) | 58.( 10.) |
| | 1500 | 48.( 12.)* | 58.( 5.) |

[a] Group means and standard deviations(SD)
* Significantly different from control at 5% level by Dunnett criteria
# Significantly different from control at 5% level by Mann-Whitney U criteria

SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

H-16728
MR-5602-001
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TABLE 4

SUMMARY OF CLINICAL URINALYSIS FINDINGS FOR MALE RATS

| TESTS | CONCENTRATION (ppm) | SAMPLING TIME 12 DAYS ON TEST | SAMPLING TIME 26 DAYS ON TEST |
|---|---|---|---|
| VOL ml | 0 | 7.2( 4.1)[a] | 10.9( 7.7) |
| | 100 | 5.1( 1.3) | 9.2( 1.6) |
| | 500 | 4.5( 1.2) | 7.6( 0.9) |
| | 1500 | 7.2( 4.2) | 10.1( 2.6) |
| OSMOL mOs | 0 | 1410.( 454.) | 1499.( 547.) |
| | 100 | 1497.( 406.) | 1847.( 405.) |
| | 500 | 1870.( 535.) | 2293.( 161.)* |
| | 1500 | 1786.(1514.) | 1426.( 257.) |
| pH | 0 | 7.6( 0.6) | 7.5( 0.6) |
| | 100 | 7.3( 0.3) | 7.3( 0.4) |
| | 500 | 6.9( 0.3)* | 6.8( 0.4) |
| | 1500 | 6.6( 0.8)* | 7.4( 0.5) |
| UROBL mg/dl | 0 | 0.1( 0.0) | 0.1( 0.0) |
| | 100 | 0.1( 0.0) | 0.1( 0.0) |
| | 500 | 0.1( 0.0) | 0.1( 0.0) |
| | 1500 | 0.1( 0.0) | 0.1( 0.0) |

[a] Group means and standard deviations(SD)
* Significantly different from control at 5% level by Dunnett criteria

TABLE 4 (CONTINUED)

SUMMARY OF CLINICAL URINALYSIS FINDINGS FOR MALE RATS

| Measurement | Concentration (ppm) | Sampling Time 12 DAYS ON TEST | Sampling Time 26 DAYS ON TEST |
|---|---|---|---|
| Blood Number Positive | 0 | 7/10++ | 1/5 |
| | 100 | 3/10 | 1/5 |
| | 500 | 1/10 | 0/5 |
| | 1500 | 5/7 | 0/4 |
| Glucose Number Positive | 0 | 0/10 | 0/5 |
| | 100 | 0/10 | 0/5 |
| | 500 | 0/10 | 0/5 |
| | 1500 | 0/7 | 0/4 |
| Protein Number Abnormal ≥ + 3 | 0 | 0/10 | 1/5 |
| | 100 | 0/10 | 0/5 |
| | 500 | 1/10 | 0/5 |
| | 1500 | 1/7 | 0/4 |
| Bilirubin Number Positive | 0 | 0/10 | 0/5 |
| | 100 | 0/10 | 0/5 |
| | 500 | 0/10 | 0/5 |
| | 1500 | 0/7 | 0/4 |
| Ketone Number Positive | 0 | 6/10 | 4/5 |
| | 100 | 5/10 | 5/5 |
| | 500 | 7/10 | 5/5 |
| | 1500 | 0/7 | 4/4 |
| Appearance (Color and Transparency) | 0 | 0/10 | 0/5 |
| | 100 | 0/10 | 0/5 |
| | 500 | 0/10 | 0/5 |
| | 1500 | 0/7 | 0/4 |
| Microscopic Number Abnormal | 0 | 5/10 | 4/5 |
| | 100 | 7/10 | 1/5 |
| | 500 | 5/10 | 4/5 |
| | 1500 | 2/7 | 3/4 |

++ Number of abnormal or positive findings/number of individual specimens examined

SUBCHRONIC INAHALTION TOXICITY STUDY WITH FORMAMIDE

APPENDIX A

H-16728, MR-5602-001, HC-17

## TERMS AND CRITERIA USED IN URINALYSES

Abbreviations for Descriptive Terms Normally Used for Gross Evaluation of Urine (other Abbreviations and Descriptive Terms may be used if they are more applicable)

Y = Yellow
LY = Light Yellow
DY = Dark Yellow
A = Amber
DA = Dark Amber
G = Green
BL = Bloody
R = Red
C = Clear
CL = Cloudy
P/PPT = Precipitate
F = Feed
FEC = Feces
QNS = Quantity not sufficient

Abbreviations for Descriptive Terms Used for Microscopic Evaluation of Urine

Epith = Epithelial Cells
hpf = high power field
lpf = low power field
RBC = Red Blood Cells
WBC = White Blood Cells
TNTC (99-99) = Too Numerous to Count

Definition of "Normal" and "Abnormal" Designations Used for Gross and Microscopic Appearance of Urine

| Appearance | Normal | Abnormal |
|---|---|---|
| Color | Light to dark yellow or amber | Color other than yellow or amber |
| Microscopic | | |
| Red Blood Cells | Average of 0 to 4 red blood cells per high power field | Average of more than 4 red blood cells per high power field |
| Casts | None observed | Average of more than 0 per low power field |
| Epithelial Cells | Average of 0 to 9 per high power field | Average of more than 9 per high power field |
| White Blood Cells | Average of 0 to 9 per high power field | Average of more than 9 per high power field |

SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

H-16728
MR-5602-001
HC-17

APPENDIX A

INDIVIDUAL HEMATOLOGIC FINDINGS FOR MALE RATS
AT 12 DAYS ON TEST

---

GROUP: I
SAMPLE DATE: 09/04/87

CONCENTRATION: 0 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | RBC $x10^6/ul$ | Hb g/dl | Ht % | MCV fl | MCH pg | MCHC g/dl | PLAT $x10^3/ul$ |
|---|---|---|---|---|---|---|---|
| 425489 | 6.85 | 14.0 | 49. | 72. | 20. | 29. | 1702. |
| 425490 | 7.09 | 14.7 | 51. | 72. | 21. | 29. | 869. |
| 425491 | 6.79 | 13.2 | 48. | 71. | 19. | 28. | 1304. |
| 425492 | 6.95 | 14.2 | 50. | 72. | 20. | 28. | 892. |
| 425493 | 8.19 | 15.4 | 57. | 69. | 19. | 27. | 1173. |
| 425494 | 8.30 | 16.1 | 58. | 70. | 19. | 28. | 991. |
| 425495 | 6.79 | 13.9 | 49. | 72. | 21. | 28. | 966. |
| 425496 | 7.61 | 14.8 | 54. | 70. | 19. | 28. | 1244. |
| 425497 | 7.15 | 14.5 | 51. | 72. | 20. | 28. | 889. |
| 425498 | 7.22 | 14.2 | 52. | 71. | 20. | 28. | 1392. |
| AVG. | 7.294 | 14.50 | 51.9 | 71.1 | 19.9 | 28.0 | 1142.2 |
| S. D. | 0.558 | 0.82 | 3.4 | 1.1 | 0.6 | 0.5 | 272.5 |
| S. E. | 0.177 | 0.26 | 1.1 | 0.3 | 0.2 | 0.2 | 86.2 |

GROUP: III
SAMPLE DATE: 09/04/87

CONCENTRATION: 100 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | RBC $x10^6/ul$ | Hb g/dl | Ht % | MCV fl | MCH pg | MCHC g/dl | PLAT $x10^3/ul$ |
|---|---|---|---|---|---|---|---|
| 425499 | 6.88 | 13.8 | 48. | 70. | 20. | 29. | 1434. |
| 425500 | 7.33 | 15.1 | 52. | 71. | 21. | 29. | 797. |
| 425501 | 7.20 | 14.4 | 51. | 71. | 20. | 28. | 1129. |
| 425502 | 7.32 | 14.5 | 52. | 71. | 20. | 28. | 1326. |
| 425503 | 7.23 | 13.9 | 51. | 71. | 19. | 27. | 1027. |
| 425504 | 7.29 | 14.4 | 51. | 70. | 20. | 28. | 1082. |
| 425505 | 7.64 | 14.8 | 54. | 71. | 19. | 28. | 984. |
| 425506 | 7.04 | 14.2 | 51. | 72. | 20. | 28. | 1063. |
| 425507 | 6.81 | 14.2 | 49. | 72. | 21. | 29. | 935. |
| 425508 | 6.94 | 14.0 | 50. | 72. | 20. | 28. | 1020. |
| AVG. | 7.168 | 14.33 | 51.0 | 71.1 | 20.0 | 28.1 | 1079.7 |
| S. D. | 0.252 | 0.40 | 1.6 | 0.7 | 0.5 | 0.6 | 184.2 |
| S. E. | 0.080 | 0.13 | 0.5 | 0.2 | 0.2 | 0.2 | 58.2 |

SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

H-16728
MR-5602-001
HC-17

APPENDIX A (continued)

INDIVIDUAL HEMATOLOGIC FINDINGS FOR MALE RATS
AT 12 DAYS ON TEST

---

GROUP: V
SAMPLE DATE: 09/04/87

CONCENTRATION: 500 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | RBC $x10^6/ul$ | Hb g/dl | Ht % | MCV fl | MCH pg | MCHC g/dl | PLAT $x10^3/ul$ |
|---|---|---|---|---|---|---|---|
| 425509 | 7.37 | 14.6 | 52. | 71. | 20. | 28. | 750. |
| 425510 | 7.09 | 14.8 | 50. | 71. | 21. | 29. | 769. |
| 425511 | 7.68 | 15.6 | 54. | 71. | 20. | 29. | 797. |
| 425512 | 7.70 | 15.6 | 56. | 72. | 20. | 28. | 1054. |
| 425513 | 7.31 | 15.3 | 52. | 71. | 21. | 29. | 872. |
| 425514 | 7.22 | 14.5 | 52. | 72. | 20. | 28. | 870. |
| 425515 | 6.82 | 15.0 | 50. | 73. | 22. | 30. | 903. |
| 425516 | 7.16 | 15.2 | 52. | 72. | 21. | 29. | 775. |
| 425517 | 7.71 | 15.4 | 55. | 71. | 20. | 28. | 938. |
| 425518 | 8.05 | 15.7 | 56. | 70. | 20. | 28. | 1096. |
| AVG. | 7.411 | 15.17 | 52.9 | 71.4 | 20.5 | 28.7 | 882.4 |
| S. D. | 0.368 | 0.43 | 2.2 | 0.8 | 0.7 | 0.8 | 119.3 |
| S. E. | 0.116 | 0.14 | 0.7 | 0.3 | 0.2 | 0.2 | 37.7 |

GROUP: VII
SAMPLE DATE: 09/04/87

CONCENTRATION: 1500 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | RBC $x10^6/ul$ | Hb g/dl | Ht % | MCV fl | MCH pg | MCHC g/dl | PLAT $x10^3/ul$ |
|---|---|---|---|---|---|---|---|
| 425519 | 7.14 | 14.1 | 50. | 70. | 20. | 28. | 791. |
| 425521 | 6.85 | 14.0 | 49. | 71. | 20. | 29. | 755. |
| 425522 | 8.39 | 16.4 | 58. | 69. | 20. | 28. | 884. |
| 425523 | 8.55 | 16.9 | 60. | 70. | 20. | 28. | 881. |
| 425525 | 7.50 | 14.9 | 53. | 70. | 20. | 28. | 774. |
| 425527 | 7.93 | 16.0 | 56. | 70. | 20. | 29. | 1017. |
| 425528 | 7.46 | 14.4 | 52. | 69. | 19. | 28. | 825. |
| AVG. | 7.689 | 15.24 | 53.7 | 69.9 | 19.8 | 28.4 | 846.7 |
| S. D. | 0.630 | 1.18 | 4.3 | 0.7 | 0.4 | 0.3 | 90.2 |
| S. E. | 0.238 | 0.45 | 1.6 | 0.3 | 0.1 | 0.1 | 34.1 |

H-16728
MR-5602-001
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APPENDIX A (continued)

INDIVIDUAL HEMATOLOGIC FINDINGS FOR MALE RATS
AT 12 DAYS ON TEST

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GROUP: I
SAMPLE DATE: 09/04/87

CONCENTRATION: 0 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | WBC $x10^3/ul$ | Neut WBCx% | Band WBCx% | Lymph WBCx% | Alym WBCx% | Mono WBCx% | Eosin WBCx% | Baso WBCx% |
|---|---|---|---|---|---|---|---|---|
| 425489 | 20.6 | 7210. | 0. | 11742. | 0. | 1648. | 0. | 0. |
| 425490 | 13.1 | 2227. | 0. | 10349. | 131. | 393. | 0. | 0. |
| 425491 | 16.6 | 3320. | 0. | 12782. | 166. | 332. | 0. | 0. |
| 425492 | 16.6 | 1992. | 0. | 14110. | 0. | 498. | 0. | 0. |
| 425493 | 9.9 | 1287. | 0. | 7821. | 0. | 792. | 0. | 0. |
| 425494 | 12.4 | 2728. | 0. | 9424. | 0. | 124. | 124. | 0. |
| 425495 | 14.8 | 3404. | 0. | 10656. | 0. | 592. | 148. | 0. |
| 425496 | 10.9 | 2289. | 0. | 8284. | 0. | 327. | 0. | 0. |
| 425497 | 17.0 | 3060. | 0. | 13430. | 0. | 510. | 0. | 0. |
| 425498 | 17.3 | 4152. | 0. | 12283. | 519. | 173. | 173. | 0. |
| AVG. | 14.92 | 3166.9 | 0.0 | 11088.1 | 81.6 | 538.9 | 44.5 | 0.0 |
| S. D. | 3.32 | 1638.7 | 0.0 | 2144.2 | 165.8 | 436.5 | 72.6 | 0.0 |
| S. E. | 1.05 | 518.2 | 0.0 | 678.1 | 52.4 | 138.0 | 23.0 | 0.0 |

