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E. I. DU PONT DE NEMOURS & COMPANY

HARRELL LABORATORY FOR TOXICOLOGY
AND INDUSTRIAL MEDICINE
ELKTON ROAD, NEWARK, DELAWARE 19711

CENTRAL RESEARCH AND DEVELOPMENT DEPARTMENT

82 APR 30 AM 9:25
(Delivered by Terry O'Brien)

April 20, 1982

SEHQ-0482-0394C Follow-up
88-8100370

Mr. Terry O'Bryan
Chemical Hazard Identification Branch
U.S. Environmental Protection Agency
401 "M" Street, S.W.
Washington, D.C. 20460

Dear Mr. O'Bryan:

At our meeting on March 12, I agreed to send you our reports on acute and subacute testing of [redacted] (FC-143). The following Haskell reports are enclosed:

Report No.	Title
329-81	Oral LD50 Test in Mice
295-81	Oral LD50 Test in Rats
291-81	Oral LD50 Test in Guinea Pigs
682-80	Skin Absorption LD50 - Female Rats
659-79	Skin Absorption LD50 - Rabbit & Rat
636-79	Skin Irritation Test on Rabbits
635-79	Eye Irritation Test in Rabbits
253-79	Inhalation Subacute
160-69	Acute Inhalation Dust Toxicity

Sincerely,

Blaine C. McKusick
Assistant Director

BCM/bjd
Enclosures

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1982 AUG 30 AM 9:25

E. I. du Pont de Nemours and Company
Haskell Laboratory for Toxicology and Industrial Medicine
Elkton Road, Newark, Delaware 19711

HASKELL LABORATORY REPORT NO. 329-81

Material Tested	Haskell No.	Other Codes
[redacted],	12,037	[redacted]

Study Initiated/Completed
5/20/81 - 6/17/81

ORAL LD50 TEST IN MICE

Procedure: The test material, as a suspension in corn oil, was administered by intragastric intubation in single doses to 6 groups of male and 6 groups of female young adult CD-1 mice, 10 per group. The surviving mice were weighed and observed during a 14-day recovery period and then sacrificed. The LD50 value was calculated from the mortality data using the method of D. J. Finney.**

Results:

Males

Dose (mg/kg)	Average Body Weight (g)	Suspension (%)	Average Dose (mL)	Mortality Ratio	LD50***
4,000†	38	15	1.01	10/10	457 mg/kg
2,000†	38	10	0.76	10/10	
1,000	38	4	0.95	10/10	
750	31	3	0.76	10/10	
500	36	2	0.89	4/10	
250	30	1	0.75	1/10	

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Results:

Dose (mg/kg)	Average Body Weight (g)	Suspension (%)	Average Dose (ml)	Mortality Ratio	LD50***
Females:					
4,000†	35	15	0.94	10/10	457 mg/kg
2,000†	34	10	0.67	10/10	
1,000	33	4	0.82	10/10	
750	25	3	0.62	10/10	
500	33	2	0.82	4/10	
250	24	1	0.60	1/10	

Clinical Signs:
Males: Stained and/or wet perineal area, weakness and weight loss in all surviving mice, eyes half closed at 1,000 and 250 mg/kg. Ruffled fur at 250 and 500 mg/kg. Ataxia at 1000, 500 and 250 mg/kg. Tremors at 500 and 750 mg/kg. All deaths occurred within 5 days after dosing.

Females: Stained and/or wet perineal area, weakness and weight loss in all surviving mice. Eyes half closed, stained face and tremors at 750 mg/kg. Ataxia at 500 mg/kg. Ruffled fur at 750 and 250 mg/kg. All deaths occurred within 7 days after dosing.

Summary: [redacted] is moderately toxic when administered orally to young adult CD-1 male and female mice; its LD50 for males and females is 457 mg/kg of body weight. Clinical signs included: stained and/or wet perineal area, ataxia, tremors, weakness, ruffled fur, eyes half-closed and weight loss. All deaths occurred within 7 days after dosing.

* Synonyms: o [redacted]
o FC-143
o [redacted]
o [redacted]

Purity: Approximately 100%

Contaminants: Mixed isomers [redacted]

** Finney, D. J., Probit Analysis, 3rd Ed., 1971, Cambridge University Press.

*** 95% Confidence Limits:

Males:
Lower: 344 mg/kg
Upper: 560 mg/kg
Slope: 6.6

Females:
Lower: 344 mg/kg
Upper: 560 mg/kg
Slope: 6.6

† 4000 and 2000 mg/kg dose levels male and female were not calculated in LD50 data due to limitations of computer.

Report by: John A. Hall
John A. Hall
Technician

Reviewed by: O. Louis Dashiell
O. Louis Dashiell
Study Director

Approved by: Gerald L. Kennedy
Gerald L. Kennedy
Chief, Acute Investigations Section

JAH:jrg
Date Issued: June 17, 1981

Report No. 329-81

E. I. du Pont de Nemours and Company
Haskell Laboratory for Toxicology and Industrial Medicine
Elkton Road, Newark, Delaware 19711

HASKELL LABORATORY REPORT NO. 295-81

Material Tested	Haskell No.	Other Codes
[redacted]	12,037	None

Study Initiated/Completed
5/20/80 - 6/17/80

ORAL LD50 TEST IN RATS

Procedure: The test material, as a suspension in corn oil, was administered by intragastric intubation in single doses to 6 groups of male and 6 groups of female young adult Crl:CD® rats, 10 per group. The surviving rats were weighed and observed during a 14-day recovery period and then sacrificed. The LD50 value was calculated from the mortality data using the method of D. J. Finney.**

Results:

Males

Dose (mg/kg)	Average Body Weight (g)	Suspension (%)	Average Dose (mL)	Mortality Ratio	LD50***
1,000	264	10	2.64	10/10	470 mg/kg
670	252	10	1.69	9/10	
500	253	10	[illegible].27	6/10	
450	241	10	1.09	4/10	
400	257	5	2.05	3/10	
200	247	1	4.93	2/10	

Results:

Females

Dose (mg/kg)	Average Body Weight (g)	Suspension (%)	Average Dose (ml.)	Mortality Ratio	LD50***
1,000	189	10	1.89	10/10	482 mg/kg
670	182	10	1.22	9/10	
500	195	5	1.95	7/10	
450	212	5	1.91	5/10	
400	197	5	1.57	0/10	
200	228	1	4.56	0/10	

Clinical Signs:

Males: Stained and/or wet perineal area, weakness and weight loss at all levels tested.

Chromodacryorrhea at 1,000 and 500 mg/kg.

Stained face at 1,000, 670, 500 and 450 mg/kg.

Moribundity, eyes half-closed and gasping at 670 mg/kg.

Humped posture at 500 mg/kg.

All deaths occurred within 4 days after dosing.

Females: Stained and wet perineal area and weight loss at all levels tested.

Stained face at all levels tested except 200 mg/kg.

Weakness at 1,000, 670, 450, and 400 mg/kg.

Chromodacryorrhea, eyes half-closed and ataxia at 670 mg/kg.

Humped posture at 670 and 450 mg/kg.

Alopecia at 400 mg/kg.

All deaths occurred within 3 days after dosing.

Summary: [redacted] is moderately toxic when administered orally to young adult CrlCD® male and female rats; its LD50 for males is 470 mg/kg and females is 482 mg/kg of body weight. Clinical signs for males and females included: stained and wet perinual area, stained face, weakness, chromodacryorrhea, and weight loss. All deaths occurred within 4 days after dosing.