GROUP: III
SAMPLE DATE: 09/04/87

CONCENTRATION: 100 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | WBC $x10^3/ul$ | Neut WBCx% | Band WBCx% | Lymph WBCx% | Alym WBCx% | Mono WBCx% | Eosin WBCx% | Baso WBCx% |
|---|---|---|---|---|---|---|---|---|
| 425499 | 12.9 | 2709. | 0. | 9159. | 516. | 516. | 0. | 0. |
| 425500 | 7.1 | 923. | 0. | 5964. | 71. | 142. | 0. | 0. |
| 425501 | 14.2 | 3408. | 0. | 9940. | 284. | 284. | 284. | 0. |
| 425502 | 14.4 | 2448. | 0. | 11520. | 0. | 432. | 0. | 0. |
| 425503 | 10.5 | 1995. | 0. | 8400. | 0. | 105. | 0. | 0. |
| 425504 | 11.0 | 3410. | 0. | 7150. | 0. | 440. | 0. | 0. |
| 425505 | 17.9 | 5907. | 0. | 10382. | 0. | 1432. | 179. | 0. |
| 425506 | 23.1 | 5313. | 0. | 16863. | 0. | 924. | 0. | 0. |
| 425507 | 13.0 | 4420. | 0. | 8190. | 0. | 390. | 0. | 0. |
| 425508 | 16.8 | 2184. | 0. | 13104. | 0. | 1512. | 0. | 0. |
| AVG. | 14.09 | 3271.7 | 0.0 | 10067.2 | 87.1 | 617.7 | 46.3 | 0.0 |
| S. D. | 4.44 | 1556.1 | 0.0 | 3164.1 | 175.1 | 503.9 | 100.7 | 0.0 |
| S. E. | 1.40 | 492.1 | 0.0 | 1000.6 | 55.4 | 159.4 | 31.8 | 0.0 |

SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

H-16728
MR-5602-001
HC-17

APPENDIX A (continued)

INDIVIDUAL HEMATOLOGIC FINDINGS FOR MALE RATS
AT 12 DAYS ON TEST

---

GROUP: V
SAMPLE DATE: 09/04/87

CONCENTRATION: 500 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | WBC x10$^3$/ul | Neut WBCx% | Band WBCx% | Lymph WBCx% | Alym WBCx% | Mono WBCx% | Eosin WBCx% | Baso WBCx% |
|---|---|---|---|---|---|---|---|---|
| 425509 | 12.3 | 3321. | 0. | 8856. | 0. | 123. | 0. | 0. |
| 425510 | 7.3 | 1825. | 0. | 4891. | 0. | 584. | 0. | 0. |
| 425511 | 13.4 | 2680. | 0. | 10184. | 0. | 268. | 268. | 0. |
| 425512 | 15.8 | 1896. | 0. | 12956. | 0. | 632. | 316. | 0. |
| 425513 | 17.1 | 4104. | 0. | 12483. | 0. | 342. | 171. | 0. |
| 425514 | 12.5 | 2875. | 0. | 9375. | 0. | 250. | 0. | 0. |
| 425515 | 19.1 | 7067. | 0. | 11460. | 191. | 191. | 191. | 0. |
| 425516 | 17.7 | 4248. | 0. | 12390. | 708. | 354. | 0. | 0. |
| 425517 | 10.8 | 2592. | 0. | 7668. | 0. | 540. | 0. | 0. |
| 425518 | 10.2 | 1224. | 0. | 8568. | 0. | 408. | 0. | 0. |
| AVG. | 13.62 | 3183.2 | 0.0 | 9883.1 | 89.9 | 369.2 | 94.6 | 0.0 |
| S. D. | 3.74 | 1670.7 | 0.0 | 2537.2 | 225.3 | 171.2 | 128.2 | 0.0 |
| S. E. | 1.18 | 528.3 | 0.0 | 802.3 | 71.3 | 54.1 | 40.5 | 0.0 |

GROUP: VII
SAMPLE DATE: 09/04/87

CONCENTRATION: 1500 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | WBC x10$^3$/ul | Neut WBCx% | Band WBCx% | Lymph WBCx% | Alym WBCx% | Mono WBCx% | Eosin WBCx% | Baso WBCx% |
|---|---|---|---|---|---|---|---|---|
| 425519 | 12.2 | 3660. | 0. | 7808. | 0. | 732. | 0. | 0. |
| 425521 | 8.7 | 1131. | 0. | 7047. | 87. | 261. | 174. | 0. |
| 425522 | 9.3 | 1674. | 0. | 6882. | 279. | 372. | 93. | 0. |
| 425523 | 9.0 | 1620. | 0. | 6750. | 0. | 540. | 90. | 0. |
| 425525 | 10.9 | 2616. | 0. | 7630. | 109. | 545. | 0. | 0. |
| 425527 | 10.5 | 3990. | 0. | 6300. | 0. | 210. | 0. | 0. |
| 425528 | 9.8 | 2940. | 0. | 6272. | 0. | 588. | 0. | 0. |
| AVG. | 10.06 | 2518.7 | 0.0 | 6955.6 | 67.9 | 464.0 | 51.0 | 0.0 |
| S. D. | 1.23 | 1087.9 | 0.0 | 596.5 | 104.1 | 188.7 | 69.3 | 0.0 |
| S. E. | 0.47 | 411.2 | 0.0 | 225.4 | 39.4 | 71.3 | 26.2 | 0.0 |

SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX A (continued)

INDIVIDUAL CLINICAL CHEMICAL FINDINGS FOR MALE RATS
AT 12 DAYS ON TEST

---

GROUP: I
SAMPLE DATE: 09/04/87

CONCENTRATION: 0 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | ALP U/L | ALT U/L | AST U/L | BUN mg/dl | CREAT mg/dl | TPROT g/dl | CHOL mg/dl |
|---|---|---|---|---|---|---|---|
| 425489 | 337. | 41. | 87. | 21. | 0.70 | 6.6 | 32. |
| 425490 | 297. | 41. | 66. | 18. | 0.60 | 6.3 | 39. |
| 425491 | 214. | 34. | 81. | 13. | 0.60 | 6.0 | 25. |
| 425492 | 330. | 38. | 67. | 15. | 0.70 | 6.5 | 31. |
| 425493 | 278. | 26. | 69. | 19. | 0.60 | 6.6 | 24. |
| 425494 | 455. | 43. | 92. | 18. | 0.70 | 7.1 | 25. |
| 425495 | 392. | 44. | 80. | 16. | 0.60 | 6.3 | 50. |
| 425496 | 572. | 48. | 94. | 18. | 0.70 | 7.2 | 31. |
| 425497 | 262. | 46. | 89. | 13. | 0.60 | 6.1 | 21. |
| 425498 | 434. | 35. | 74. | 14. | 0.60 | 6.5 | 28. |
| AVG. | 357.1 | 39.6 | 79.9 | 16.5 | 0.640 | 6.52 | 30.6 |
| S. D. | 107.2 | 6.6 | 10.5 | 2.7 | 0.052 | 0.39 | 8.5 |
| S. E. | 33.9 | 2.1 | 3.3 | 0.9 | 0.016 | 0.12 | 2.7 |

GROUP: III
SAMPLE DATE: 09/04/87

CONCENTRATION: 100 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | ALP U/L | ALT U/L | AST U/L | BUN mg/dl | CREAT mg/dl | TPROT g/dl | CHOL mg/dl |
|---|---|---|---|---|---|---|---|
| 425499 | 221. | 28. | 59. | 14. | 0.60 | 5.9 | 32. |
| 425500 | 454. | 36. | 70. | 16. | 0.60 | 6.5 | 25. |
| 425501 | 189. | 31. | 97. | 17. | 0.60 | 6.0 | 19. |
| 425502 | 580. | 35. | 59. | 13. | 0.60 | 6.4 | 30. |
| 425503 | 325. | 35. | 81. | 12. | 0.60 | 6.2 | 23. |
| 425504 | 335. | 26. | 67. | 14. | 0.60 | 6.4 | 26. |
| 425505 | 407. | 36. | 66. | 17. | 0.70 | 6.6 | 39. |
| 425506 | 361. | 94. | 122. | 15. | 0.70 | 6.7 | 28. |
| 425507 | 255. | 38. | 66. | 14. | 0.60 | 6.8 | 22. |
| 425508 | 380. | 39. | 55. | 12. | 0.60 | 6.2 | 32. |
| AVG. | 350.7 | 39.8 | 74.2 | 14.4 | 0.620 | 6.37 | 27.6 |
| S. D. | 115.7 | 19.5 | 20.8 | 1.8 | 0.042 | 0.29 | 5.9 |
| S. E. | 36.6 | 6.2 | 6.6 | 0.6 | 0.013 | 0.09 | 1.9 |

SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX A (continued)

INDIVIDUAL CLINICAL CHEMICAL FINDINGS FOR MALE RATS
AT 12 DAYS ON TEST

---

GROUP: V
SAMPLE DATE: 09/04/87

CONCENTRATION: 500 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | ALP U/L | ALT U/L | AST U/L | BUN mg/dl | CREAT mg/dl | TPROT g/dl | CHOL mg/dl |
|---|---|---|---|---|---|---|---|
| 425509 | 519. | 28. | 84. | 15. | 0.60 | 6.1 | 15. |
| 425510 | 290. | 30. | 61. | 13. | 0.60 | 6.6 | 39. |
| 425511 | 207. | 27. | 64. | 18. | 0.60 | 6.5 | 29. |
| 425512 | 524. | 32. | 71. | 14. | 0.70 | 6.7 | 36. |
| 425513 | 588. | 37. | 73. | 12. | 0.60 | 6.1 | 39. |
| 425514 | 570. | 34. | 76. | 14. | 0.60 | 6.6 | 18. |
| 425515 | 290. | 37. | 70. | 15. | 0.60 | 6.0 | 44. |
| 425516 | 583. | 31. | 63. | 16. | 0.60 | 6.5 | 39. |
| 425517 | 276. | 33. | 69. | 17. | 0.60 | 6.9 | 57. |
| 425518 | 263. | 26. | 82. | 16. | 0.70 | 7.0 | 58. |
| AVG. | 411.0 | 31.5 | 71.3 | 15.0 | 0.620 | 6.50 | 37.4 |
| S. D. | 156.9 | 3.9 | 7.7 | 1.8 | 0.042 | 0.34 | 14.2 |
| S. E. | 49.6 | 1.2 | 2.4 | 0.6 | 0.013 | 0.11 | 4.5 |

GROUP: VII
SAMPLE DATE: 09/04/87

CONCENTRATION: 1500 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | ALP U/L | ALT U/L | AST U/L | BUN mg/dl | CREAT mg/dl | TPROT g/dl | CHOL mg/dl |
|---|---|---|---|---|---|---|---|
| 425519 | 286. | 47. | 87. | 20. | 0.60 | 6.2 | 41. |
| 425521 | 432. | 30. | 76. | 19. | 0.60 | 5.7 | 50. |
| 425522 | 422. | 35. | 94. | 25. | 0.60 | 6.5 | 55. |
| 425523 | 366. | 24. | 86. | 21. | 0.60 | 7.0 | 33. |
| 425525 | 502. | 58. | 97. | 23. | 0.60 | 6.5 | 41. |
| 425527 | 533. | 33. | 76. | 26. | 0.70 | 6.9 | 44. |
| 425528 | 184. | 46. | 93. | 13. | 0.60 | 5.9 | 71. |
| AVG. | 389.3 | 39.0 | 87.0 | 21.0 | 0.614 | 6.39 | 47.9 |
| S. D. | 122.2 | 11.8 | 8.4 | 4.4 | 0.038 | 0.48 | 12.4 |
| S. E. | 46.2 | 4.5 | 3.2 | 1.6 | 0.014 | 0.18 | 4.7 |

SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX A (continued)

INDIVIDUAL CLINICAL URINALYSIS FINDINGS FOR MALE RATS
AT 12 DAYS ON TEST

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GROUP: I
SAMPLE DATE: 09/04/87

CONCENTRATION: 0 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | VOL ml | OSMOL mOs | BLOOD | GLUCOSE | PRO-TEIN | pH | BILI-RUBIN | UROBL mg/dl | Ke-tone |
|---|---|---|---|---|---|---|---|---|---|
| 425489 | 17.6 | 780. | +1 | - | +2 | 8.5 | - | 0.1 | - |
| 425490 | 3.2 | 2286. | - | - | +2 | 7.0 | - | 0.1 | - |
| 425491 | 7.0 | 2027. | +1 | - | +2 | 7.0 | - | 0.1 | +1 |
| 425492 | 5.6 | 1474. | +1 | - | +2 | 7.5 | - | 0.1 | + |
| 425493 | 5.2 | 1293. | +1 | - | +2 | 8.5 | - | 0.1 | - |
| 425494 | 3.8 | 1421. | +1 | - | +2 | 7.5 | - | 0.1 | + |
| 425495 | 7.4 | 1142. | +1 | - | +1 | 7.5 | - | 0.1 | + |
| 425496 | 10.0 | 958. | - | - | - | 7.0 | - | 0.1 | - |
| 425497 | 6.0 | 1416. | +2 | - | +2 | 7.5 | - | 0.1 | +1 |
| 425498 | 6.0 | 1300. | - | - | +1 | 7.5 | - | 0.1 | + |
| AVG. | 7.18 | 1409.7 | | | | 7.55 | | 0.10 | |
| S. D. | 4.12 | 453.5 | | | | 0.55 | | 0.00 | |
| S. E. | 1.30 | 143.4 | | | | 0.17 | | 0.00 | |

GROUP: III
SAMPLE DATE: 09/04/87

CONCENTRATION: 100 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | VOL ml | OSMOL mOs | BLOOD | GLUCOSE | PRO-TEIN | pH | BILI-RUBIN | UROBL mg/dl | Ke-tone |
|---|---|---|---|---|---|---|---|---|---|
| 425499 | 6.6 | 1324. | - | - | +2 | 7.5 | - | 0.1 | + |
| 425500 | 3.4 | 2358. | +1 | - | +2 | 7.5 | - | 0.1 | - |
| 425501 | 5.4 | 942. | - | - | + | 6.5 | - | 0.1 | + |
| 425502 | 4.0 | 1280. | - | - | - | 7.5 | - | 0.1 | - |
| 425503 | 5.0 | 1461. | - | - | + | 7.5 | - | 0.1 | + |
| 425504 | 4.6 | 1408. | - | - | +2 | 7.5 | - | 0.1 | - |
| 425505 | 4.8 | 2037. | - | - | +2 | 7.0 | - | 0.1 | + |
| 425506 | 7.6 | 1293. | +1 | - | +2 | 7.5 | - | 0.1 | - |
| 425507 | 4.0 | 1488. | - | - | +2 | 7.0 | - | 0.1 | + |
| 425508 | 5.2 | 1379. | + | - | + | 7.5 | - | 0.1 | - |
| AVG. | 5.06 | 1497.0 | | | | 7.30 | | 0.10 | |
| S. D. | 1.26 | 405.9 | | | | 0.35 | | 0.00 | |
| S. E. | 0.40 | 128.4 | | | | 0.11 | | 0.00 | |

SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX A (continued)

INDIVIDUAL CLINICAL URINALYSIS FINDINGS FOR MALE RATS
AT 12 DAYS ON TEST

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GROUP: V
SAMPLE DATE: 09/04/87