* Synonyms: o FC-143

[redacted]

Purity: Approximately 100%

Contaminants: Mixed isomers [redacted]

CAS Registry No.: [redacted]

** Finney, D. J., Probit Analysis, 3rd Ed., 1971, Cambridge University Press.

*** 95% Confidence Limits:

Males	
Lower:	403 mg/kg
Upper:	536 mg/kg
Slope:	8.6
Females	
Lower:	438 mg/kg
Upper:	541 mg/kg
Slope:	12.3

Report by: John A. Hall
Technician

Reviewed by: O. Louis Dashiell
Study Director

Approved by: Gerald L. Kennedy
Chief, Acute Investigations Section

JAH:jrg
Date Issued: June 1, 1981

Report No. 295-81

(47)

E. I. du Pont de Nemours and Company
Haskell Laboratory for Toxicology and Industrial Medicine
Elkton Road, Newark, Delaware 19711

HASKELL LABORATORY REPORT NO. 291-81

Material Tested	Haskell No.	Other Codes
[redacted]	12,037	None

Study Initiated/Completed
5/20/80 - 6/17/81

ORAL LD50 TEST IN GUINEA PIGS

Procedure: The test material, as a suspension in corn oil, was administered by intragastric intubation in single doses to 6 groups of male and 6 groups of female young adult Duncan Hartley guinea pigs, 10 per group. The surviving guinea pigs were weighed and observed during a 14-day recovery period and then sacrificed. The LD50 value was calculated from the mortality data using the method of D. J. Finney.**

Results:

Males

Dose (mg/kg)	Average Body Weight (g)	Suspension (%)	Average Dose (ml)	Mortality Ratio	LD50***
670	419	10	2.80	10/10	178 mg/kg
400	492	10	1.97	10/10	
300	522	5	3.13	10/10	
250	433	5	2.15	9/10	
200	461	5	2.13	6/10	
150	425	2	3.19	3/10	

Results: (Cont'd.)

Females

Dose (mg/kg)	Average Body Weight (g)	Suspension (%)	Average Dose (ml)	Mortality Ratio	LD50***
670	450	10	3.02	10/10	217 mg/kg
400	499	10	2.00	10/10	
300	477	5	2.86	9/10	
250	419	5	2.10	8/10	
200	493	5	1.97	1/10	
150	411	2	3.09	2/10	

Clinical Signs:

Males: Stained and/or wet perineal area, weakness at all levels tested except 670 and 400 mg/kg.

Stained face at 670, 200 and 150 mg/kg.

Eyes half closed at 300 and 200 mg/kg.

Lacrimation at 200 and 150 mg/kg.

Salivation at 300 and 150 mg/kg.

Ataxia at 670 mg/kg.

Tremors at 150 mg/kg.

Humped posture at 200 mg/kg.

Weight loss at all levels tested except at 670 and 400 mg/kg.

All deaths occurred within 1-4 days after dosing.

Clinical Signs: (Cont'd.)

Females: Stained and/or wet perineal area and weakness at all levels tested except 670 and 400 mg/kg.

Convulsions, ataxia, gasping at 670 mg/kg

Eyes half closed at 250 and 150 mg/kg.

Tremors at 400 mg/kg.

Lacrimation at 250 mg/kg.

Stained face at 200 mg/kg.

Lethargy at 150 mg/kg.

Weight loss at all levels tested except for 670 mg/kg.

All deaths occurred within 1-6 days after dosing.

Summary: [redacted] is moderately toxic when administered orally to young adult outbred albino male and female guinea pigs; its LD50 for males is 178 mg/kg and females 217 mg/kg of body weight. Clinical signs for males and females included: stained and/or wet perineal area, convulsions, gasping, stained face, eyes half-closed, and weight loss. All deaths occurred within 1-6 days after dosing.

* Synonyms: o [redacted]
o
o
o FC-143

Contaminants: Mixed isomers and [redacted]

Purity: Approximately 100%

CAS Registry No.: [redacted]

** Finney, D. J., Probit Analysis, 3rd Ed., 1971, Cambridge University Press.

*** 95% Confidence Limits:

Males:
Lower: 144 mg/kg
Upper: 202 mg/kg
Slope: 8.9

Females:
Lower: 187 mg/kg
Upper: 246 mg/kg
Slope: 8.6

Report by: John A. Hall
Technician

Reviewed by: O. Louis Bashiell
Study Director

Approved by: Gerald L. Kennedy
Chief, Acute Investigations Section

JAH:jrg
Date Issued: June 1, 1981

Report No. 291-81

E. I. du Pont de Nemours and Company
Haskell Laboratory for Toxicology and Industrial Medicine
Elkton Road, Newark, Delaware 19711

HASKELL LABORATORY REPORT NO. 682-80

Material Tested	Haskell No.	Other Codes
[redacted]	12,037	None

Study Initiated/Completed
8/12/80 - 9/3/80

SKIN ABSORPTION LD50 - FEMALE RATS

Procedure: Two groups of CHR-CD® female rats, 5 rats per group, were clipped free of hair over the back and trunk area. The test material, as a 50/50 aqueous suspension was applied to the back of each rat under a square of aluminum foil and held in place with 3" Elastoplast®. After 24 hours exposure the rats were unwrapped, sponged off with a mild detergent, rinsed, dried and returned to cages for 14 days observation or until death. Surviving rats were sacrificed.

Results:

No. of Animals	Dose (mg/kg)	Active Ingredient Average Dose (g)	Average Weight (g) Initial	Average Weight (g) Final	Mortality
5	7,500	1.38	183	226	1/5
5	5,000	0.96	191	235	0/5

Clinical Signs:

7,500 mg/kg Mild skin irritation, stained face, wet and stained perineal area and initial weight loss. Death occurred 3 days after treatment.

5,000 mg/kg Mild skin irritation and intermittent weight loss.

Summary: [redacted] is slightly toxic in female rats by skin absorption; its LD50 is greater than 7,500 mg/kg, the maximum feasible dose.

All rats dosed at 7,500 and 5,000 mg/kg had mild skin irritation and initial weight loss.

Other Name: FC 143, [redacted]

Composition: Approximately 100%

Contaminants: Mixed isomers [redacted]

Report by: John E. Henry
John E. Henry
Technician

Approved by: Gerald L. Kennedy
Gerald L. Kennedy
Chief, Acute Investigations Section

JEH:jrg
Study Director: O. L. Dashiell
Date Issued: September 22, 1980

Report No. 682-80

E. I. du Pont de Nemours and Company
Haskell Laboratory for Toxicology and Industrial Medicine
Elkton Road, Newark, Delaware 19711

HASKELL LABORATORY REPORT NO. 659-79

Material Tested	Haskell No.	Other Codes	Study Initiated/ Completed
[redacted]	12,037	None	8/21-9/12/79 (rabbits) 8/22-9/11/79 (rats)

SKIN ABSORPTION LD50 - RABBIT AND RAT

Procedure: (Rabbits)

Four groups of male albino rabbits were clipped free of hair over the back and trunk area and equipped with plastic collars. The proper dose of test material (made into a slurry with water) was applied to the back of each rabbit and wrapped successively with layers of Saran® Wrap, Kling® gauze bandages and Elastoplast® elastic bandages. After 24 hours of exposure, the animals were unwrapped, washed with water, dried and returned to cages for 14 or 15 days observation or until death. During the observation period, the animals were weighed and observed for clinical signs. Gross pathology was done on all survivors and 1 animal that was found dead at 3,000 mg/kg. The LD50 values were calculated from the mortality data using the method of D. J. Finney.[†]

Procedure: (Rats)

Three groups of CRL-CD male rats, 5 rats per group, were clipped free of hair over the back and trunk area. The proper dose of test material[1], as a 50/50 aqueous suspension, was applied to the back of each rat under a square of aluminum foil and held in place with 3" Elastoplast®. After 24 hours exposure, the rats were unwrapped, sponged off with a mild detergent, rinsed, dried and returned to cages for 13 days observation or until death. During the observation period, the rats were weighed and observed for clinical signs. Gross pathology was done on all survivors and 1 rat that died at 3,500 mg/kg. The LD50 values were calculated from the mortality data using the method of D. J. Finney.[†]

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* Other Name: FC 143, [redacted] Composition: ~100% (contaminants: mixed isomers- [redacted]

† Finney, D. J., Probit Analysis, 3rd Ed., 1971, Cambridge University Press. (Data with MR file)

[1] One rat dosed at 3,500 mg/kg did not have liver weight recorded at pathology.

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Results: (Rabbits)

No. of Animals	Dose (mg/kg)	Average Dose (g) (Aqueous Slurry)	Average Weight Initial/Final	Mortality#	Clinical Signs
2	7,500	25.28	3370.5/ -	1D - 2 d. 1D - 3 d.	Weight loss, labored breathing, cyanosis, body wet underneath and moderate skin irritation (erythema).
5	5,000	16.63	3326 / 2872	2D - 3 d. 1D - 4 d. 2S - 14 d.	Nasal discharge, shallow breathing, pallor, diarrhea, wet underneath body, weakness, weight loss and skin irritation with necrotic spots.
5	3,000	10.39	3463.2/2827.2	1D - 7 d. 2S - 14 d. 2S - 15 d.	Labored breathing, lethargy, skin irritation and weight loss.
5	1,500	4.99	3320 / 3002	5S - 14 d.	Labored breathing, skin irritation with crusty hard area and weight loss.