CONCENTRATION: 500 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | VOL ml | OSMOL mOs | BLOOD | GLUCOSE | PRO-TEIN | pH | BILI-RUBIN | UROBL mg/dl | Ke-tone |
|---|---|---|---|---|---|---|---|---|---|
| 425509 | 4.0 | 1726. | - | - | +1 | 7.0 | - | 0.1 | - |
| 425510 | 3.4 | 2139. | - | - | +2 | 6.5 | - | 0.1 | + |
| 425511 | 3.8 | 2079. | - | - | +2 | 7.5 | - | 0.1 | +1 |
| 425512 | 2.6 | 2902. | - | - | +3 | 7.0 | - | 0.1 | +1 |
| 425513 | 5.0 | 1331. | - | - | + | 7.0 | - | 0.1 | - |
| 425514 | 4.2 | 2115. | - | - | +2 | 7.0 | - | 0.1 | + |
| 425515 | 6.4 | 1399. | - | - | +1 | 6.5 | - | 0.1 | + |
| 425516 | 4.4 | 2332. | - | - | +1 | 6.5 | - | 0.1 | +1 |
| 425517 | 6.0 | 1241. | + | - | + | 7.0 | - | 0.1 | + |
| 425518 | 5.4 | 1434. | - | - | +2 | 7.0 | - | 0.1 | - |
| AVG. | 4.52 | 1869.8 | | | | 6.90 | | 0.10 | |
| S. D. | 1.18 | 534.7 | | | | 0.32 | | 0.00 | |
| S. E. | 0.37 | 169.1 | | | | 0.10 | | 0.00 | |

GROUP: VII
SAMPLE DATE: 09/04/87

CONCENTRATION: 1500 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | VOL ml | OSMOL mOs | BLOOD | GLUCOSE | PRO-TEIN | pH | BILI-RUBIN | UROBL mg/dl | Ke-tone |
|---|---|---|---|---|---|---|---|---|---|
| 425519 | 13.8 | 824. | +1 | - | +1 | 7.0 | - | 0.1 | - |
| 425521 | 9.0 | 1065. | +1 | - | + | 6.5 | - | 0.1 | - |
| 425522 | 4.4 | 2174. | +2 | - | + | 7.5 | - | 0.1 | - |
| 425523 | 1.1 | 5070. | - | - | +4 | 5.0 | - | 0.1 | - |
| 425525 | 9.0 | 1010. | - | - | +1 | 6.5 | - | 0.1 | - |
| 425527 | 4.2 | 1323. | +1 | - | + | 7.0 | - | 0.1 | - |
| 425528 | 9.0 | 1039. | +1 | - | + | 7.0 | - | 0.1 | - |
| AVG. | 7.21 | 1786.4 | | | | 6.64 | | 0.10 | |
| S. D. | 4.23 | 1514.1 | | | | 0.80 | | 0.00 | |
| S. E. | 1.60 | 572.3 | | | | 0.30 | | 0.00 | |

SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX A (continued)

INDIVIDUAL CLINICAL URINALYSIS FINDINGS FOR MALE RATS
AT 12 DAYS ON TEST

---

GROUP: I
SAMPLE DATE: 09/04/87

CONCENTRATION: 0 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | RBC /hpf | WBC /hpf | Epith /hpf | Cast /lpf | APPEARANCE |
|---|---|---|---|---|---|
| 425489 | 0-0 | 6-8 | 0-0 | 0-0 | Y CL PPT |
| 425490 | 8-10 | 0-1 | 0-0 | 0-0 | Y C PPT |
| 425491 | 0-1 | 0-2 | 0-0 | 0-0 | Y C PPT |
| 425492 | 2-4 | 0-2 | 0-0 | 0-0 | Y C PPT |
| 425493 | 15-20 | 4-5 | 0-0 | 0-0 | A C PPT |
| 425494 | 10-12 | 2-3 | 10-12 | 0-0 | Y C PPT |
| 425495 | 4-5 | 25-30 | 0-0 | 0-0 | Y C PPT |
| 425496 | 0-1 | 0-0 | 0-1 | 0-0 | Y C |
| 425497 | 2-3 | 2-3 | 0-0 | 0-0 | A CL PPT FEED |
| 425498 | 4-5 | 9-10 | 0-0 | 0-0 | Y C PPT |

GROUP: III
SAMPLE DATE: 09/04/87

CONCENTRATION: 100 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | RBC /hpf | WBC /hpf | Epith /hpf | Cast /lpf | APPEARANCE |
|---|---|---|---|---|---|
| 425499 | 2-3 | 6-8 | 4-5 | 0-0 | Y C PPT |
| 425500 | 5-6 | 0-2 | 0-0 | 0-0 | Y C PPT |
| 425501 | 0-0 | 2-3 | 0-0 | 0-0 | Y C |
| 425502 | 1-2 | 1-2 | 0-0 | 0-0 | Y C PPT |
| 425503 | 12-15 | 12-15 | 0-0 | 0-0 | Y C PPT |
| 425504 | 5-6 | 3-4 | 0-0 | 0-0 | Y CL PPT |
| 425505 | 8-9 | 10-12 | 0-0 | 0-0 | Y C PPT |
| 425506 | 20-25 | 30-40 | 0-0 | 0-0 | Y CL PPT |
| 425507 | 10-12 | 15-20 | 0-0 | 0-0 | Y CL PPT |
| 425508 | 5-6 | 10-15 | 0-0 | 0-0 | Y C PPT |

SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX A (continued)

INDIVIDUAL CLINICAL URINALYSIS FINDINGS FOR MALE RATS
AT 12 DAYS ON TEST

---

GROUP: V
SAMPLE DATE: 09/04/87

CONCENTRATION: 500 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | RBC /hpf | WBC /hpf | Epith /hpf | Cast /lpf | APPEARANCE |
|---|---|---|---|---|---|
| 425509 | 4-5 | 8-10 | 0-0 | 0-0 | Y CL PPT |
| 425510 | 0-1 | 0-1 | 0-0 | 0-0 | Y C PPT |
| 425511 | 8-10 | 15-20 | 0-0 | 0-0 | Y CL PPT |
| 425512 | 2-3 | 0-1 | 0-0 | 0-0 | Y C PPT |
| 425513 | 4-5 | 8-10 | 2-3 | 0-0 | Y C PPT |
| 425514 | 0-0 | 5-6 | 0-0 | 0-0 | Y C PPT |
| 425515 | 0-0 | 8-10 | 0-0 | 0-0 | Y C PPT |
| 425516 | 8-10 | 15-20 | 0-0 | 0-0 | Y CL PPT |
| 425517 | 8-10 | 10-12 | 0-0 | 0-0 | Y CL PPT |
| 425518 | 0-0 | 0-2 | 0-0 | 0-0 | Y C PPT |

GROUP: VII
SAMPLE DATE: 09/04/87

CONCENTRATION: 1500 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | RBC /hpf | WBC /hpf | Epith /hpf | Cast /lpf | APPEARANCE |
|---|---|---|---|---|---|
| 425519 | 6-7 | 12-15 | 0-0 | 0-0 | Y CL PPT |
| 425521 | 2-3 | 8-10 | 0-0 | 0-0 | Y C PPT |
| 425522 | 0-0 | 0-0 | 0-0 | 0-0 | Y C PPT |
| 425523 | 0-0 | 0-2 | 0-0 | 0-0 | Y C PPT |
| 425525 | 0-1 | 0-2 | 0-0 | 0-0 | Y C |
| 425527 | 0-0 | 2-3 | 0-0 | 0-0 | Y C |
| 425528 | 4-5 | 8-10 | 0-0 | 0-0 | Y C PPT |

SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX A (continued)

INDIVIDUAL HEMATOLOGIC FINDINGS FOR MALE RATS
AT 26 DAYS ON TEST

---

GROUP: I
SAMPLE DATE: 09/18/87

CONCENTRATION: 0 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | RBC $x10^6/ul$ | Hb g/dl | Ht % | MCV fl | MCH pg | MCHC g/dl | PLAT $x10^3/ul$ |
|---|---|---|---|---|---|---|---|
| 425489 | 7.17 | 14.0 | 51. | 71. | 20. | 27. | 1548. |
| 425490 | 7.46 | 15.1 | 54. | 72. | 20. | 28. | 883. |
| 425492 | 7.06 | 14.2 | 51. | 72. | 20. | 28. | 967. |
| 425495 | 7.25 | 15.3 | 52. | 72. | 21. | 29. | 1316. |
| 425496 | 7.84 | 15.2 | 55. | 70. | 19. | 28. | 1188. |
| AVG. | 7.356 | 14.76 | 52.4 | 71.4 | 20.1 | 28.2 | 1180.4 |
| S. D. | 0.308 | 0.61 | 1.7 | 0.9 | 0.7 | 0.7 | 268.1 |
| S. E. | 0.138 | 0.27 | 0.7 | 0.4 | 0.3 | 0.3 | 119.9 |

GROUP: III
SAMPLE DATE: 09/18/87

CONCENTRATION: 100 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | RBC $x10^6/ul$ | Hb g/dl | Ht % | MCV fl | MCH pg | MCHC g/dl | PLAT $x10^3/ul$ |
|---|---|---|---|---|---|---|---|
| 425499 | 7.44 | 15.0 | 52. | 70. | 20. | 29. | 1196. |
| 425500 | 7.21 | 14.6 | 51. | 71. | 20. | 28. | 1032. |
| 425501 | 7.28 | 14.5 | 52. | 71. | 20. | 28. | 1212. |
| 425504 | 7.08 | 13.9 | 49. | 70. | 20. | 28. | 1163. |
| 425507 | 7.12 | 14.8 | 51. | 71. | 21. | 29. | 924. |
| AVG. | 7.226 | 14.56 | 51.1 | 70.6 | 20.1 | 28.5 | 1105.4 |
| S. D. | 0.143 | 0.42 | 1.1 | 0.5 | 0.4 | 0.4 | 123.7 |
| S. E. | 0.064 | 0.19 | 0.5 | 0.2 | 0.2 | 0.2 | 55.3 |

SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX A (continued)

INDIVIDUAL HEMATOLOGIC FINDINGS FOR MALE RATS
AT 26 DAYS ON TEST

---

GROUP: V
SAMPLE DATE: 09/18/87

CONCENTRATION: 500 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | RBC $x10^6$/ul | Hb g/dl | Ht % | MCV fl | MCH pg | MCHC g/dl | PLAT $x10^3$/ul |
|---|---|---|---|---|---|---|---|
| 425510 | 7.33 | 14.9 | 52. | 71. | 20. | 29. | 744. |
| 425511 | 8.00 | 16.3 | 57. | 71. | 20. | 29. | 832. |
| 425513 | 7.69 | 15.7 | 55. | 71. | 20. | 29. | 860. |
| 425515 | 7.15 | 15.7 | 53. | 74. | 22. | 30. | 926. |
| 425516 | 7.33 | 15.5 | 53. | 72. | 21. | 29. | 792. |
| AVG. | 7.500 | 15.62 | 53.7 | 71.8 | 20.8 | 29.1 | 830.8 |
| S. D. | 0.341 | 0.50 | 1.9 | 1.3 | 0.7 | 0.5 | 68.8 |
| S. E. | 0.153 | 0.22 | 0.9 | 0.6 | 0.3 | 0.2 | 30.8 |

GROUP: VII
SAMPLE DATE: 09/18/87

CONCENTRATION: 1500 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | RBC $x10^6$/ul | Hb g/dl | Ht % | MCV fl | MCH pg | MCHC g/dl | PLAT $x10^3$/ul |
|---|---|---|---|---|---|---|---|
| 425522 | 7.55 | 16.0 | 54. | 72. | 21. | 30. | 911. |
| 425525 | 7.33 | 15.5 | 53. | 72. | 21. | 29. | 842. |
| 425527 | 7.32 | 15.5 | 53. | 72. | 21. | 30. | 925. |
| 425528 | 6.75 | 14.0 | 48. | 70. | 21. | 30. | 309. |
| AVG. | 7.238 | 15.25 | 51.8 | 71.5 | 21.1 | 29.5 | 746.8 |
| S. D. | 0.342 | 0.87 | 2.9 | 1.0 | 0.2 | 0.2 | 294.1 |
| S. E. | 0.171 | 0.43 | 1.5 | 0.5 | 0.1 | 0.1 | 147.0 |

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APPENDIX A (continued)

INDIVIDUAL HEMATOLOGIC FINDINGS FOR MALE RATS
AT 26 DAYS ON TEST

GROUP: I
SAMPLE DATE: 09/18/87

CONCENTRATION: 0 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | WBC $x10^3/ul$ | Neut WBCx% | Band WBCx% | Lymph WBCx% | Alym WBCx% | Mono WBCx% | Eosin WBCx% | Baso WBCx% |
|---|---|---|---|---|---|---|---|---|
| 425489 | 17.6 | 4752. | 0. | 11616. | 0. | 1056. | 176. | 0. |
| 425490 | 17.4 | 4698. | 0. | 11658. | 0. | 1044. | 0. | 0. |
| 425492 | 16.3 | 2282. | 0. | 13529. | 0. | 489. | 0. | 0. |
| 425495 | 20.4 | 4080. | 0. | 15096. | 0. | 1020. | 204. | 0. |
| 425496 | 12.2 | 2562. | 0. | 8784. | 0. | 854. | 0. | 0. |
| AVG. | 16.78 | 3674.8 | 0.0 | 12136.6 | 0.0 | 892.6 | 76.0 | 0.0 |
| S. D. | 2.97 | 1177.9 | 0.0 | 2368.4 | 0.0 | 239.9 | 104.5 | 0.0 |
| S. E. | 1.33 | 526.8 | 0.0 | 1059.2 | 0.0 | 107.3 | 46.8 | 0.0 |

GROUP: III
SAMPLE DATE: 09/18/87

CONCENTRATION: 100 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | WBC $x10^3/ul$ | Neut WBCx% | Band WBCx% | Lymph WBCx% | Alym WBCx% | Mono WBCx% | Eosin WBCx% | Baso WBCx% |
|---|---|---|---|---|---|---|---|---|
| 425499 | 14.3 | 1716. | 0. | 11297. | 429. | 715. | 143. | 0. |
| 425500 | 11.8 | 944. | 0. | 10266. | 118. | 472. | 0. | 0. |
| 425501 | 16.9 | 3211. | 0. | 12506. | 169. | 1014. | 0. | 0. |
| 425504 | 13.4 | 4020. | 0. | 9246. | 0. | 134. | 0. | 0. |
| 425507 | 16.8 | 3864. | 0. | 11760. | 336. | 840. | 0. | 0. |
| AVG. | 14.64 | 2751.0 | 0.0 | 11015.0 | 210.4 | 635.0 | 28.6 | 0.0 |
| S. D. | 2.21 | 1359.9 | 0.0 | 1279.5 | 171.8 | 342.6 | 64.0 | 0.0 |
| S. E. | 0.99 | 608.2 | 0.0 | 572.2 | 76.8 | 153.2 | 28.6 | 0.0 |

SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX A (continued)

INDIVIDUAL HEMATOLOGIC FINDINGS FOR MALE RATS
AT 26 DAYS ON TEST

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GROUP: V
SAMPLE DATE: 09/18/87

CONCENTRATION: 500 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | WBC $x10^3/ul$ | Neut WBCx% | Band WBCx% | Lymph WBCx% | Alym WBCx% | Mono WBCx% | Eosin WBCx% | Baso WBCx% |
|---|---|---|---|---|---|---|---|---|
| 425510 | 12.8 | 3840. | 0. | 8448. | 0. | 512. | 0. | 0. |
| 425511 | 12.6 | 3780. | 0. | 8316. | 0. | 504. | 0. | 0. |
| 425513 | 16.9 | 3042. | 0. | 13351. | 169. | 169. | 169. | 0. |
| 425515 | 20.1 | 5025. | 0. | 14472. | 201. | 402. | 0. | 0. |
| 425516 | 17.5 | 4550. | 0. | 11550. | 175. | 1225. | 0. | 0. |
| AVG. | 15.98 | 4047.4 | 0.0 | 11227.4 | 109.0 | 562.4 | 33.8 | 0.0 |
| S. D. | 3.23 | 763.8 | 0.0 | 2799.2 | 100.2 | 395.4 | 75.6 | 0.0 |
| S. E. | 1.44 | 341.6 | 0.0 | 1251.8 | 44.8 | 176.8 | 33.8 | 0.0 |

GROUP: VII
SAMPLE DATE: 09/18/87

CONCENTRATION: 1500 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | WBC $x10^3/ul$ | Neut WBCx% | Band WBCx% | Lymph WBCx% | Alym WBCx% | Mono WBCx% | Eosin WBCx% | Baso WBCx% |
|---|---|---|---|---|---|---|---|---|
| 425522 | 12.3 | 2214. | 0. | 9348. | 123. | 492. | 123. | 0. |
| 425525 | 13.5 | 3510. | 0. | 9180. | 0. | 675. | 135. | 0. |
| 425527 | 13.5 | 4725. | 0. | 7965. | 0. | 810. | 0. | 0. |
| 425528 | 6.0 | 720. | 0. | 4980. | 120. | 180. | 0. | 0. |
| AVG. | 11.32 | 2792.3 | 0.0 | 7868.3 | 60.8 | 539.3 | 64.5 | 0.0 |
| S. D. | 3.59 | 1720.4 | 0.0 | 2021.7 | 70.2 | 272.7 | 74.6 | 0.0 |
| S. E. | 1.80 | 860.2 | 0.0 | 1010.8 | 35.1 | 136.3 | 37.3 | 0.0 |

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APPENDIX A (continued)

INDIVIDUAL CLINICAL CHEMICAL FINDINGS FOR MALE RATS
AT 26 DAYS ON TEST

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GROUP: I
SAMPLE DATE: 09/18/87

CONCENTRATION: 0 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | ALP U/L | ALT U/L | AST U/L | BUN mg/dl | CREAT mg/dl | TPROT g/dl | CHOL mg/dl |
|---|---|---|---|---|---|---|---|
| 425489 | 377. | 40. | 78. | 27. | 0.70 | 6.5 | 53. |
| 425490 | 251. | 37. | 69. | 14. | 0.60 | 6.7 | 75. |
| 425492 | 307. | 45. | 73. | 18. | 0.70 | 6.3 | 52. |
| 425495 | 450. | 49. | 84. | 17. | 0.90 | 7.4 | 89. |
| 425496 | 552. | 43. | 63. | 18. | 0.70 | 6.6 | 53. |
| AVG. | 387.4 | 42.8 | 73.4 | 18.8 | 0.720 | 6.70 | 64.4 |
| S. D. | 118.5 | 4.6 | 8.1 | 4.9 | 0.110 | 0.42 | 16.8 |
| S. E. | 53.0 | 2.1 | 3.6 | 2.2 | 0.049 | 0.19 | 7.5 |

GROUP: III
SAMPLE DATE: 09/18/87

CONCENTRATION: 100 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | ALP U/L | ALT U/L | AST U/L | BUN mg/dl | CREAT mg/dl | TPROT g/dl | CHOL mg/dl |
|---|---|---|---|---|---|---|---|
| 425499 | 279. | 38. | 56. | 20. | 0.60 | 6.4 | 62. |
| 425500 | 466. | 38. | 64. | 16. | 0.70 | 5.9 | 49. |
| 425501 | 282. | 42. | 68. | 16. | 0.60 | 6.3 | 57. |
| 425504 | 361. | 33. | 60. | 16. | 0.60 | 6.2 | 56. |
| 425507 | 263. | 43. | 58. | 15. | 0.60 | 6.6 | 49. |
| AVG. | 330.2 | 38.8 | 61.2 | 16.6 | 0.620 | 6.28 | 54.6 |
| S. D. | 84.9 | 4.0 | 4.8 | 1.9 | 0.045 | 0.26 | 5.6 |
| S. E. | 38.0 | 1.8 | 2.2 | 0.9 | 0.020 | 0.12 | 2.5 |

SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX A (continued)

INDIVIDUAL CLINICAL CHEMICAL FINDINGS FOR MALE RATS
AT 26 DAYS ON TEST

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GROUP: V
SAMPLE DATE: 09/18/87

CONCENTRATION: 500 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | ALP U/L | ALT U/L | AST U/L | BUN mg/dl | CREAT mg/dl | TPROT g/dl | CHOL mg/dl |
|---|---|---|---|---|---|---|---|
| 425510 | 290. | 31. | 54. | 16. | 0.60 | 6.5 | 43. |
| 425511 | 245. | 48. | 70. | 14. | 0.60 | 5.9 | 54. |
| 425513 | 624. | 65. | 82. | 17. | 0.60 | 6.5 | 69. |
| 425515 | 298. | 41. | 69. | 16. | 0.60 | 5.9 | 64. |
| 425516 | 558. | 46. | 70. | 18. | 0.70 | 6.5 | 60. |
| AVG. | 403.0 | 46.2 | 69.0 | 16.2 | 0.620 | 6.26 | 58.0 |
| S. D. | 174.4 | 12.4 | 9.9 | 1.5 | 0.045 | 0.33 | 10.0 |
| S. E. | 78.0 | 5.5 | 4.4 | 0.7 | 0.020 | 0.15 | 4.5 |

GROUP: VII
SAMPLE DATE: 09/18/87

CONCENTRATION: 1500 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | ALP U/L | ALT U/L | AST U/L | BUN mg/dl | CREAT mg/dl | TPROT g/dl | CHOL mg/dl |
|---|---|---|---|---|---|---|---|
| 425522 | 475. | 25. | 52. | 17. | 0.60 | 6.1 | 60. |
| 425525 | 451. | 42. | 63. | 15. | 0.60 | 6.0 | 54. |
| 425527 | 454. | 36. | 70. | 17. | 0.60 | 5.8 | 54. |
| 425528 | 328. | 52. | 79. | 15. | 0.60 | 5.6 | 64. |
| AVG. | 427.0 | 38.8 | 66.0 | 16.0 | 0.600 | 5.88 | 58.0 |
| S. D. | 66.9 | 11.3 | 11.4 | 1.2 | 0.000 | 0.22 | 4.9 |
| S. E. | 33.4 | 5.6 | 5.7 | 0.6 | 0.000 | 0.11 | 2.4 |

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APPENDIX A (continued)

INDIVIDUAL CLINICAL URINALYSIS FINDINGS FOR MALE RATS
AT 26 DAYS ON TEST

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GROUP: I
SAMPLE DATE: 09/18/87

CONCENTRATION: 0 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | VOL ml | OSMOL mOs | BLOOD | GLUCOSE | PRO-TEIN | pH | BILI-RUBIN | UROBL mg/dl | Ke-tone |
|---|---|---|---|---|---|---|---|---|---|
| 425489 | 23.2 | 853. | +3 | - | +4 | 8.5 | - | 0.1 | - |
| 425490 | 5.0 | 1816. | - | - | +2 | 7.0 | - | 0.1 | + |
| 425492 | 5.6 | 2223. | - | - | +2 | 7.5 | - | 0.1 | + |
| 425495 | 13.6 | 1104. | - | - | + | 7.5 | - | 0.1 | + |
| 425496 | 7.2 | 1498. | - | - | + | 7.0 | - | 0.1 | + |
| AVG. | 10.92 | 1498.8 | | | | 7.50 | | 0.10 | |
| S. D. | 7.67 | 547.3 | | | | 0.61 | | 0.00 | |
| S. E. | 3.43 | 244.7 | | | | 0.27 | | 0.00 | |

GROUP: III
SAMPLE DATE: 09/18/87

CONCENTRATION: 100 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | VOL ml | OSMOL mOs | BLOOD | GLUCOSE | PRO-TEIN | pH | BILI-RUBIN | UROBL mg/dl | Ke-tone |
|---|---|---|---|---|---|---|---|---|---|
| 425499 | 8.6 | 1976. | + | - | +2 | 7.0 | - | 0.1 | +1 |
| 425500 | 10.6 | 1687. | - | - | +2 | 7.5 | - | 0.1 | + |
| 425501 | 10.0 | 1597. | - | - | +2 | 7.0 | - | 0.1 | + |
| 425504 | 10.2 | 1480. | - | - | +2 | 8.0 | - | 0.1 | + |
| 425507 | 6.8 | 2493. | - | - | +2 | 7.0 | - | 0.1 | +1 |
| AVG. | 9.24 | 1846.6 | | | | 7.30 | | 0.10 | |
| S. D. | 1.56 | 405.2 | | | | 0.45 | | 0.00 | |
| S. E. | 0.70 | 181.2 | | | | 0.20 | | 0.00 | |

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APPENDIX A (continued)

INDIVIDUAL CLINICAL URINALYSIS FINDINGS FOR MALE RATS
AT 26 DAYS ON TEST

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GROUP: V
SAMPLE DATE: 09/18/87

CONCENTRATION: 500 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | VOL ml | OSMOL mOs | BLOOD | GLUCOSE | PRO-TEIN | pH | BILI-RUBIN | UROBL mg/dl | Ke-tone |
|---|---|---|---|---|---|---|---|---|---|
| 425510 | 6.6 | 2188. | - | - | +2 | 6.5 | - | 0.1 | +1 |
| 425511 | 8.6 | 2128. | - | - | + | 7.5 | - | 0.1 | +1 |
| 425513 | 7.0 | 2268. | - | - | +2 | 7.0 | - | 0.1 | + |
| 425515 | 7.2 | 2543. | - | - | +2 | 6.5 | - | 0.1 | + |
| 425516 | 8.6 | 2340. | - | - | +2 | 6.5 | - | 0.1 | + |
| AVG. | 7.60 | 2293.4 | | | | 6.80 | | 0.10 | |
| S. D. | 0.94 | 160.9 | | | | 0.45 | | 0.00 | |
| S. E. | 0.42 | 72.0 | | | | 0.20 | | 0.00 | |

GROUP: VII
SAMPLE DATE: 09/18/87

CONCENTRATION: 1500 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | VOL ml | OSMOL mOs | BLOOD | GLUCOSE | PRO-TEIN | pH | BILI-RUBIN | UROBL mg/dl | Ke-tone |
|---|---|---|---|---|---|---|---|---|---|
| 425522 | 10.2 | 1545. | - | - | +1 | 7.0 | - | 0.1 | + |
| 425525 | 10.2 | 1302. | - | - | +1 | 8.0 | - | 0.1 | + |
| 425527 | 6.8 | 1718. | - | - | + | 7.5 | - | 0.1 | + |
| 425528 | 13.2 | 1138. | - | - | + | 7.0 | - | 0.1 | + |
| AVG. | 10.10 | 1425.8 | | | | 7.38 | | 0.10 | |
| S. D. | 2.62 | 256.7 | | | | 0.48 | | 0.00 | |
| S. E. | 1.31 | 128.4 | | | | 0.24 | | 0.00 | |

SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX A (continued)

INDIVIDUAL CLINICAL URINALYSIS FINDINGS FOR MALE RATS
AT 26 DAYS ON TEST

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GROUP: I
SAMPLE DATE: 09/18/87

CONCENTRATION: 0 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | RBC /hpf | WBC /hpf | Epith /hpf | Cast /lpf | APPEARANCE |
|---|---|---|---|---|---|
| 425489 | 0-0 | TNTC | 0-0 | 0-0 | LY CL PPT |
| 425490 | 0-1 | 0-2 | 0-0 | 0-0 | Y C PPT |
| 425492 | 8-10 | 2-3 | 0-0 | 0-0 | Y C PPT |
| 425495 | 6-7 | 0-2 | 0-0 | 0-0 | Y C PPT |
| 425496 | 7-8 | 0-1 | 0-0 | 0-0 | Y C PPT |

GROUP: III
SAMPLE DATE: 09/18/87

CONCENTRATION: 100 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | RBC /hpf | WBC /hpf | Epith /hpf | Cast /lpf | APPEARANCE |
|---|---|---|---|---|---|
| 425499 | 10-15 | 0-2 | 0-0 | 0-0 | Y C PPT |
| 425500 | 3-4 | 8-9 | 0-0 | 0-0 | Y CL PPT |
| 425501 | 2-3 | 8-10 | 0-0 | 0-0 | Y C PPT |
| 425504 | 0-1 | 3-4 | 0-0 | 0-0 | Y CL PPT |
| 425507 | 0-2 | 0-2 | 0-0 | 0-0 | Y CL PPT |

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APPENDIX A (continued)

INDIVIDUAL CLINICAL URINALYSIS FINDINGS FOR MALE RATS
AT 26 DAYS ON TEST

---

GROUP: V
SAMPLE DATE: 09/18/87

CONCENTRATION: 500 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | RBC /hpf | WBC /hpf | Epith /hpf | Cast /lpf | APPEARANCE |
|---|---|---|---|---|---|
| 425510 | 10-12 | 2-3 | 0-0 | 0-0 | Y C PPT |
| 425511 | 15-20 | 3-4 | 0-0 | 0-0 | Y CL PPT |
| 425513 | 4-5 | 10-15 | 0-0 | 0-0 | Y C PPT |
| 425515 | 3-4 | 3-4 | 0-0 | 0-0 | Y CL PPT FEED |
| 425516 | 8-10 | 5-6 | 0-0 | 0-0 | DY CL PPT |

GROUP: VII
SAMPLE DATE: 09/18/87

CONCENTRATION: 1500 ppm
BIRTH DATE: 06/29/87

| ANIMAL#: | RBC /hpf | WBC /hpf | Epith /hpf | Cast /lpf | APPEARANCE |
|---|---|---|---|---|---|
| 425522 | 6-7 | 0-2 | 0-0 | 0-0 | Y C PPT |
| 425525 | 15-18 | 3-4 | 0-0 | 0-0 | Y CL PPT |
| 425527 | 0-0 | 5-6 | 0-0 | 0-0 | DY CL PPT |
| 425528 | 8-10 | 2-3 | 0-0 | 0-0 | Y C PPT |

Subchronic Inhalation Toxicity Study with Formamide

Appendix F

Pathology Report No. 19-87

ES-3862 REV. 12-85

DU PONT

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E. I. DU PONT DE NEMOURS & COMPANY
INCORPORATED

HASKELL LABORATORY FOR TOXICOLOGY
AND INDUSTRIAL MEDICINE
P.O. BOX 50, ELKTON ROAD
NEWARK, DELAWARE 19714

CENTRAL RESEARCH AND DEVELOPMENT DEPARTMENT



PATHOLOGY REPORT NO. 2-88

MEDICAL RESEARCH PROJECT NO. 5602

HASKELL LABORATORY NO. 16,728

# SUBCHRONIC INHALATION TOXICITY STUDY IN RATS WITH FORMAMIDE

CENTRAL RESEARCH AND DEVELOPMENT DEPARTMENT

DATE ISSUED: APRIL 5, 1988

# SUBCHRONIC INHALATION TOXICITY STUDY IN RATS WITH FORMAMIDE


## SUMMARY

Male Crl:CD®BR rats exposed nose-only to formamide by inhalation at design concentrations of 0, 100, 500, or 1500 ppm were examined grossly and selected organs were weighed and/or examined microscopically. There were treatment-related microscopic changes in the kidneys of the high concentration exposure rats. Nephrosis was characterized by necrosis and regeneration of renal tubule cells of deep cortical nephrons. Necrosis and regeneration were prominent at 0 day recovery but after 14 recovery days regeneration of tubule cells was the only feature of the lesion. The high concentration exposure group had statistically and biologically significant lower mean final body weights and higher relative kidney weights at 0 day recovery. Mean absolute kidney weights of this group at 0 day recovery were elevated, significant biologically but not statistically. After 14 recovery days, the same group had statistically and biologically significant low mean final body weights and elevated mean absolute and relative kidney weights. Microscopic changes were correlated with changes in kidney weights.

Based on the renal lesion produced by formamide exposure under the conditions of this study, the no-effect level for histopathology is 500 ppm.



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PER/WCK/wfd
ROSS1 1.8

## INTRODUCTION AND METHODS

Body and organ weight data and gross and microscopic findings from male Crl:CD®BR rats exposed via inhalation to formamide are summarized in this report. Exposure groups were as follows:

| GROUP | DESIGN CONCENTRATION OF FORMAMIDE (ppm) |
|---|---|
| I | 0.00 (air-exposed control) |
| III | 100 |
| V | 500 |
| VII | 1500 |

Four groups of ten male rats each were exposed nose-only, 6 hours/day, 5 days/week for 2 weeks to design concentrations of 0, 100, 500, and 1500 ppm of formamide vapor in air. Five rats per group were killed and examined after the last exposure and the remaining five per group were killed and examined after a 14 day recovery period. At study termination, rats were anesthetized by intraperitoneal administration of pentobarbital and exsanguinated. Lungs, liver, kidneys, spleen, and testes were weighed. The following tissues were processed and examined microscopically: liver, kidneys, urinary bladder, lungs, heart, pancreas, thymus, spleen, adrenal glands, thyroid gland, trachea, esophagus, brain, stomach, duodenum, jejunum, ileum, cecum, colon, rectum, mesenteric lymph node, testes, epididymides, eyes, sternum, bone marrow, nose, and gross lesions. Testes, epididymides, sternum, and eyes were fixed in Bouin's solution. All other organs were fixed in 10% neutral buffered formalin. Processed tissues were embedded in paraffin, cut at 5 microns, and stained with hematoxylin and eosin.

Mean body weights, mean absolute organ weights, and mean relative (organ-to-body weight ratios) organ weights were analyzed using a one-way analysis of variance. Test groups were compared with controls by the Least Significant Difference (LSD) test and Dunnett's test when the ratio of variance (F) indicated a significant among-to-within group variation. Significance was judged at the 0.05 probability level.

The grading scale for microscopic lesions was minimal, mild, moderate, and severe.

## RESULTS AND DISCUSSION

Tables 1 and 2 contain mean final body and organ weights. Tables 3 and 4 contain incidences of microscopic observations. Appendix A contains

individual animal final body and absolute and relative (organ-to-body weight ratios) organ weights. Appendix B contains individual animal gross and microscopic pathology data.

SURVIVAL

One high concentration exposure group rat was found dead on study day 3 and another was found dead on study day 9. One moribund rat from this group was humanely killed on study day 11. The rat found dead on study day 3 had no gross or microscopic lesions which would suggest cause of death. The other two rats had moderate and severe nephrosis, revealed by microscopic examination of kidneys.

BODY AND ORGAN WEIGHTS

The high concentration exposure group had statistically and biologically significant lower mean final body weights and higher relative kidney weights at 0 day recovery. There were no statistically significant changes in mean absolute organ weights at 0 day recovery but compared to controls, group VII kidney weights were 29% higher, spleen weights were 33% lower, liver weights were 13% lower, and testis weights were 10% lower. After 14 recovery days, the high concentration exposure group had statistically and biologically significant low mean final body weights and elevated mean absolute and relative kidney weights. Although not statistically significant, the mean absolute and relative spleen weights of this group were elevated, as were the mean relative testis weights.

The changes in kidney weights reflect target organ toxicity and the changes in liver, spleen, and testis weights reflect primarily weight gain inhibition and stress.

GROSS FINDINGS

The only treatment-associated gross observations were slightly enlarged kidneys in one group VII rat and an area of tan discoloration on the kidney of another.

MICROSCOPIC FINDINGS

Treatment-related microscopic lesions were in the kidneys of the high concentration exposure rats. The change, diagnosed nephrosis, was zonal in the inner cortex and outer medulla and was characterized by degeneration and necrosis of tubule epithelium. All tubule segments of deep cortical nephrons were affected. At 0 day recovery, the minimal to severe renal lesions consisted of necrosis and regeneration of tubule epithelium. Tubules were lined by basophilic regenerative cells, some of which were in mitosis, and desquamated necrotic cells filled the lumens. Some tubules were dilated and

lined by flattened epithelium. Occasionally, mineralized necrotic debris was surrounded by granulomatous inflammation. After 14 recovery days, the mild renal lesion consisted of regeneration of tubule epithelium with no necrosis present.

A number of changes diagnosed microscopically are not considered to be specifically induced by exposure to formamide. These include depletion of lymphocytes in the spleen, thymus, and lymph nodes, gastric erosion, degeneration of seminiferous epithelium in the testes, and atrophy of bone marrow. Such changes are not uncommon or unexpected in stressed rats with weight gain inhibition.

Other diagnoses made but not specifically mentioned so far are usual background lesions in rats of this type and age.

One of the high concentration exposure rats found dead was necropsied but, inadvertently, only nose was saved for microscopic examination.

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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

TABLE I
MEAN FINAL BODY AND ORGAN WEIGHTS FROM MALE RATS
0 DAY RECOVERY

MEAN FINAL BODY WEIGHTS (grams)

| GROUP | CONC. (PPM) | FINAL BODY |
|---|---|---|
| I | 0 | 281.9 ( 27.7) |
| III | 100 | 300.6 ( 16.1) |
| V | 500 | 271.4 ( 27.9) |
| VII | 1500 | 228.1 ( 23.5)# |

MEAN ABSOLUTE ORGAN WEIGHTS (grams)

| GROUP | CONC. (PPM) | LIVER | KIDNEYS | LUNGS | SPLEEN | TESTES |
|---|---|---|---|---|---|---|
| I | 0 | 9.272 (1.445) | 2.130 (0.451) | 1.346 (0.147) | 0.626 (0.152) | 2.741 (0.285) |
| III | 100 | 10.110 (0.734) | 2.020 (0.125) | 1.392 (0.079) | 0.635 (0.110) | 2.770 (0.206) |
| V | 500 | 8.783 (1.989) | 1.946 (0.239) | 1.223 (0.080) | 0.537 (0.044) | 2.788 (0.312) |
| VII | 1500 | 8.005 (1.953) | 2.760 (0.942) | 1.211 (0.097) | 0.416 (0.084) | 2.462 (0.414) |

MEAN RELATIVE ORGAN WEIGHTS (% of body weight)

| GROUP | CONC. (PPM) | LIVER | KIDNEYS | LUNGS | SPLEEN | TESTES |
|---|---|---|---|---|---|---|
| I | 0 | 3.2758 (.2474) | 0.7499 (.1049) | 0.4911 (.0383) | 0.2207 (.0407) | 0.9749 (.0842) |
| III | 100 | 3.3613 (.0885) | 0.6723 (.0321) | 0.4645 (.0428) | 0.2110 (.0339) | 0.9229 (.0742) |
| V | 500 | 3.2065 (.3781) | 0.7161 (.0331) | 0.4524 (.0297) | 0.1987 (.0195) | 1.0398 (.1775) |
| VII | 1500 | 3.4759 (.5110) | 1.1901 (.2968)# | 0.5320 (.0158) | 0.1812 (.0201) | 1.0745 (.0734) |

STANDARD DEVIATION IN PARENTHESES
+ - SIGNIFICANTLY DIFFERENT (P<0.05) FROM CONTROL GROUP BY LSD
# - SIGNIFICANTLY DIFFERENT (P<0.05) FROM CONTROL GROUP BY LSD AND DUNNETT'S TEST



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

TABLE 2
MEAN FINAL BODY AND ORGAN WEIGHTS FROM MALE RATS
14 DAY RECOVERY

MEAN FINAL BODY WEIGHTS (grams)

| GROUP | CONC. (PPM) | FINAL BODY |
|---|---|---|
| I | 0 | 362.8 ( 17.9) |
| III | 100 | 368.6 ( 6.2) |
| V | 500 | 356.7 ( 32.7) |
| VII | 1500 | 310.6 ( 12.0)# |

MEAN ABSOLUTE ORGAN WEIGHTS (grams)

| GROUP | CONC. (PPM) | LIVER | KIDNEYS | LUNGS | SPLEEN | TESTES |
|---|---|---|---|---|---|---|
| I | 0 | 13.307 (1.427) | 2.520 (0.094) | 1.696 (0.224) | 0.710 (0.139) | 2.989 (0.224) |
| III | 100 | 13.085 (1.377) | 2.517 (0.087) | 1.598 (0.102) | 0.692 (0.128) | 2.980 (0.161) |
| V | 500 | 12.840 (1.606) | 2.634 (0.247) | 1.601 (0.153) | 0.792 (0.199) | 3.053 (0.272) |
| VII | 1500 | 11.977 (1.556) | 3.247 (0.268)# | 1.421 (0.094) | 1.043 (0.688) | 3.033 (0.212) |

MEAN RELATIVE ORGAN WEIGHTS (% of body weight)

| GROUP | CONC. (PPM) | LIVER | KIDNEYS | LUNGS | SPLEEN | TESTES |
|---|---|---|---|---|---|---|
| I | 0 | 3.6635 (.3050) | 0.6961 (.0457) | 0.4659 (.0396) | 0.1954 (.0347) | 0.8265 (.0862) |
| III | 100 | 3.5472 (.3343) | 0.6830 (.0286) | 0.4335 (.0254) | 0.1878 (.0344) | 0.8083 (.0417) |
| V | 500 | 3.5971 (.2787) | 0.7403 (.0648) | 0.4490 (.0202) | 0.2198 (.0369) | 0.8567 (.0362) |
| VII | 1500 | 3.8493 (.3968) | 1.0445 (.0559)# | 0.4573 (.0143) | 0.3330 (.2126) | 0.9849 (.0597)# |

STANDARD DEVIATION IN PARENTHESES
+ - SIGNIFICANTLY DIFFERENT (P<0.05) FROM CONTROL GROUP BY LSD
# - SIGNIFICANTLY DIFFERENT (P<0.05) FROM CONTROL GROUP BY LSD AND DUNNETT'S TEST



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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TABLE 3
INCIDENCES OF MICROSCOPIC OBSERVATIONS IN MALE RATS

(ANIMALS NECROPSIED FROM DAY 1 TO DAY 12)

| TISSUE/LESION | GROUP DESIGNATION: I<br>DOSE (ppm): 0<br>NUMBER IN GROUP: 5 | III<br>100<br>5 | V<br>500<br>5 | VII<br>1500<br>6 |
|---|---|---|---|---|
| LIVER | 5 | 5 | 5 | 5 |
| HEPATITIS, SUBACUTE/CHRONIC | 5 | 5 | 5 | 3 |
| NECROSIS, FOCAL | 1 | - | - | - |
| KIDNEYS | 5 | 5 | 5 | 5 |
| ECTASIA [TUBULES] | - | 1 | - | - |
| HYDRONEPHROSIS | - | - | 1 | - |
| NEPHROSIS | - | - | - | 5 |
| PYELITIS, CHRONIC | - | - | - | - |
| URINARY BLADDER | 5 | 5 | 5 | 5 |
| CALCULI, MULTIPLE | - | - | - | - |
| CYSTITIS, CHRONIC | - | - | - | - |
| HYPERPLASIA [TRANSITIONAL EPITHELIUM] | - | - | - | - |
| LUNGS | 5 | 5 | 5 | 5 |
| PNEUMONIA, SUBACUTE/CHRONIC | 1 | 1 | - | 1 |
| HEART | 5 | 5 | 5 | 5 |
| MYOCARDITIS, SUBACUTE/CHRONIC | - | - | 1 | - |
| SPLEEN | 5 | 5 | 5 | 5 |
| DEPLETION, LYMPHOCYTE [WHITE PULP] | - | - | - | 2 |
| THYMUS | 5 | 5 | 5 | 5 |
| DEPLETION, LYMPHOCYTE [CORTEX] | - | - | - | 3 |
| PANCREAS | 5 | 5 | 5 | 5 |
| PANCREATITIS, SUBACUTE/CHRONIC | - | - | - | - |
| ADRENALS | 5 | 5 | 5 | 5 |
| TRACHEA | 5 | 5 | 5 | 5 |
| ESOPHAGUS | 5 | 5 | 5 | 5 |
| THYROID | 5 | 5 | 5 | 5 |
| BRAIN | 5 | 5 | 5 | 5 |



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

TABLE 3 (continued)
INCIDENCES OF MICROSCOPIC OBSERVATIONS IN MALE RATS

(ANIMALS NECROPSIED FROM DAY 1 TO DAY 12)

| TISSUE/LESION | I | III | V | VII |
|---|---|---|---|---|
| GROUP DESIGNATION: | I | III | V | VII |
| DOSE (ppm): | 0 | 100 | 500 | 1500 |
| NUMBER IN GROUP: | 5 | 5 | 5 | 6 |
| STOMACH | 5 | 5 | 5 | 5 |
| EROSION [BODY] | - | - | - | 1 |
| DUODENUM | 5 | 5 | 5 | 5 |
| JEJUNUM | 5 | 5 | 5 | 5 |
| ILEUM | 5 | 5 | 5 | 5 |
| CECUM | 5 | 5 | 5 | 5 |
| COLON | 5 | 5 | 5 | 5 |
| RECTUM | 5 | 5 | 5 | 5 |
| MESENTERIC LYMPH NODE | 5 | 5 | 5 | 5 |
| DEPLETION, LYMPHOCYTE | - | - | - | 1 |
| TESTES | 5 | 5 | 5 | 5 |
| DEGENERATION [SEMINIFEROUS EPITHELIUM] | - | 1 | - | 3 |
| EPIDIDYMIDES | 5 | 5 | 5 | 5 |
| HYPOSPERMIA | - | - | - | - |
| SPERM GRANULOMA | 1 | - | - | - |
| STERNUM | 5 | 5 | 5 | 5 |
| ATROPHY [BONE MARROW] | - | - | - | 1 |
| EYES | 5 | 5 | 5 | 5 |
| FOLD/ROSETTE [RETINA] | 1 | - | - | 1 |
| NOSE | 5 | 5 | 5 | 6 |
| RHINITIS, SUBACUTE | - | - | - | - |
| SQUAMOUS METAPLASIA [EPITHELIUM] | - | - | - | - |

NOTES:
o THE NUMBER OF ORGANS EXAMINED FOR EACH GROUP IS UNDERLINED.