LD50 = 4,218 mg/kg 95% Confidence Limits: Lower: 2,369 mg/kg Upper: 9,814 mg/kg
Slope: 6.2584

Results: (Rats)

No. of Animals	Dose (mg/kg)	Average Dose (g) (Aqueous Slurry)	Average Weight Initial/Final	Mortality#	Clinical Signs
5	7,500	1.9	254 / 258	3D - 1 d. 1D - 2 d. 1S - 14 d.	Lethargy, chromodacryorrhea, stained nose, wet and stained perineal area and initial weight loss.
	Gross Pathology: 2 rats: 1 FD at 1 day - liver weight not taken. No other compound-related signs noted. 1 Survivor (14 days) - Increase in liver weight.				
5	5,000	1.4	276 / 316	5S - 14 d.	Lethargy, wet perineal area and initial weight loss.
	Gross Pathology: 5/5 Rats: Increase in liver weight.				
5	3,000	0.87	290 / 345	5S - 14 d.	Initial weight loss only.
	Gross Pathology: 5/5 Rats: Increase in liver weight.				

LD50 = 6,958 mg/kg 95% Confidence Limits not defined - Slope: 25.5

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Summary: (Rabbits)

[redacted] is moderately toxic by skin absorption in rabbits; its LD50 is 4,278 mg/kg of body weight.

Gross pathological examination showed no compound-related changes; however, there was skin irritation at all levels. Clinical signs included weight loss and labored breathing at all levels and wet underneath the body, cyanosis, diarrhea and lethargy appearing at most levels.

Summary: (Rats)

[redacted] is slightly toxic in male rats by skin absorption; its LD50 is 6,913 mg/kg of body weight.

All rats dosed at 7,500, 5,000 and 3,000 mg/kg had initial weight loss. Rats dosed at 7,500 and 5,000 mg/kg were lethargic on the day of treatment and the majority had wet and/or stained perineal areas. Chromodacryorrhea was seen in rats treated at 7,500 mg/kg.

Gross pathology showed an increase in liver weights in all surviving rats examined at 14 days after treatment.

Report by: Doris F. Edwards
Doris F. Edwards
Toxicologist

John E. Henry
John E. Henry
Technician

Approved by: Gerald L. Kennedy
Gerald L. Kennedy
Chief, Acute Investigations Section

DFE/jhe:wp
Project No. 6[illegible]-79
Date Typed: October 26, 1979

Date Reviewed: February 26, 1980

E. I. du Pont de Nemours and Company
Haskell Laboratory for Toxicology and Industrial Medicine
Elkton Road, Newark, Delaware 19711

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HASKELL LABORATORY REPORT NO. 636-78

Material Tested	Haskell No.	Other Codes	Study Initiated/ Completed
[redacted]	12,037	None	8/15-8/17/79

SKIN IRRITATION TEST ON RABBITS

Procedure: Six male albino rabbits were clipped free of hair on the trunk and lateral areas and placed in FDA-type stocks. Doses of 0.5 gm solid test material were applied as an aqueous paste to intact skin under 1-1/2" x 1-1/2" 12-ply gauze squares. Rubber sheeting was then loosely wrapped around the trunk and secured with adhesive tape. After 24 hours, the rabbits were removed from the stocks, the patches taken off and the reactions observed. Observations were also made at 48 hours.

Results:

24-Hour Observation				48-Hour Observation			
Erythema		Edema		Erythema		Edema	
Moderate	3/6	Mild	1/6	Moderate	2/6	Mild	1/6
Mild	3/6	Slight	3/6	Mild	3/6	Slight	2/6
		None	2/6	Slight	1/6	None	3/6

Summary: [redacted] (FC-143) caused mild to moderate skin irritation in 24 hours and slight to moderate irritation in 48 hours when tested on the shaved intact skin of rabbits under semi-occluded conditions.

FC-143 may cause mild skin irritation upon repeated contact. Good industrial hygiene practice would be to minimize skin contact. In the event of any skin contact, wash thoroughly with soap and water.

* Composition: 100% Other Names: FC-143, [redacted]
Contaminants:
Alkali Isomers: [redacted]

Report by: Doris F. Edwards
Toxicologist

Approved by: Gerald L. Kennedy
Chief, Acute Investigations Section

Date Issued: October 5, 1979

E. I. du Pont de Nemours and Company
Haskell Laboratory for Toxicology and Industrial Medicine
Elkton Road, Newark, Delaware 19711

HASKELL LABORATORY REPORT NO. 635-79

Material Tested	Haskell No.	Other Codes	Study Initiated/ Completed
[redacted]	12,037	None	8/13-9/11/79

EYE IRRITATION TEST IN RABBITS

Procedure: One-tenth milliliter (38.3 mg) of solid test material was placed into the right conjunctival sac of each of 2 albino rabbits. After 20 seconds, 1 treated eye was washed with tap water for 1 minute. The treated eye of the other rabbit was not washed. Observations of the cornea, iris and conjunctiva were made with a hand-slit lamp at 1 and 4 hours, and at 1, 2, 3, 7, 14, 21 and 28 days; Fluor-i-strip® stain and a binocrostope were used at examinations after the day of treatment.

Results:

Dose	Treatment of Eyes	Ocular Effects: Cornea	Iris	Conjunctiva
0.1 ml (38.3 mg) solid test material	Not Washed	Generalized moderate opacity 1 hour-3 days. At 2 days, a small area in the lower cornea had severe opacity. The opacity gradually receded to generalized mild at 7 days except for the area in the lower cornea which had moderate opacity with vascularization. This area of opacity persisted through 14 days but gradually receded in size and degree to localized mild opacity with vascularization 21-28 days.	Slight injection at 4 hours. Moderate congestion at 1 day. Slight injection at 2 days. Moderate congestion at 14 days.	Redness: Slight 1-4 hours. Mild at 1 day. Moderate at 2 days. Mild 3-14 days. Swelling: Mild at 1 hour. Moderate at 4 hours. Mild 1-2 days. Slight at 3 and 1 days. Discharge: Copious 1 hour and 1 day. Moderate 4 hours 2 and 3 days (Hemastix®-positive 1 hour-3 days.) Mil at 14 days.

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Results: (continued)

Dose	Treatment of Eyes	Ocular Effects: Cornea	Iris	Conjunctiva
0.1 ml (25.3 mg) solid test material	Washed	Small area of mild opacity at 1 hour increasing to moderate opacity at 1 day and receding to a small area of slight opacity at 3 days.	None.	Redness: Mild 1 hour-7 days. Swelling: Mild 1 hour-1 day. Slight at 2 days. Discharge: Copious 1-4 hours. Moderate at 1 day (Bonastix®-positive 1 hour-1 day.

Summary: [redacted] (EC-143) caused generalized moderate corneal opacity with a small area of severe opacity. Intermittent moderate iritis and moderate conjunctivitis when tested in a rabbit eye. The ocular effects gradually receded; however, the small area of corneal opacity persisted and at 21-28 days was mild with vascularization (sign of healing). An eye dosed with the test material and promptly washed had a small area of slight to moderate corneal opacity and moderate to slight conjunctivitis with no iritic effect. The eye was normal within 7 days except for mild conjunctival redness, which was normal within 14 days.

EC-143 is a mild to moderate eye irritant, capable of causing persistent mild corneal opacity. Eye contact with this compound should be avoided. In the event of any eye contact, flush copiously with water and obtain medical attention.

* Other Names: EC-143, [redacted]

Specification: 1002 Contaminants: Mixed isomers [redacted]

Report by: Curtis F. Edwards
Toxicologist

Approved by: Gerald L. Kennedy
Chief, Acute Toxicity Investigations Section

Sherwin
Report No. (AC-2)
Date: Month October 5, 1971

E. I. du Pont de Nemours and Company
Haskell Laboratory for Toxicology and Industrial Medicine

HASKELL LABORATORY REPORT NO. 258-79

Material Tested	Haskell No.	Other Codes	Sample Ready for Testing
[redacted]	12,037	[redacted]	1/5/78

INHALATION SUBACUTE

Introduction: Existing data (HLR No. 160-69) indicate that [redacted] causes significant liver enlargement following acute exposure via inhalation or oral routes. This experiment was designed to investigate a "no effect" level.

Procedure: Houseline air (.20 l/min) was passed through a cyclone-head dust generator connected to a particle agitator-reservoir which contained [redacted] The resulting airborne particulate was passed into a 30 l battery jar exposure chamber.

The atmospheric concentration of [redacted] in the exposure chamber was monitored at 30-min intervals with Gelman glass fiber filters (type AE, 47 mm). The particulate concentration was determined by weight gain of the filters. Particle size was determined on a Brink cascade impactor.

Sixty CRL-CD® albino male rats (20/group) were exposed to design level atmospheric concentrations of 0, 0.008 or 0.08 mg/l [redacted] Rats were exposed, head only, for 5 consecutive days, 6 hr per day. After 5 days, the rats were given a 2-day recovery (weekend) which was followed by 5 daily, consecutive 6-hr exposures.

All rats were weighed and observed daily (except weekends) during the exposure and recovery periods. Purina® Laboratory Chow and water were available *ad libitum* at all times other than during actual exposure.

Clinical laboratory examinations were performed on 10 rats from each group at 0, 14, and 28 days post-exposure (details in Appendix B). After a total of 10 exposures, 5 rats from each of the 3 groups were pathologically evaluated at 0, 14, 32 and 42 days post-exposure (details in Appendix C). Select organs were weighed; absolute and relative organ weights were calculated.

On the 5th and 9th days of exposure, 10 rats were selected from each group for eye examinations.

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(C)

Results:

Design	Atmospheric [redacted] Concentrations (mg/l) Atmospheric ± S.D.	Mean Mass Median Diameter ± S.D. (μ)
0.0 (control)	0.0	0.0
0.009	0.011 ± 0.005	1.63 ± 0.70
0.080	0.083 ± 0.017	4.47 ± 3.41

Weight Gain: Rats exposed to [redacted] showed a suppression of body weight throughout the test. The 0.083 mg/l group was more severely affected during exposure (loss of body weight) and for 14 days of recovery (Appendix A).

Clinical Observations: During each exposure, sporadic cases of blinking, pawing, chewing and red eye and nasal discharge were seen in all groups.

Clinical Pathology: Some rats exposed to [redacted] displayed elevated alkaline phosphatase activity. Effects were seen in glutamic-pyruvic transaminase and glutamic-oxaloacetic transaminase after 0, 14 and 28 recovery days. The incidence was related to dose; higher activities were found at the higher exposure level. However, only the latter activity at 0.083 mg/l was statistically different from controls. (Clinical Laboratory Report by Walter B. Roelecki, Clinical Chemist, Appendix B.)

Pathology: Pathologic evaluations showed cloudy swelling or granular degeneration of hepatocytes in the livers of rats (5 of 5 examined) exposed to [redacted] for 10 days with no recovery. This effect was not seen after a 14-day or longer recovery period. No other compound-related histologic changes were noted. (Pathology Report No. 2-79 by Ross B. C. Chen, Senior Research Pathologist, Appendix C.)

Organ/Body Weights: Various organ weight effects were evident in rats exposed to [redacted]. These effects were not seen after 32 or 48 recovery days and in the absence of related histologic abnormalities were not considered compound-related (Appendix D).

The dose-related increase in liver weights correlates with existing Lara (HLS 150-83) and hepatocyte changes detailed above.

Eye Examinations: No corneal, iritic or conjunctival effects were seen in any of the rats examined after 5 or 9 exposure days (Appendix E).

Summary: Groups of 30 male rats were exposed, head only, to particulate atmospheres of 0, 0.011 or 0.083 mg/l [redacted], 6 hr /day, 5 days/wk for 2 wks with 42 days recovery.

Rats exposed to [redacted] showed a dose-related suppression of body weight.

Rats exposed to [redacted] had dose-related elevations of plasma enzyme activities for up to 28 days of recovery; liver injury or dysfunction was suggested.

Liver degeneration was detected at the end of the 2-week exposure period in all examined rats exposed to [redacted]. This liver effect was not detected after 14, 32 or 42 days of recovery.

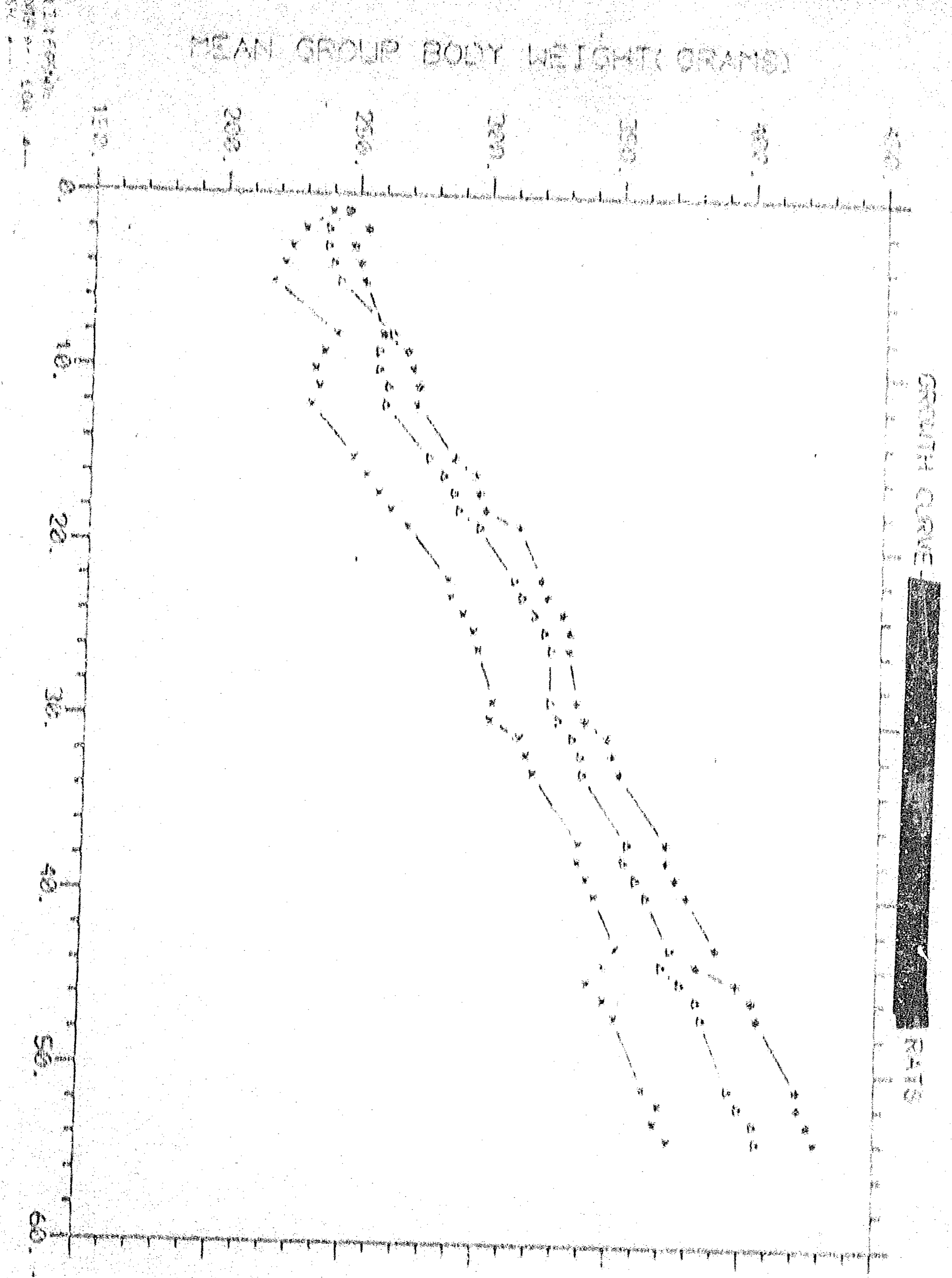
Eye examinations revealed no compound-related effects.

Report by: George T. Hall
George T. Hall
Toxicologist

Approved by: Gerald L. Kennedy
Gerald L. Kennedy
Chief, Acute Investigations Section

CTH:scg
Report No. 253-79
Date Issued: July 20, 1979

000004


MEAN GROUP BODY WEIGHT(GRAMS)
GROWTH CURVE - RATS

APPENDIX B

SUBACUTE INHALATION OF [redacted]

Medical Research Project No. 2733

Haskell Laboratory No. 12037

Clinical Laboratory Reports

Samples of urine were collected overnight (16 hours) from groups of ten rats that were exposed nine times for four hours per day, five days per week over a two-week period to 0 mg/L, 0.008 mg/L or 0.08 mg/L [redacted] dust. Blood was taken from the tail of these rats after the tenth exposure. Fourteen and 28 days after the last exposure blood and urine (24 hour) samples were again collected from the animals.