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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

TABLE 4
INCIDENCES OF MICROSCOPIC OBSERVATIONS IN MALE RATS

(ANIMALS NECROPSIED FROM DAY 24 TO DAY 26)

| TISSUE/LESION | GROUP DESIGNATION: I<br>DOSE (ppm): 0<br>NUMBER IN GROUP: 5 | III<br>100<br>5 | V<br>500<br>5 | VII<br>1500<br>4 |
|---|---|---|---|---|
| LIVER | 5 | 5 | 5 | 4 |
| HEPATITIS, SUBACUTE/CHRONIC | 3 | 5 | 5 | 3 |
| NECROSIS, FOCAL | - | - | - | - |
| KIDNEYS | 5 | 5 | 5 | 4 |
| ECTASIA [TUBULES] | - | - | - | - |
| HYDRONEPHROSIS | 1 | - | - | - |
| NEPHROSIS | - | - | - | 4 |
| PYELITIS, CHRONIC | 1 | - | - | - |
| URINARY BLADDER | 4 | 5 | 5 | 4 |
| CALCULI, MULTIPLE | 1 | - | - | - |
| CYSTITIS, CHRONIC | 1 | - | - | - |
| HYPERPLASIA [TRANSITIONAL EPITHELIUM] | 1 | - | - | - |
| LUNGS | 5 | 5 | 5 | 4 |
| PNEUMONIA, SUBACUTE/CHRONIC | 1 | - | - | 1 |
| HEART | 5 | 5 | 5 | 4 |
| MYOCARDITIS, SUBACUTE/CHRONIC | - | - | - | - |
| SPLEEN | 5 | 5 | 5 | 4 |
| DEPLETION, LYMPHOCYTE [WHITE PULP] | - | - | - | - |
| THYMUS | 5 | 5 | 5 | 4 |
| DEPLETION, LYMPHOCYTE [CORTEX] | - | - | - | - |
| PANCREAS | 5 | 5 | 5 | 4 |
| PANCREATITIS, SUBACUTE/CHRONIC | - | 1 | - | - |
| ADRENALS | 5 | 5 | 5 | 4 |
| TRACHEA | 5 | 5 | 5 | 4 |
| ESOPHAGUS | 5 | 5 | 5 | 4 |
| THYROID | 5 | 5 | 5 | 3 |
| BRAIN | 5 | 5 | 5 | 4 |



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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TABLE 4 (continued)
INCIDENCES OF MICROSCOPIC OBSERVATIONS IN MALE RATS

(ANIMALS NECROPSIED FROM DAY 24 TO DAY 26)

| TISSUE/LESION | I | III | V | VII |
|---|---|---|---|---|
| GROUP DESIGNATION: | I | III | V | VII |
| DOSE (ppm): | 0 | 100 | 500 | 1500 |
| NUMBER IN GROUP: | 5 | 5 | 5 | 4 |
| STOMACH | 5 | 5 | 5 | 4 |
| EROSION [BODY] | - | - | - | - |
| DUODENUM | 5 | 5 | 5 | 4 |
| JEJUNUM | 5 | 5 | 5 | 4 |
| ILEUM | 5 | 5 | 5 | 4 |
| CECUM | 5 | 5 | 5 | 4 |
| COLON | 5 | 5 | 5 | 4 |
| RECTUM | 5 | 5 | 4 | 4 |
| MESENTERIC LYMPH NODE | 5 | 5 | 5 | 4 |
| DEPLETION, LYMPHOCYTE | - | - | - | - |
| TESTES | 5 | 5 | 5 | 4 |
| DEGENERATION [SEMINIFEROUS EPITHELIUM] | 1 | 1 | - | 1 |
| EPIDIDYMIDES | 5 | 5 | 5 | 4 |
| HYPOSPERMIA | - | - | - | 1 |
| SPERM GRANULOMA | - | - | - | - |
| STERNUM | 5 | 5 | 5 | 4 |
| ATROPHY [BONE MARROW] | - | - | - | - |
| EYES | 5 | 5 | 5 | 4 |
| FOLD/ROSETTE [RETINA] | - | 1 | - | - |
| NOSE | 5 | 5 | 5 | 4 |
| RHINITIS, SUBACUTE | 1 | - | - | 1 |
| SQUAMOUS METAPLASIA [EPITHELIUM] | 1 | - | - | 1 |

NOTES:
o THE NUMBER OF ORGANS EXAMINED FOR EACH GROUP IS UNDERLINED.

SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX A
INDIVIDUAL ANIMAL FINAL BODY AND ORGAN WEIGHTS
0 DAY RECOVERY

FINAL BODY AND ABSOLUTE ORGAN WEIGHTS (grams) FROM MALE RATS

GROUP : 1 - CONTROL

| ANIMAL NUMBER | FINAL BODY | LIVER | KIDNEYS | LUNGS | SPLEEN | TESTES |
|---|---|---|---|---|---|---|
| 425491 | 294.9 | 10.462 | 2.511 | 1.503 | 0.860 | 3.030 |
| 425493 | 255.1 | 8.431 | 1.954 | 1.368 | 0.493 | 2.741 |
| 425494 | 250.0 | 7.214 | 1.439 | 1.147 | 0.487 | 2.393 |
| 425497 | 296.9 | 9.611 | 2.231 | 1.365 | 0.633 | 2.528 |
| 425498 | 312.7 | 10.643 | 2.517 | NW | 0.658 | 3.014 |
| GROUP MEAN | 281.9 | 9.272 | 2.130 | 1.346 | 0.626 | 2.741 |
| STD. DEV. | 27.7 | 1.445 | 0.451 | 0.147 | 0.152 | 0.285 |

NW = NOT WEIGHED



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

APPENDIX A (continued)
INDIVIDUAL ANIMAL FINAL BODY AND ORGAN WEIGHTS
0 DAY RECOVERY

FINAL BODY AND ABSOLUTE ORGAN WEIGHTS (grams) FROM MALE RATS

GROUP : III - 100 PPM

| ANIMAL NUMBER | FINAL BODY | LIVER | KIDNEYS | LUNGS | SPLEEN | TESTES |
|---|---|---|---|---|---|---|
| 425502 | 298.8 | 9.975 | 1.905 | 1.290 | 0.511 | 2.989 |
| 425503 | 283.2 | 9.124 | 1.977 | 1.448 | 0.562 | 2.801 |
| 425505 | 326.5 | 11.128 | 2.211 | 1.377 | 0.735 | 2.837 |
| 425506 | 301.4 | 10.410 | 1.932 | 1.353 | 0.601 | 2.793 |
| 425508 | 292.9 | 9.912 | 2.073 | 1.491 | 0.765 | 2.430 |
| GROUP MEAN | 300.6 | 10.110 | 2.020 | 1.392 | 0.635 | 2.770 |
| STD. DEV. | 16.1 | 0.734 | 0.125 | 0.079 | 0.110 | 0.206 |



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

APPENDIX A (continued)
INDIVIDUAL ANIMAL FINAL BODY AND ORGAN WEIGHTS
0 DAY RECOVERY

FINAL BODY AND ABSOLUTE ORGAN WEIGHTS (grams) FROM MALE RATS

GROUP : V - 500 PPM

| ANIMAL NUMBER | FINAL BODY | LIVER | KIDNEYS | LUNGS | SPLEEN | TESTES |
|---|---|---|---|---|---|---|
| 425509 | 269.5 | 8.791 | 1.868 | 1.159 | 0.557 | 3.070 |
| 425512 | 316.3 | 12.103 | 2.277 | 1.316 | 0.581 | 2.412 |
| 425514 | 270.4 | 8.174 | 2.011 | 1.304 | 0.537 | 2.627 |
| 425517 | 260.5 | 8.031 | 1.956 | 1.179 | 0.463 | 3.151 |
| 425518 | 240.2 | 6.818 | 1.616 | 1.155 | 0.545 | 2.681 |
| GROUP MEAN | 271.4 | 8.783 | 1.946 | 1.223 | 0.537 | 2.788 |
| STD. DEV. | 27.9 | 1.989 | 0.239 | 0.080 | 0.044 | 0.312 |

SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

H# 16,728
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APPENDIX A (continued)
INDIVIDUAL ANIMAL FINAL BODY AND ORGAN WEIGHTS
0 DAY RECOVERY

FINAL BODY AND ABSOLUTE ORGAN WEIGHTS (grams) FROM MALE RATS

GROUP : VII - 1500 PPM

| ANIMAL NUMBER | FINAL BODY | LIVER | KIDNEYS | LUNGS | SPLEEN | TESTES |
|---|---|---|---|---|---|---|
| 425519 | 233.5 | 8.002 | 2.807 | 1.214 | 0.453 | 2.545 |
| 425521 | 248.4 | 9.960 | 3.678 | 1.307 | 0.476 | 2.829 |
| 425523 | 202.4 | 6.054 | 1.796 | 1.113 | 0.320 | 2.013 |
| GROUP MEAN | 228.1 | 8.005 | 2.760 | 1.211 | 0.416 | 2.462 |
| STD. DEV. | 23.5 | 1.953 | 0.942 | 0.097 | 0.084 | 0.414 |



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX A (continued)
INDIVIDUAL ANIMAL FINAL BODY AND ORGAN WEIGHTS
0 DAY RECOVERY

RELATIVE ORGAN WEIGHTS (% of body weight) FROM MALE RATS

GROUP : 1 - CONTROL

| ANIMAL NUMBER | LIVER | KIDNEYS | LUNGS | SPLEEN | TESTES |
|---|---|---|---|---|---|
| 425491 | 3.5476 | 0.8515 | 0.5097 | 0.2916 | 1.0275 |
| 425493 | 3.3050 | 0.7660 | 0.5363 | 0.1933 | 1.0745 |
| 425494 | 2.8856 | 0.5756 | 0.4588 | 0.1948 | 0.9572 |
| 425497 | 3.2371 | 0.7514 | 0.4598 | 0.2132 | 0.8515 |
| 425498 | 3.4036 | 0.8049 | NW | 0.2104 | 0.9639 |
| GROUP MEAN | 3.2758 | 0.7499 | 0.4911 | 0.2207 | 0.9749 |
| STD. DEV. | 0.2474 | 0.1049 | 0.0383 | 0.0407 | 0.0842 |

NW = NOT WEIGHED



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

H# 16,728
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APPENDIX A (continued)
INDIVIDUAL ANIMAL FINAL BODY AND ORGAN WEIGHTS
0 DAY RECOVERY

RELATIVE ORGAN WEIGHTS (% of body weight) FROM MALE RATS

GROUP : II,I - 100 PPM

| ANIMAL NUMBER | LIVER | KIDNEYS | LUNGS | SPLEEN | TESTES |
|---|---|---|---|---|---|
| 425502 | 3.3384 | 0.6376 | 0.4317 | 0.1710 | 1.0003 |
| 425503 | 3.2218 | 0.6981 | 0.5113 | 0.1984 | 0.9891 |
| 425505 | 3.4083 | 0.6772 | 0.4217 | 0.2251 | 0.8689 |
| 425506 | 3.4539 | 0.6410 | 0.4489 | 0.1994 | 0.9267 |
| 425508 | 3.3841 | 0.7078 | 0.5090 | 0.2612 | 0.8296 |
| GROUP MEAN | 3.3613 | 0.6723 | 0.4645 | 0.2110 | 0.9229 |
| STD. DEV. | 0.0885 | 0.0321 | 0.0428 | 0.0339 | 0.0742 |



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX A (continued)
INDIVIDUAL ANIMAL FINAL BODY AND ORGAN WEIGHTS
0 DAY RECOVERY

RELATIVE ORGAN WEIGHTS (% of body weight) FROM MALE RATS

GROUP : V - 500 PPM

| ANIMAL NUMBER | LIVER | KIDNEYS | LUNGS | SPLEEN | TESTES |
|---|---|---|---|---|---|
| 425509 | 3.2620 | 0.6931 | 0.4301 | 0.2067 | 1.1391 |
| 425512 | 3.8264 | 0.7199 | 0.4161 | 0.1837 | 0.7626 |
| 425514 | 3.0229 | 0.7437 | 0.4822 | 0.1986 | 0.9715 |
| 425517 | 3.0829 | 0.7509 | 0.4526 | 0.1777 | 1.2096 |
| 425518 | 2.8385 | 0.6728 | 0.4808 | 0.2269 | 1.1162 |
| GROUP MEAN | 3.2065 | 0.7161 | 0.4524 | 0.1987 | 1.0398 |
| STD. DEV. | 0.3781 | 0.0331 | 0.0297 | 0.0195 | 0.1775 |



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX A (continued)
INDIVIDUAL ANIMAL FINAL BODY AND ORGAN WEIGHTS
0. DAY RECOVERY