The examination of the blood and urine included the following:

Hematology: Erythrocyte count (RBC), hemoglobin (Hb), hematocrit (Ht), total leukocyte count (WBC), relative number of neutrophils (Neut), lymphocytes (Lymph), eosinophils (Eosin), monocytes (Mono) and basophils (Baso). The indices, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC), were calculated from these data.

Chemistry: Alkaline phosphatase (AP), glutamic-pyruvic transaminase (GPT), glutamic-oxalacetic transaminase (GOT), gamma-glutamyl transpeptidase (gGTP), bilirubin (BILRN), urea nitrogen (BUN) and total protein (TPROT).

Urinalysis: A measure of the volume (VOL), osmolality (mOs) and pH; a semi-quantitative test for sugar, protein and urobilinogen (UROBL); a test for blood and bilirubin; a microscopic examination of the sediment from pooled specimens.

The data were analyzed by a one-way analysis of variance (AOV) to compare the exposed animals with the controls at each sampling interval and by a nested AOV for the three sampling intervals. Significance was judged at the 0.05 probability level.

Results:

The results of the clinical laboratory measurements or observations are summarized in Table 1, and for the statistical analyses in Table 2. Measurements on individual animals are listed in the computer print-out attached to this report.

Higher than normal activity was found for the plasma enzymes AP, GPT and GOT in some rats exposed to [redacted] dust after the last exposure and 14 and 28 days later. The incidence of elevated enzyme activity was related to the dose, occurring more frequently in the rats exposed to 0.08 mg/L [redacted] dust. The statistical analysis, however, indicated that only the GOT activity of the rats exposed to 0.08 mg/L was significantly elevated.

Increased activity of these enzymes is associated with liver injury or dysfunction. A similar effect was seen in an earlier study with dogs that were given a single non-lethal oral dose of [redacted] (1). These results therefore, suggest that the livers of rats, exposed by inhalation to [redacted] dust, may be affected by the exposure and that the effect may persist for 28 days or longer.

---

(1) Effect of Fluorocarbon Dispersing Agents on the Livers of Rats and Dogs. Haskell Laboratory Report No. 123-65.

Report by: Walter B. Koniecki

Walter B. Koniecki
Clinical Chemist

Approved by: John R. Barnes

John R. Barnes
Chief, Clinical Pathology Section

WBK:JRB:lljm

Date: October 19, 1978

TABLE I

SUMMARY OF CLINICAL LABORATORY [illegible] EXAMINATIONS ON RATS
EXPOSED TO [redacted]

	0 mg/l			0.008 mg/l			0.04 mg/l		
		Recovery			Recovery			Recovery	
	Test	14	28	Test	14	28	Test	14	28
HEMATOLOGY									
Erythrocytes x $10^6/mm^3$	5.86	6.30	6.25	5.87	6.12	6.24	5.99	6.37	6.3[illegible]
Hemoglobin g %	15.1	16.8	14.9	14.7	14.3	14.7	15.2	14.5	15.2
Hematocrit %	46	44	47	45	45	47	46	46	48
MCV μ^3	78	72	75	77	73	75	76	75	8[illegible]
MCH $\mu\mu g$	26	23	24	25	23	24	25	23	7[illegible]
MCHC %	33	22	32	33	32	32	33	31	32
Leukocytes x $10^3/mm^3$	15.15	17.76	15.73	10.37	13.17	12.92	13.64	17.0[illegible]	15.8[illegible]
Neutrophils %	18	22	18	19	19	15	18	17	14
Lymphocytes %	81	75	76	79	78	81	78	81	1[illegible]
Eosinophils %	0.8	1.2	2.7	0.6	1.3	1.3	0.8	0.9	0.8
Monocytes %	1.0	2.1	3.4	1.2	1.6	2.6	1.6	1.1	2.2
Basophils %	0	0	0	0	0	0	0	0	0
CHEMISTRY									
AP IU	201	226	270	242	296	291	244	275	307
SGPT IU	23	23	25	28	25	26	27	25	29
SGOT IU	62	68	66	72	74	67	72	76	84
g-GTP IU	1.7	0.9	1.0	1.2	0.7	0.8	1.1	0.6	0.6
Bilirubin mg%	0.3	0.5	0.3	0.3	0.4	0.3	0.4	0.5	0.3
Urea nitrogen mg%	16	21	18	19	22	29	23	24	22
Total Protein g%	6.6	6.7	6.7	6.3	6.7	6.8	6.6	6.6	6.7
URINALYSIS									
Volume ml	7	18	14	6	16	12	8	16	15
Osmolality mOs	2519	1527	1706	2337	1490	1818	1624	1596	1461
pH	7.2	7.1	6.7	7.2	6.9	7.3	7.5	7.7	7.5
Blood, number positive	0	0	0	0	0	1	0	0	0
Sugar, number abnormal	0	0	0	0	0	0	0	0	0
Protein, number abnormal	0	0	1	0	0	0	0	0	0
Urobilinogen, Ehrlich units	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Bilirubin, number positive	0	0	0	0	0	0	0	0	0
Microscopic, number abnormal	0	0	0	0	0	1	0	0	0

002008

TABLE 2

SUMMARY OF STATISTICAL DATA
F: RATIO OF VARIANCE

	Tenth Exposure	14-Day Post-Exposure	28-Day Post-Exposure	All Data
Erythrocytes	0.5	1.5	1.0	0.7
Hemoglobin	1.3	1.7	1.7	2.2
Hematocrit	1.1	1.5	0.7	1.8
MCV	0.8	2.0	0.2	0.3
MCH	1.7	0.0	0.5	1.4
MCHC	0.1	2.9	0.4	0.4
Leukocytes	7.4	4.4	2.2	5.2
Neutrophils	0.4	1.6	1.0	0.5
Lymphocytes	0.7	2.7	2.9	1.4
Eosinophils	0.2	0.5	4.9	2.9
Monocytes	0.7	1.2	2.0	1.2
Basophils	0.0	0.0	0.0	0.0
AP	4.4	2.0	1.6	2.3
GPT	1.4	0.8	1.4	2.1
GOT	1.5	1.1	5.4	2.7
gGTP	1.3	0.6	1.8	1.6
Bilirubin	3.0	2.1	2.5	6.1
Urea nitrogen	4.8	1.4	1.8	3.2
Total Protein	1.9	0.3	0.4	0.1
Urine VOL	2.0	0.3	0.8	0.6
Urine sOs	7.4	0.9	1.0	1.0

000009

APPENDIX A

PATHOLOGY REPORT NO. 1-29

[redacted]

H-12637 MR-2793-001 - PV42 Compressors

Inhalation Subacute - CDR-CD Rats

February 27, 1979

Summary and Conclusion

Sixty young adult male rats were divided equally into three groups with Group I serving as a negative control and exposed only to air. Groups II and III were exposed to [redacted] at concentrations of 0.01 and 0.08 mg/l respectively, 6 hrs/day, 5 days/week for 2 weeks. On 0, 14, 32, and 42 days post-exposure, 5 animals from each group were sacrificed for pathological evaluation. At necropsy, the animals were examined grossly, and the following tissues or organs saved for histopathologic evaluation: external ear, abdominal skin, trachea, lungs*, heart*, thyroid, adrenals, thymus*, mediastinal tissue, spleen*, sternebrae with bone marrow, stomach, small intestine, large intestine, liver*, kidneys*, testes*, epididymis, brain and eyes.

The results of pathologic findings are summarized in Table 1. As the table shows [illegible] apparent compound-induced toxic effect consisting of a cloudy swelling [illegible] vacuolar degeneration of hepatocytes was detected in the livers of all five rats (5/5) in both Group II (0.01 mg/l) and Group III (0.08 mg/l) at the end of the two-week exposure period. However, the hepatotoxic effect was not detected after a 14-day or longer post-exposure recovery period. All of the remaining pathologic findings listed in the table are considered to be spontaneous or the result of intercurrent disease.