RELATIVE ORGAN WEIGHTS (% of body weight) FROM MALE RATS

GROUP : VII - 1500 PPM

| ANIMAL NUMBER | LIVER | KIDNEYS | LUNGS | SPLEEN | TESTES |
|---|---|---|---|---|---|
| 425519 | 3.4270 | 1.2021 | 0.5199 | 0.1940 | 1.0899 |
| 425521 | 4.0097 | 1.4807 | 0.5262 | 0.1916 | 1.1389 |
| 425523 | 2.9911 | 0.8874 | 0.5499 | 0.1581 | 0.9946 |
| GROUP MEAN | 3.4759 | 1.1901 | 0.5320 | 0.1812 | 1.0745 |
| STD. DEV. | 0.5110 | 0.2968 | 0.0158 | 0.0201 | 0.0734 |



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX A (continued)
INDIVIDUAL ANIMAL FINAL BODY AND ORGAN WEIGHTS
14 DAY RECOVERY

FINAL BODY AND ABSOLUTE ORGAN WEIGHTS (grams) FROM MALE RATS

GROUP : 1 - CONTROL

| ANIMAL NUMBER | FINAL BODY | LIVER | KIDNEYS | LUNGS | SPLEEN | TESTES |
|---|---|---|---|---|---|---|
| 425489 | 352.1 | 13.129 | 2.493 | 1.632 | 0.805 | 3.095 |
| 425490 | 342.2 | 11.046 | 2.588 | 1.400 | 0.606 | 2.935 |
| 425492 | 363.0 | 14.824 | 2.383 | 1.655 | 0.735 | 3.088 |
| 425495 | 389.7 | 14.142 | 2.512 | 2.015 | 0.871 | 2.625 |
| 425496 | 367.2 | 13.395 | 2.625 | 1.776 | 0.533 | 3.200 |
| GROUP MEAN | 362.8 | 13.307 | 2.520 | 1.696 | 0.710 | 2.989 |
| STD. DEV. | 17.9 | 1.427 | 0.094 | 0.224 | 0.139 | 0.224 |



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX A (continued)
INDIVIDUAL ANIMAL FINAL BODY AND ORGAN WEIGHTS
14 DAY RECOVERY

FINAL BODY AND ABSOLUTE ORGAN WEIGHTS (grams) FROM MALE RATS

GROUP : III - 100 PPM

| ANIMAL NUMBER | FINAL BODY | LIVER | KIDNEYS | LUNGS | SPLEEN | TESTES |
|---|---|---|---|---|---|---|
| 425499 | 374.5 | 14.843 | 2.531 | 1.729 | 0.638 | 2.984 |
| 425500 | 374.2 | 14.185 | 2.392 | 1.511 | 0.618 | 2.983 |
| 425501 | 362.9 | 12.524 | 2.479 | 1.487 | 0.630 | 3.120 |
| 425504 | 361.3 | 12.347 | 2.559 | 1.601 | 0.655 | 2.714 |
| 425507 | 370.3 | 11.528 | 2.624 | 1.663 | 0.920 | 3.098 |
| GROUP MEAN | 368.6 | 13.085 | 2.517 | 1.598 | 0.692 | 2.980 |
| STD. DEV. | 6.2 | 1.377 | 0.087 | 0.102 | 0.128 | 0.161 |



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX A (continued)
INDIVIDUAL ANIMAL FINAL BODY AND ORGAN WEIGHTS
14 DAY RECOVERY

FINAL BODY AND ABSOLUTE ORGAN WEIGHTS (grams) FROM MALE RATS

GROUP : V - 500 PPM

| ANIMAL NUMBER | FINAL BODY | LIVER | KIDNEYS | LUNGS | SPLEEN | TESTES |
|---|---|---|---|---|---|---|
| 425510 | 345.9 | 14.076 | 2.864 | 1.561 | 0.654 | 3.034 |
| 425511 | 322.1 | 10.995 | 2.541 | 1.506 | 0.632 | 2.885 |
| 425513 | 344.7 | 11.792 | 2.335 | 1.436 | 0.667 | 2.758 |
| 425515 | 361.2 | 12.460 | 2.513 | 1.676 | 0.933 | 3.115 |
| 425516 | 409.6 | 14.876 | 2.915 | 1.826 | 1.073 | 3.474 |
| GROUP MEAN | 356.7 | 12.840 | 2.634 | 1.601 | 0.792 | 3.053 |
| STD. DEV. | 32.7 | 1.606 | 0.247 | 0.153 | 0.199 | 0.272 |



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX A (continued)
INDIVIDUAL ANIMAL FINAL BODY AND ORGAN WEIGHTS
14 DAY RECOVERY

FINAL BODY AND ABSOLUTE ORGAN WEIGHTS (grams) FROM MALE RATS

GROUP : VII - 1500 PPM

| ANIMAL NUMBER | FINAL BODY | LIVER | KIDNEYS | LUNGS | SPLEEN | TESTES |
|---|---|---|---|---|---|---|
| 425522 | 315.7 | 13.845 | 3.388 | 1.424 | 0.730 | 2.905 |
| 425525 | 315.9 | 11.708 | 3.500 | 1.487 | 0.746 | 3.278 |
| 425527 | 292.6 | 10.077 | 2.887 | 1.288 | 0.623 | 2.917 |
| 425528 | 318.0 | 12.280 | 3.212 | 1.486 | 2.072 | NW |
| GROUP MEAN | 310.6 | 11.977 | 3.247 | 1.421 | 1.043 | 3.033 |
| STD. DEV. | 12.0 | 1.556 | 0.268 | 0.094 | 0.688 | 0.212 |

NW = NOT WEIGHED



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

APPENDIX A (continued)
INDIVIDUAL ANIMAL FINAL BODY AND ORGAN WEIGHTS
14 DAY RECOVERY

RELATIVE ORGAN WEIGHTS (% of body weight) FROM MALE RATS

GROUP : I - CONTROL

| ANIMAL NUMBER | LIVER | KIDNEYS | LUNGS | SPLEEN | TESTES |
|---|---|---|---|---|---|
| 425489 | 3.7288 | 0.7080 | 0.4635 | 0.2286 | 0.8790 |
| 425490 | 3.2279 | 0.7563 | 0.4091 | 0.1771 | 0.8577 |
| 425492 | 4.0837 | 0.6565 | 0.4559 | 0.2025 | 0.8507 |
| 425495 | 3.6289 | 0.6446 | 0.5171 | 0.2235 | 0.6736 |
| 425496 | 3.6479 | 0.7149 | 0.4837 | 0.1452 | 0.8715 |
| GROUP MEAN | 3.6635 | 0.6961 | 0.4659 | 0.1954 | 0.8265 |
| STD. DEV. | 0.3050 | 0.0457 | 0.0396 | 0.0347 | 0.0862 |



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX A (continued)
INDIVIDUAL ANIMAL FINAL BODY AND ORGAN WEIGHTS
14 DAY RECOVERY

RELATIVE ORGAN WEIGHTS (% of body weight) FROM MALE RATS

GROUP : III - 100 PPM

| ANIMAL NUMBER | LIVER | KIDNEYS | LUNGS | SPLEEN | TESTES |
|---|---|---|---|---|---|
| 425499 | 3.9634 | 0.6758 | 0.4617 | 0.1704 | 0.7968 |
| 425500 | 3.7908 | 0.6392 | 0.4038 | 0.1652 | 0.7972 |
| 425501 | 3.4511 | 0.6831 | 0.4098 | 0.1736 | 0.8597 |
| 425504 | 3.4174 | 0.7083 | 0.4431 | 0.1813 | 0.7512 |
| 425507 | 3.1132 | 0.7086 | 0.4491 | 0.2484 | 0.8366 |
| GROUP MEAN | 3.5472 | 0.6830 | 0.4335 | 0.1878 | 0.8083 |
| STD. DEV. | 0.3343 | 0.0286 | 0.0254 | 0.0344 | 0.0417 |



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

H# 16,728
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APPENDIX A (continued)
INDIVIDUAL ANIMAL FINAL BODY AND ORGAN WEIGHTS
14 DAY RECOVERY

RELATIVE ORGAN WEIGHTS (% of body weight) FROM MALE RATS

GROUP : V - 500 PPM

| ANIMAL NUMBER | LIVER | KIDNEYS | LUNGS | SPLEEN | TESTES |
|---|---|---|---|---|---|
| 425510 | 4.0694 | 0.8280 | 0.4513 | 0.1891 | 0.8771 |
| 425511 | 3.4135 | 0.7889 | 0.4676 | 0.1962 | 0.8957 |
| 425513 | 3.4209 | 0.6774 | 0.4166 | 0.1935 | 0.8001 |
| 425515 | 3.4496 | 0.6957 | 0.4640 | 0.2583 | 0.8624 |
| 425516 | 3.6318 | 0.7117 | 0.4458 | 0.2620 | 0.8481 |
| GROUP MEAN | 3.5971 | 0.7403 | 0.4490 | 0.2198 | 0.8567 |
| STD. DEV. | 0.2787 | 0.0648 | 0.0202 | 0.0369 | 0.0362 |



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

H# 16,728
MR 5602
HC 17

APPENDIX A (continued)
INDIVIDUAL ANIMAL FINAL BODY AND ORGAN WEIGHTS
14 DAY RECOVERY

RELATIVE ORGAN WEIGHTS (% of body weight) FROM MALE RATS

GROUP : VII - 1500 PPM

| ANIMAL NUMBER | LIVER | KIDNEYS | LUNGS | SPLEEN | TESTES |
|---|---|---|---|---|---|
| 425522 | 4.3855 | 1.0732 | 0.4511 | 0.2312 | 0.9202 |
| 425525 | 3.7062 | 1.1079 | 0.4707 | 0.2362 | 1.0377 |
| 425527 | 3.4440 | 0.9867 | 0.4402 | 0.2129 | 0.9969 |
| 425528 | 3.8616 | 1.0101 | 0.4673 | 0.6516 | NW |
| GROUP MEAN | 3.8493 | 1.0445 | 0.4573 | 0.3330 | 0.9849 |
| STD. DEV. | 0.3968 | 0.0559 | 0.0143 | 0.2126 | 0.0597 |

NW = NOT WEIGHED



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

APPENDIX B
INDIVIDUAL ANIMAL PATHOLOGY DATA

HN-16728
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MALE RAT GROUP: I DOSE: CONTROL

ANIMAL #: 425489 DAYS ON TEST: 26 MODE OF DEATH: SD

GROSS OBSERVATIONS:
URINARY BLADDER
- THICK, MODERATE
- CALCULUS, (< 6 MM IN DIAMETER), WHITE, SEVERAL

MICROSCOPIC OBSERVATIONS:
KIDNEYS - PYELITIS, CHRONIC, MILD
LIVER - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL
LUNGS - PNEUMONIA, SUBACUTE/CHRONIC, MINIMAL
URINARY BLADDER - CALCULI, MULTIPLE
- CYSTITIS, CHRONIC, MILD
- HYPERPLASIA [TRANSITIONAL EPITHELIUM], MILD

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES: NONE



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

HN-16728
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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: I DOSE: CONTROL

ANIMAL #: 425490 DAYS ON TEST: 26 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:
LIVER - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, KIDNEYS, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: I DOSE: CONTROL

ANIMAL #: 425491 DAYS ON TEST: 12 MODE OF DEATH: SD

GROSS OBSERVATIONS:
PERIOCULAR - CHROMODACRYORRHEA, BILATERAL, SLIGHT
LIVER - ADHESION, ATTACHED TO DIAPHRAGM, RIGHT LOBE
- DISCOLORATION, YELLOW, BENEATH ADHESION SITE

MICROSCOPIC OBSERVATIONS:
LIVER - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL
- NECROSIS, FOCAL, MODERATE

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, KIDNEYS, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES: NONE



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: I DOSE: CONTROL

ANIMAL #: 425492 DAYS ON TEST: 26 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS: NONE

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, KIDNEYS, LIVER, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: I DOSE: CONTROL

ANIMAL #: 425493 DAYS ON TEST: 12 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:
LIVER - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, KIDNEYS, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: I DOSE: CONTROL

ANIMAL #: 425494 DAYS ON TEST: 12 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:

| | |
|---|---|
| EPIDIDYMIDES | - SPERM GRANULOMA |
| EYES | - FOLD/ROSETTE [RETINA] |
| LIVER | - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL |
| LUNGS | - PNEUMONIA, SUBACUTE/CHRONIC, MINIMAL |

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, ESOPHAGUS, HEART, ILEUM, JEJUNUM, KIDNEYS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: I DOSE: CONTROL

ANIMAL #: 425495 DAYS ON TEST: 26 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:
TESTES - DEGENERATION [SEMINIFEROUS EPITHELIUM], MINIMAL

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, KIDNEYS, LIVER, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: I DOSE: CONTROL

ANIMAL #: 425496 DAYS ON TEST: 26 MODE OF DEATH: SD

GROSS OBSERVATIONS:
RENAL PELVIS - DILATATION, LEFT, MODERATE

MICROSCOPIC OBSERVATIONS:
KIDNEYS - HYDRONEPHROSIS, MODERATE
LIVER - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL
NOSE - RHINITIS, SUBACUTE, MINIMAL
- SQUAMOUS METAPLASIA [EPITHELIUM], MINIMAL

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, LUNGS, MESENTERIC LYMPH NODE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: URINARY BLADDER

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: I DOSE: CONTROL

ANIMAL #: 425497 DAYS ON TEST: 12 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:
LIVER - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, KIDNEYS, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: I DOSE: CONTROL

ANIMAL #: 425498 DAYS ON TEST: 12 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:
LIVER - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, KIDNEYS, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: III DOSE: 100 ppm

ANIMAL #: 425499 DAYS ON TEST: 26 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:
LIVER - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, KIDNEYS, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: III DOSE: 100 ppm

ANIMAL #: 425500 DAYS ON TEST: 26 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:
LIVER - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, KIDNEYS, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

HN-16728
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MALE RAT GROUP: III DOSE: 100 ppm

ANIMAL #: 425501 DAYS ON TEST: 26 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:

| | |
|---|---|
| EYES | - FOLD/ROSETTE [RETINA] |
| LIVER | - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL |
| PANCREAS | - PANCREATITIS, SUBACUTE/CHRONIC, MINIMAL |
| TESTES | - DEGENERATION [SEMINIFEROUS EPITHELIUM], MINIMAL |

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, HEART, ILEUM, JEJUNUM, KIDNEYS, LUNGS, MESENTERIC LYMPH NODE, NOSE, RECTUM, SPLEEN, STERNUM, STOMACH, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: III DOSE: 100 ppm

ANIMAL #: 425502 DAYS ON TEST: 12 MODE OF DEATH: SD

GROSS OBSERVATIONS:
PERIOCULAR - CHROMODACRYORRHEA, BILATERAL, SLIGHT

MICROSCOPIC OBSERVATIONS:
KIDNEYS - ECTASIA (TUBULES), MINIMAL
LIVER - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: III DOSE: 100 ppm

ANIMAL #: 425503 DAYS ON TEST: 12 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:
LIVER - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL
LUNGS - PNEUMONIA, SUBACUTE/CHRONIC, MINIMAL

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, KIDNEYS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

HN-16728
HC-17
MR-5602

APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: III DOSE: 100 ppm

ANIMAL #: 425504 DAYS ON TEST: 26 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:
LIVER - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, KIDNEYS, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: III DOSE: 100 ppm

ANIMAL #: 425505 DAYS ON TEST: 12 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:
LIVER - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, KIDNEYS, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: III DOSE: 100 ppm

ANIMAL #: 425506 DAYS ON TEST: 12 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:
LIVER - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, KIDNEYS, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: III DOSE: 100 ppm

ANIMAL #: 425507 DAYS ON TEST: 26 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:
LIVER - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, KIDNEYS, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: III DOSE: 100 ppm

ANIMAL #: 425508 DAYS ON TEST: 12 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:
LIVER - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL
TESTES - DEGENERATION [SEMINIFEROUS EPITHELIUM], MINIMAL

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, KIDNEYS, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: V DOSE: 500 ppm

ANIMAL #: 425509 DAYS ON TEST: 12 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:
LIVER - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, KIDNEYS, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: V DOSE: 500 ppm

ANIMAL #: 425510 DAYS ON TEST: 26 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:
LIVER - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, KIDNEYS, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: RECTUM

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: V DOSE: 500 ppm

ANIMAL #: 425511 DAYS ON TEST: 26 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:
LIVER - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, KIDNEYS, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: V DOSE: 500 ppm

ANIMAL #: 425512 DAYS ON TEST: 12 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:
HEART - MYOCARDITIS, SUBACUTE/CHRONIC, MINIMAL
LIVER - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, ILEUM, JEJUNUM, KIDNEYS, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: V DOSE: 500 ppm

ANIMAL #: 425513 DAYS ON TEST: 26 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:
LIVER - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, KIDNEYS, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: V DOSE: 500 ppm

ANIMAL #: 425514 DAYS ON TEST: 12 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:
LIVER - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, KIDNEYS, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

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MALE RAT GROUP: V DOSE: 500 ppm

ANIMAL #: 425515 DAYS ON TEST: 26 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:
LIVER - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, KIDNEYS, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: V DOSE: 500 ppm

ANIMAL #: 425516 DAYS ON TEST: 26 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:
LIVER - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, KIDNEYS, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: V DOSE: 500 ppm

ANIMAL #: 425517 DAYS ON TEST: 12 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:
KIDNEYS - HYDRONEPHROSIS, MILD
LIVER - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: V DOSE: 500 ppm

ANIMAL #: 425518 DAYS ON TEST: 12 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:
LIVER - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, KIDNEYS, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: VII DOSE: 1500 ppm

ANIMAL #: 425519 DAYS ON TEST: 12 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:

| | |
|---|---|
| KIDNEYS | - NEPHROSIS, MODERATE |
| LIVER | - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL |
| LUNGS | - PNEUMONIA, SUBACUTE/CHRONIC, MINIMAL |

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: VII DOSE: 1500 ppm

ANIMAL #: 425520 DAYS ON TEST: 11 MODE OF DEATH: SE

GROSS OBSERVATIONS:
NASAL CAVITY - DISCHARGE, BROWN, SLIGHT

MICROSCOPIC OBSERVATIONS:

| | |
|---|---|
| EYES | - FOLD/ROSETTE [RETINA] |
| KIDNEYS | - NEPHROSIS, MODERATE |
| MESENTERIC LYMPH NODE | - DEPLETION, LYMPHOCYTE, MILD |
| SPLEEN | - DEPLETION, LYMPHOCYTE [WHITE PULP], SEVERE |
| STERNUM | - ATROPHY [BONE MARROW], MILD |
| STOMACH | - EROSION [BODY] |
| TESTES | - DEGENERATION [SEMINIFEROUS EPITHELIUM], MILD |
| THYMUS | - DEPLETION, LYMPHOCYTE [CORTEX], SEVERE |

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, HEART, ILEUM, JEJUNUM, LIVER, LUNGS, NOSE, PANCREAS, RECTUM, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES: NONE



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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: VII DOSE: 1500 ppm

ANIMAL #: 425521 DAYS ON TEST: 12 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:

| | |
|---|---|
| KIDNEYS | - NEPHROSIS, MODERATE |
| LIVER | - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL |
| THYMUS | - DEPLETION, LYMPHOCYTE [CORTEX], MINIMAL |

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



Du Pont HLR 139-88

SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

HN-16728
HC-17
MR-5602

APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: VII DOSE: 1500 ppm

ANIMAL #: 425522 DAYS ON TEST: 26 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:
KIDNEYS - NEPHROSIS, MILD
LIVER - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: THYROID

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



Du Pont HLR 139-88

SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

HN-16728
HC-17
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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: VII DOSE: 1500 ppm

ANIMAL #: 425523 DAYS ON TEST: 12 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:

| | |
|---|---|
| KIDNEYS | - NEPHROSIS, MINIMAL |
| LIVER | - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL |
| TESTES | - DEGENERATION [SEMINIFEROUS EPITHELIUM], MILD |

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



Du Pont HLR 139-88

SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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MR-5602

APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: VII DOSE: 1500 ppm

ANIMAL #: 425524 DAYS ON TEST: 3 MODE OF DEATH: FD

GROSS OBSERVATIONS:

| | |
|---|---|
| WHOLE BODY | - AUTOLYSIS, MILD |
| SKIN | - STAIN, PERINEUM, BROWN, MILD |
| NASAL CAVITY | - DISCHARGE, RED, SLIGHT |

MICROSCOPIC OBSERVATIONS: NONE

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: NOSE

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, KIDNEYS, LIVER, LUNGS, MESENTERIC LYMPH NODE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: VII DOSE: 1500 ppm

ANIMAL #: 425525 DAYS ON TEST: 26 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:

| | |
|---|---|
| KIDNEYS | - NEPHROSIS, MILD |
| LUNGS | - PNEUMONIA, SUBACUTE/CHRONIC, MINIMAL |
| NOSE | - RHINITIS, SUBACUTE, MINIMAL |
| | - SQUAMOUS METAPLASIA [EPITHELIUM], MINIMAL |

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, LIVER, MESENTERIC LYMPH NODE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

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HC-17
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APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: VII DOSE: 1500 ppm

ANIMAL #: 425526 DAYS ON TEST: 9 MODE OF DEATH: FD

GROSS OBSERVATIONS:

| | |
|---|---|
| WHOLE BODY | - AUTOLYSIS, SLIGHT |
| KIDNEYS | - LARGE, SLIGHT, BILATERAL |

MICROSCOPIC OBSERVATIONS:

| | |
|---|---|
| KIDNEYS | - NEPHROSIS, SEVERE |
| SPLEEN | - DEPLETION, LYMPHOCYTE (WHITE PULP), MILD |
| TESTES | - DEGENERATION (SEMINIFEROUS EPITHELIUM), MINIMAL |
| THYMUS | - DEPLETION, LYMPHOCYTE (CORTEX), MODERATE |

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, LIVER, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, STERNUM, STOMACH, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: CECUM

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE



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SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

HN-16728
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MR-5602

APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: VII DOSE: 1500 ppm

ANIMAL #: 425527 DAYS ON TEST: 26 MODE OF DEATH: SD

GROSS OBSERVATIONS:
NO ABNORMALITIES DETECTED

MICROSCOPIC OBSERVATIONS:
KIDNEYS - NEPHROSIS, MILD
LIVER - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, EPIDIDYMIDES, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, TESTES, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: CECUM

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES:
NONE

SUBCHRONIC INHALATION TOXICITY STUDY WITH FORMAMIDE

HN-16728
HC-17
MR-5602

APPENDIX B (continued)
INDIVIDUAL ANIMAL PATHOLOGY DATA

MALE RAT GROUP: VII DOSE: 1500 ppm

ANIMAL #: 425528 DAYS ON TEST: 26 MODE OF DEATH: SD

GROSS OBSERVATIONS:

| | |
|---|---|
| KIDNEYS | - DISCOLORATION, RIGHT, SURFACE, (2 MM IN DIAMETER), TAN |
| TESTES | - SMALL, RIGHT |

MICROSCOPIC OBSERVATIONS:

| | |
|---|---|
| EPIDIDYMIDES | - HYPOSPERMIA, MODERATE |
| KIDNEYS | - NEPHROSIS, MILD |
| LIVER | - HEPATITIS, SUBACUTE/CHRONIC, MINIMAL |
| TESTES | - DEGENERATION [SEMINIFEROUS EPITHELIUM], MILD |

THE FOLLOWING TISSUES WERE UNREMARKABLE MICROSCOPICALLY: ADRENALS, BRAIN, CECUM, COLON, DUODENUM, ESOPHAGUS, EYES, HEART, ILEUM, JEJUNUM, LUNGS, MESENTERIC LYMPH NODE, NOSE, PANCREAS, RECTUM, SPLEEN, STERNUM, STOMACH, THYMUS, THYROID, TRACHEA, URINARY BLADDER

THE FOLLOWING TISSUES WERE AUTOLYZED; DEGREE OF AUTOLYSIS DID NOT PRECLUDE MICROSCOPIC EXAMINATION: NONE

THE FOLLOWING TISSUES WERE SEVERELY AUTOLYZED; MICROSCOPIC DIAGNOSES NOT MADE, ORGAN NOT COUNTED IN INCIDENCE TABLES: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE NOT PRESENT FOR MICROSCOPIC EXAMINATION: NONE

SECTIONS OF THE FOLLOWING TISSUES WERE INSUFFICIENT FOR MICROSCOPIC EXAMINATION; ORGAN NOT COUNTED IN INCIDENCE TABLES: NONE



Du Pont HLR 139-88

# Triage of 8(e) Submissions

Date sent to triage: _____ NON-CAP (CAP)

Submission number: 13176A TSCA Inventory: (Y) N D

---

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX (SBTOX) SEN w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX CTOX EPI RTOX GTOX

STOX/ONCO CTOX/ONCO IMMUNO CYTO NEUR

Other (FATE, EXPO, MET, etc.): _____

---

Notes:

**THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY**

**For Contractor Use Only**

**entire document:** (0) 1 2 **pages** 1,9 **pages** _____

**Notes:**

**Contractor reviewer :** JW **Date:** 1/24/96

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ- 0992-13176 SEQ. A

TYPE: INT SUPP FLWP

SUBMITTER NAME: E. I. Dupont de Nemours and Company

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
0639 REFER TO CHEMICAL SCREENING
0678 CAP NOTICE

VOLUNTARY ACTIONS:
0401 NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKER/OTHERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

SUB. DATE: 09/11/92 OTS DATE: 09/22/92 CSRAD DATE: 03/27/95

CHEMICAL NAME:

CAS#
75-12-7

| INFORMATION TYPE: | | P F C |
|---|---|---|
| 0201 | ONCO (HUMAN) | 01 02 04 |
| 0202 | ONCO (ANIMAL) | 01 02 04 |
| 0203 | CELL TRANS (IN VITRO) | 01 02 04 |
| 0204 | MUTA (IN VITRO) | 01 02 04 |
| 0205 | MUTA (IN VIVO) | 01 02 04 |
| 0206 | REPRO/TERATO (HUMAN) | 01 02 04 |
| 0207 | REPRO/TERATO (ANIMAL) | 01 02 04 |
| 0208 | NEURO (HUMAN) | 01 02 04 |
| 0209 | NEURO (ANIMAL) | 01 02 04 |
| 0210 | ACUTE TOX. (HUMAN) | 01 02 04 |
| 0211 | CHR. TOX. (HUMAN) | 01 02 04 |
| 0212 | ACUTE TOX. (ANIMAL) | 01 02 04 |
| 0213 | SUB ACUTE TOX (ANIMAL) | 01 02 04 |
| 0214 | SUB CHRONIC TOX (ANIMAL) | 01 02 04 |
| 0215 | CHRONIC TOX (ANIMAL) | 01 02 04 |

| INFORMATION TYPE: | | P F C |
|---|---|---|
| 0216 | EPI/CLIN | 01 02 04 |
| 0217 | HUMAN EXPOS (PROD CONTAM) | 01 02 04 |
| 0218 | HUMAN EXPOS (ACCIDENTAL) | 01 02 04 |
| 0219 | HUMAN EXPOS (MONITORING) | 01 02 04 |
| 0220 | ECO/AQUA TOX | 01 02 04 |
| 0221 | ENV. OCCC/REL/FATE | 01 02 04 |
| 0222 | EMER INCI OF ENV CONTAM | 01 02 04 |
| 0223 | RESPONSE REQEST DELAY | 01 02 04 |
| 0224 | PROD/COMP/CHEM ID | 01 02 04 |
| 0225 | REPORTING RATIONALE | 01 02 04 |
| 0226 | CONFIDENTIAL | 01 02 04 |
| 0227 | ALLERG (HUMAN) | 01 02 04 |
| 0228 | ALLERG (ANIMAL) | 01 02 04 |
| 0239 | METAB/PHARMACO (ANIMAL) | 01 02 04 |
| 0240 | METAB/PHARMACO (HUMAN) | 01 02 04 |

| INFORMATION TYPE: | | P F C |
|---|---|---|
| 0241 | IMMUNO (ANIMAL) | 01 02 04 |
| 0242 | IMMUNO (HUMAN) | 01 02 04 |
| 0243 | CHEM/PHYS PROP | 01 02 04 |
| 0244 | CLASTO (IN VITRO) | 01 02 04 |
| 0245 | CLASTO (ANIMAL) | 01 02 04 |
| 0246 | CLASTO (HUMAN) | 01 02 04 |
| 0247 | DNA DAM/REPAIR | 01 02 04 |
| 0248 | PROD/USE/PROC | 01 02 04 |
| 0251 | MSDS | 01 02 04 |
| 0299 | OTHER | 01 02 04 |

| TRIAGE DATE: | NON-CBI INVENTORY | ONGOING REVIEW | SPECIES | TOXICOLOGICAL CONCERN: | USE: | PRODUCTION: |
|---|---|---|---|---|---|---|
| | YES | YES (DROP/REFER) | RAT | LOW | solvent in manuf. and processing of plastics | |
| CAS SR | NO | NO (CONTINUE) | | MED Subacute Inhalation Toxicity | | |
| | DETERMINE | REFER | | HIGH | | |

[illegible]

13176A

M

Subacute inhalation toxicity is of medium concern based on mortality in rats exposed to 0, 100, 500 and 1500 ppm for 6 hours/day, 5 days/week for 2 weeks. There were 3/10 deaths at the 1500 ppm dose. Clinical signs included weakness and hunched posture (1500); pathological findings included persistent thrombocytopenia (≥500) and nephrosis (1500).