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* Organs weighed

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

Approved by: William C. Krause
William C. Krause, D.V.M.
Chief, Pathology Section

HHCC:WCK:mjb

[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	Group
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	Dose (mg/L)
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	Days on test
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	Recovery days
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	Lungs: Chronic mycoplasma pneumonia, early stage
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	Lungs: Focal alveolar emphysema
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	Liver: Non-specific micro granuloma/foci of extra-medullary hemopoiesis
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	Liver: Cloudy swelling/granular degeneration of hepatocytes
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	Liver: Focal perihepatitis
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	Liver: Focal perihepatitis with capsule adhesion
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	Kidneys: Chronic progressive nephrosis, early stage
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	Kidneys: Hydronephrosis, unilateral
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	Testes: Focal atrophy/degeneration of seminiferous tubules
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	Testes: Testicular atrophy, focal, unilateral
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	Thymus: Atrophy
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	External Ear: Focal necrosis of cartilage (early stage of chondrosarcoma)
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	Heart: Chronic focal myocarditis

000011

#	Group	Dose (mg/L)	Days on test	Recovery days	Lungs: Chronic murine pneumonia, early stage	Lungs: Focal alveolar emphysema	Liver: Nonspecific micro-granulomas/foci of extramedullary hematopoiesis	Liver: Cloudy swelling/granular degeneration of of hepatocytes	Liver: Focal periportal cirrhosis	Liver: Focal portovenitis with lobar cirrhosis	Kidneys: Chronic progressive nephrosis, early stage	Kidneys: Hydronephrosis, unilateral	Testes: Focal atrophy/degeneration of seminiferous tubules	Testes: Testicular atrophy, focal, unilateral	Thymus: Atrophy	Mesenteric lymph node: Focal necrosis of lymphoid early stage of lymphonodrosis	Heart: Chronic focal myocarditis
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
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[illegible] [redacted]

Animal No.	Group	Dose (mg/l)	Days on test	Necropsy date	Lungs: Chronic murine pneumonia, early stage	Lungs: Focal alveolar histiocytosis	Liver: Subcapsular/focal [illegible]	Liver: Cloudy swelling/[illegible] degeneration of hepatocytes	Liver: Focal [illegible]	Liver: Focal peritonitis with liver invasion	Kidney: Chronic progressive nephrosis, early stage	Kidney: Hydronephrosis, unilateral	Testes: Focal atrophy/degeneration of seminiferous tubules	Testis: Testicular atrophy, [illegible], unilateral	Thymus: Atrophy	External ear: Focal necrosis of cartilage, early stage of [illegible]	Heart: Chronic focal myocarditis
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	-	[illegible]	[illegible]	-	-	[illegible]	-	-	-	-	-	-
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	-	[illegible]	-	-	-	[illegible]	-	-	-	-	-	-
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[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	-	[illegible]	-	-	-	[illegible]	-	-	-	-	-	-
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[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	-	[illegible]	-	-	-	[illegible]	-	-	-	-	-	-
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	-	[illegible]	-	-	-	[illegible]	-	-	-	-	-	-
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	-	[illegible]	-	-	-	[illegible]	-	-	-	-	-	-
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	-	[illegible]	-	-	-	[illegible]	-	-	-	-	-	-
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	-	[illegible]	-	-	-	-	[illegible]	-	-	-	-	-
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	-	[illegible]	-	-	-	-	-	-	-	-	-	-
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[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	-	[illegible]	-	-	-	[illegible]	-	-	-	-	-	-

Code: - : No lesion 1: Very mild change 2: Slight change 3: Moderate change P: Lesion present X: Grossly normal

Animal No.	Group	Dose (mg/L)	Days on test	Recovery days	Lungs: Chronic murine pneumonia, early stage	Lungs: Focal alveolar emphysema	Liver: Non-specific microgranuloma/foci of extramedullary hemopoiesis	Liver: Cloudy swelling/granular degeneration of hepatocytes	Liver: Focal periportal hepatitis	Liver: Focal peritonitis with lobar adhesion	Kidneys: Chronic progressive nephrosis, early stage	Kidneys: Hydronephrosis, unilateral	Testes: Focal atrophy/degeneration of seminiferous tubules	Testes: Testicular atrophy, head, unilateral	Thymus: Atrophy	External Ear: Focal necrolysis of cartilage, early stage of osteochondromatosis	Heart: Chronic focal myocarditis
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	N	-	N	-	-	-	-	-	-	-	-	-	-
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	N	-	N	-	N	-	N	-	-	-	N	-	-
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	N	-	N	-	-	-	-	-	-	-	-	-	-
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	N	N	N	N	-	-	-	-	N	-	-	-	-
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	N	-	N	-	-	-	N	-	-	-	-	-	-
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	N	-	N	-	-	-	-	-	-	-	-	-	-
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	N	-	N	-	-	-	-	-	-	-	-	-	-
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	N	-	N	-	-	-	-	-	-	-	-	-	-
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	N	-	N	-	-	-	-	-	-	-	-	-	-
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	N	-	N	-	-	-	-	-	-	-	-	-	-

[illegible]

000014

PCC - 2 WEEKS
F 344 RATS - 2 SEX - 2 DOSE - 2 TREATMENT - 10 RATS PER GROUP

Sex	Group	Dose (mg/l)	Days on test	Recovery days	Lungs: Chronic murine pneumonia, early stage	Lungs: Focal alveolar emphysema	Liver: Non-specific micro-granuloma/focal of extramedullary hematopoiesis	Liver: Cloudy swelling/granular degeneration of hepatocytes	Liver: Focal periportal hepatitis	Liver: Focal periportal fibrosis with lobar adhesion	Kidneys: Chronic progressive nephropathy, early stage	Kidneys: Pyelonephrosis, unilateral	Testes: Focal atrophy/degeneration of seminiferous tubules	Testes: Testicular atrophy, head, unilateral	Thymus: Atrophy	External ears: Focal hedgehogs of cartilage, early stage of osteochondrophosis	Hearts: Chronic focal myocarditis
M	M	0	5	5	-	-	-	-	-	-	-	-	-	-	-	-	-
M	M	0	5	5	-	-	-	-	-	-	-	-	-	-	-	-	-
M	M	0	5	5	-	-	-	-	-	-	-	-	-	-	-	-	-
M	M	0	5	5	-	-	-	-	-	-	-	-	-	-	-	-	-
M	M	0	5	5	-	-	-	-	-	-	-	-	-	-	-	-	-
M	M	0	5	5	-	-	-	-	-	-	-	-	-	-	-	-	-
M	M	0	5	5	-	-	-	-	-	-	-	-	-	-	-	-	-
M	M	0	5	5	-	-	-	-	-	-	-	-	-	-	-	-	-
M	M	0	5	5	-	-	-	-	-	-	-	-	-	-	-	-	-
M	M	0	5	5	-	-	-	-	-	-	-	-	-	-	-	-	-

MEAN RELATIVE ORGAN AND BODY WEIGHTS FOR MALE RATS EXPOSED TO [redacted] VIA INHAL. (SUBACUTE-0 RECOVERY DAYS)

GROUP	HEART	LUNGS	LIVER	HELEEN	KIDNEY
I CONTROL	0.3540	0.6206	4.7259	0.2075	0.936
II LOW LEVEL	0.3243	0.5447+	4.9997	0.1665+	0.892
III HIGH LEVEL	0.3254	0.6083	5.9326+	0.1455+	0.929
F RATIO(1)	1.235	4.569*	4.316*	17.638*	0.27
LSD(2)	0.0406	0.0587	0.9299	0.0232	0.137
DUNNETT(3)	0.0466	0.0674	1.0670	0.0266	0.175
WMS(4)	0.0009	0.0018	0.4554	0.0003	0.007

GROUP	TESTIS	THYMUS
I CONTROL	1.0253	0.2410
II LOW LEVEL	1.0059	0.1804+
III HIGH LEVEL	1.1105	0.1430+
F RATIO(1)	1.036	7.713*
LSD(2)	0.1266	0.0349
DUNNETT(3)	0.1492	0.0629
WMS(4)	0.0084	0.0016

(1) RATIO OF AMONG- TO WITHIN-GROUP VARIATION--ONE-FACTOR ANALYSIS OF VARIANC

(2) LEAST SIGNIFICANT DIFFERENCE--GIVEN A SIGNIFICANT (ALPHA=0.05) F RATIO, ANY TWO MEANS DIFFERING BY MORE THAN THE LSD ARE SIGNIFICATLY DIFFERENT WITH A VARIABLE-WISE FALSE POSITIVE (ALPHA) ERROR RATE OF 0.05.

(3) DUNNETT TEST--ANY TREATMENT MEAN DIFFERING FROM THE CONTROL MEAN BY MORE THAN THE DUNNETT STATISTIC IS SIGNIFICANTLY DIFFERENT FROM THE CONTROL MEAN WITH A VARIABLE-WIDE FALSE POSITIVE (ALPHA) ERROR RATE OF 0.05.

(4) WITHIN-GROUP MEAN SQUARE.

\+ SIGNIFICANTLY DIFFERENT (P<0.05) FROM CONTROL GROUP BY LSD.

\# SIGNIFICANTLY DIFFERENT (P<0.05) FROM CONTROL GROUP BY DUNNETT TEST.

* SIGNIFICANT AT THE 0.05 PROBABILITY LEVEL.

MEAN ABSOLUTE ORGAN AND BODY WEIGHTS OF MALE RATS EXPOSED TO [redacted] VIA INHAL. (SUBACUTE-14 RECOVERY DAYS)

GROUP	FINAL BW	HEART	LUNGS	LIVER	SPLEEN
I CONTROL	341.2000	1.1660	1.0480	14.4900	0.7500
II LOW LEVEL	341.0000	1.1720	1.6700	16.0540	0.6[illegible]
III HIGH LEVEL	303.8000	1.0400	1.6640	15.0360	0.5[illegible]
F RATIO(1)	2.604	1.010	1.224	0.604	3.02[illegible]
LSD(2)	41.1241	0.1601	0.2771	2.9474	0.1[illegible]
DUNNETT(3)	47.1067	0.1930	0.3180	3.3012	0.1[illegible]
WMS(4)	890.6333	0.0135	0.0465	4.5750	0.012[illegible]

GROUP	KIDNEY	TESTIS	THYMUS
I CONTROL	2.8520	3.3260	0.6040
II LOW LEVEL	3.0060	3.1580	0.6520
III HIGH LEVEL	2.6360	2.7040*	0.6020
F RATIO(1)	1.293	3.949*	0.250
LSD(2)	0.4270	0.5740	0.1743
DUNNETT(3)	0.4908	0.6586	0.2000
WMS(4)	0.0964	0.1735	0.0160

(1) RATIO OF AMONG- TO WITHIN-GROUP VARIATION--ONE-FACTOR ANALYSIS OF VARIANC[illegible]

(2) LEAST SIGNIFICANT DIFFERENCE--GIVEN A SIGNIFICANT (ALPHA=0.05) F RATIO, ANY TWO MEANS DIFFERING BY MORE THAN THE LSD ARE SIGNIFICANTLY DIFFERENT WITH A VARIABLE-WISE FALSE POSITIVE (ALPHA) ERROR RATE OF 0.05.

(3) DUNNETT TEST--ANY TREATMENT MEAN DIFFERING FROM THE CONTROL MEAN BY MORE THAN THE DUNNETT STATISTIC IS SIGNIFICANTLY DIFFERENT FROM THE CONTROL MEAN WITH A VARIABLE-WISE FALSE POSITIVE (ALPHA) ERROR RATE OF 0.05.

(4) WITHIN-GROUP MEAN SQUARE.

+ SIGNIFICANTLY DIFFERENT (P<0.05) FROM CONTROL GROUP BY LSD.

* SIGNIFICANTLY DIFFERENT (P<0.05) FROM CONTROL GROUP BY DUNNETT [illegible]

* SIGNIFICANT AT THE 0.05 PROBABILITY LEVEL.

000017

MEAN RELATIVE ORGAN AND BODY WEIGHTS FOR MALE RATS EXPOSED
TO [redacted] VIA INHAL. (SUBACUTE+14 RECOVERY DAYS)

GROUP	HEART	LUNGS	LIVER	SPLEEN	KIDNEY
I CONTROL	0.3420	0.5392	4.2487	0.2180	0.036
II LOW LEVEL	0.3430	0.4965	4.7164	0.1830*	0.003
III HIGH LEVEL	0.3450	0.5514	4.9095*	0.1925*	0.064
F RATIO(1)	0.029	1.952	3.330	5.090*	0.62
LSD(2)	0.0339	0.0637	0.5720	0.0243	0.093
DUNNETT(3)	0.0389	0.0731	0.6563	0.0279	0.105
WMS(4)	0.0006	0.0021	0.1733	0.0003	0.004

GROUP	TESTIS	THYMUS
I CONTROL	0.9650	0.1773
II LOW LEVEL	0.9263	0.1916
III HIGH LEVEL	0.8528	0.2003
F RATIO(1)	1.004	0.400
LSD(2)	0.1763	0.0560
DUNNETT(3)	0.2023	0.0642
WMS(4)	0.0164	0.0017

(1) RATIO OF AMONG- TO WITHIN-GROUP VARIATION--ONE-FACTOR ANALYSIS OF VARIANCE

(2) LEAST SIGNIFICANT DIFFERENCE--GIVEN A SIGNIFICANT (ALPHA=0.05) F RATIO, ANY TWO MEANS DIFFERING BY MORE THAN THE LSD ARE SIGNIFICANTLY DIFFERENT WITH A VARIABLE-WISE FALSE POSITIVE (ALPHA) ERROR RATE OF 0.05.

(3) DUNNETT TEST--ANY TREATMENT MEAN DIFFERING FROM THE CONTROL MEAN BY MORE THAN THE DUNNETT STATISTIC IS SIGNIFICANTLY DIFFERENT FROM THE CONTROL MEAN WITH A VARIABLE-WISE FALSE POSITIVE (ALPHA) ERROR RATE OF 0.05.

(4) WITHIN-GROUP MEAN SQUARE.

* SIGNIFICANTLY DIFFERENT (P<0.05) FROM CONTROL GROUP BY LSD.

*, SIGNIFICANTLY DIFFERENT (P<0.05) FROM CONTROL GROUP BY DUNNETT TEST.

000018

MEAN ABSOLUTE ORGAN AND BODY WEIGHTS OF MALE RATS EXPOSED TO [redacted] VIA INHAL. (SUBACUTE-33 RECOVERY DAYS)

GROUP	FINAL BW	HEART	LUNGS	LIVER	SPLEEN
I CONTROL	367.2000	1.1100	1.7940	12.2440	0.6900
II LOW LEVEL	361.6000	1.1260	1.6840	12.4240	0.5960
III HIGH LEVEL	351.6000	1.1340	1.7600	12.5760	0.595[illegible]
F RATIO(1)	0.494	0.054	0.375	0.097	1.39[illegible]
LSD(2)	34.6507	0.1628	0.2209	1.6546	0.072[illegible]
DUNNETT(3)	39.7401	0.1040	0.2626	1.9634	0.10[illegible]
WMS(4)	632.6000	0.0140	0.0276	1.3409	0.004[illegible]

GROUP	KIDNEY	TESTIS	THYMUS
I CONTROL	2.6740	3.0520	0.5900
II LOW LEVEL	2.8200	3.2400	0.5320
III HIGH LEVEL	2.6660	3.1060	0.6340
F RATIO(1)	0.279	0.891	1.816
LSD(2)	0.3050	0.4159	0.1290
DUNNETT(3)	0.3003	0.3625	0.1400
WMS(4)	0.1347	0.0326	0.0000

(1) RATIO OF AMONG- TO WITHIN-GROUP VARIATION--ONE-FACTOR ANALYSIS OF VARIANC[illegible]

(2) LEAST SIGNIFICANT DIFFERENCE--GIVEN A SIGNIFICANT (ALPHA=0.05) F RATIO, ANY TWO MEANS DIFFERING BY MORE THAN THE LSD ARE SIGNIFICANTLY DIFFERENT WITH A VARIABLE-WISE FALSE POSITIVE (ALPHA) ERROR RATE OF 0.05.

(3) DUNNETT TEST--ANY TREATMENT MEAN DIFFERING FROM THE CONTROL MEAN BY MORE THAN THE DUNNETT STATISTIC IS SIGNIFICANTLY DIFFERENT FROM THE CONTROL MEAN WITH A VARIABLE-WISE FALSE POSITIVE (ALPHA) ERROR RATE OF 0.05.

(4) WITHIN-GROUP MEAN SQUARE.

* SIGNIFICANTLY DIFFERENT (P<0.05) FROM CONTROL GROUP BY LSD.

\# SIGNIFICANTLY DIFFERENT (P<0.05) FROM CONTROL GROUP BY DUNNETT TEST.

MEAN RELATIVE ORGAN AND BODY WEIGHTS FOR MALE RATS EXPOSED
TO [redacted] VIA INHAL. (SUBACUTE-32 RECOVERY DAYS)

GROUP	HEART	LUNGS	LIVER	SPLEEN	KIDNEY
I CONTROL	0.3020	0.4204	3.3304	0.1789	0.731
II LOW LEVEL	0.3104	0.4662	3.4320	0.1661	0.774
III HIGH LEVEL	0.3221	0.5094	3.5735	0.1704	0.750
F RATIO(1)	1.379	1.449	1.472	0.765	0.30
LSD(2)	0.0255	0.0443	0.3004	0.0351	0.11
DUNNETT(3)	0.0293	0.0509	0.3447	0.0265	0.139
WMS(4)	0.0003	0.0010	0.0475	0.0003	0.006

GROUP	TESTIS	THYMUS
I CONTROL	0.0336	0.1627
II LOW LEVEL	0.0391	0.1439
III HIGH LEVEL	0.0049	0.1310
F RATIO(1)	1.067	1.913
LSD(2)	0.1029	0.0413
DUNNETT(3)	0.1180	0.0474
WMS(4)	0.0056	0.0009

(1) RATIO OF AMONG- TO WITHIN-GROUP VARIATION--ONE-FACTOR ANALYSIS OF VARIANCE

(2) LEAST SIGNIFICANT DIFFERENCE--GIVEN A SIGNIFICANT (ALPHA=0.05) F RATIO, ANY TWO MEANS DIFFERING BY MORE THAN THE LSD ARE SIGNIFICANTLY DIFFERENT WITH A VARIABLE-WISE FALSE POSITIVE (ALPHA) ERROR RATE OF 0.05.

(3) DUNNETT TEST--ANY TREATMENT MEAN DIFFERING FROM THE CONTROL MEAN BY MORE THAN THE DUNNETT STATISTIC IS SIGNIFICANTLY DIFFERENT FROM THE CONTROL MEAN WITH A VARIABLE-WISE FALSE POSITIVE (ALPHA) ERROR RATE OF 0.05.

(4) WITHIN-GROUP MEAN SQUARE.

* SIGNIFICANTLY DIFFERENT (P<0.05) FROM CONTROL GROUP BY LSD.

* SIGNIFICANTLY DIFFERENT (P<0.05) FROM CONTROL GROUP BY DUNNETT TEST.

MEAN ABSOLUTE ORGAN AND BODY WEIGHTS OF MALE RATS EXPOSED TO [redacted] VIA INHAL. *SUBACUT-42 RECOVERY DAYS*

GROUP	FINAL BW	HEART	LUNGS	LIVER	SPLEEN
I CONTROL	427.0000	1.3460	1.2230	14.5906	[illegible]
II LOW LEVEL	409.0000	1.2420	1.0920	15.4160	[illegible]
III HIGH LEVEL	372.0000*	1.1640	1.0430	13.7460	[illegible]
F RATIO(1)	3.469	3.078	0.985	2.455	[illegible]
LSD(2)	46.3909	0.1664	0.3270	[illegible]	[illegible]
DUNNETT(3)	53.2290	0.1040	0.3258	[illegible]	[illegible]
WMS(4)	1135.3462	0.0139	0.0567	[illegible]	[illegible]

GROUP	KIDNEY	TESTIS	THYMUS
I CONTROL	3.2100	3.3000	0.6040
II LOW LEVEL	3.2220	3.2560	0.5920
III HIGH LEVEL	2.0500	3.2160	0.5440
F RATIO(1)	1.241	0.239	0.540
LSD(2)	0.5846	0.2862	0.1331
DUNNETT(3)	0.6708	0.3284	0.1527
WMS(4)	0.1800	0.0431	0.0693

(1) RATIO OF AMONG- TO WITHIN-GROUP VARIATION--ONE-FACTOR ANALYSIS OF VARIANCE

(2) LEAST SIGNIFICANT DIFFERENCE--GIVEN A SIGNIFICANT (ALPHA=0.05) F RATIO, ANY TWO MEANS DIFFERING BY MORE THAN THE LSD ARE SIGNIFICANTLY DIFFERENT WITH A VARIABLE-WISE FALSE POSITIVE (ALPHA) ERROR RATE OF 0.05.

(3) DUNNETT TEST--ANY TREATMENT MEAN DIFFERING FROM THE CONTROL MEAN BY MORE THAN THE DUNNETT STATISTIC IS SIGNIFICANTLY DIFFERENT FROM THE CONTROL MEAN WITH A VARIABLE-WISE FALSE POSITIVE (ALPHA) ERROR RATE OF 0.05.

(4) WITHIN-GROUP MEAN SQUARE.

* SIGNIFICANTLY DIFFERENT (P<0.05) FROM CONTROL GROUP BY LSD.

\# SIGNIFICANTLY DIFFERENT (P<0.05) FROM CONTROL GROUP BY DUNNETT [illegible]

TO [redacted] MEAN RELATIVE OR [illegible] WEIGHTS FOR MALE RATS EXPOSED [illegible] (SUBACUTE-42 RECOVERY DAYS)

GROUP	KIDNEY	LUNGS	LIVER	SPLEEN	KIDNEY
I CONTROL	0.3[illegible]	[illegible].4451	3.8604	0.1047	0.74
II LOW LEVEL	0.3029	[illegible].4629	3.7516	0.1613	0.78
III HIGH LEVEL	0.3135	0.4956	3.6035	0.1075	0.76
F RATIO(1)	0.405	1.530	0.573	2.002	0.3[illegible]
LSD(2)	0.0333	0.0629	0.3007	0.0307	0.0[illegible]
DUNNETT(3)	0.0382	0.0723	0.4360	0.0352	0.10[illegible]
WMS(4)	0.0006	0.0021	0.0763	0.0005	0.00[illegible]

GROUP	TESTIS	EPIDIDYMIS
I CONTROL	0.7245	0.1423
II LOW LEVEL	0.7982	0.1451
III HIGH LEVEL	0.8630	0.1456
F RATIO(1)	2.687	0.027
LSD(2)	0.0861	0.0345
DUNNETT(3)	0.0900	0.0396
WMS(4)	0.0039	0.0006

(1) RATIO OF AMONG- TO WITHIN-GROUP VARIATION--ONE-FACTOR ANALYSIS OF VARIANCE

(2) LEAST SIGNIFICANT DIFFERENCE--GIVEN A SIGNIFICANT (ALPHA=0.05) F RATIO, ANY TWO MEANS DIFFERING BY MORE THAN THE LSD ARE SIGNIFICANTLY DIFFERENT WITH A VARIABLE-WISE FALSE POSITIVE (ALPHA) ERROR RATE OF 0.05.

(3) DUNNETT TEST--ANY TREATMENT MEAN DIFFERING FROM THE CONTROL MEAN BY MORE THAN THE DUNNETT STATISTIC IS SIGNIFICANTLY DIFFERENT FROM THE CONTROL MEAN WITH A VARIABLE-WISE FALSE POSITIVE (ALPHA) ERROR RATE OF 0.05.

(4) WITHIN-GROUP MEAN SQUARE.

F SIGNIFICANTLY DIFFERENT (P<0.05) FROM CONTROL GROUP BY LSD.

D SIGNIFICANTLY DIFFERENT (P<0.05) FROM CONTROL GROUP BY DUNNETT TEST.

APPENDIX E

INHALATION TOXICITY OF [redacted]

MR PROJECT NO. 2753-001
HASKELL NO. 12,037
OCULAR TOXICITY REPORT

Procedure: Sixty ChR-CD® young adult male rats were divided into three groups of 20 rats each and exposed (head-only) six hours per day, five days per week for a total of 10 exposures over a two-week period to 0.00, 0.01 or 0.08 mg/l [redacted] particulate. Ten rats were selected from each group for eye examination on the 5th and 9th days of exposure. Observations of the cornea, iris and conjunctiva were made with a hand-slit lamp and a biomicroscope after using Fluor-i-strip® stain.

Results: The results of the eye examinations for each rat are presented in Tables I, II and III. When rats were exposed by inhalation to [redacted] particulate at 0.01 mg/l, two of ten rats at five days and five of ten rats at nine days had dried reddish brown discharge around their eyes. When exposed to 0.08 mg/l of test material, two of ten rats had dried reddish brown discharge at five days and five of ten had brown discharge and one had dried reddish brown discharge at nine days. This discharge (chromodacryorrhea) is often seen in animals under stress. No corneal or iritic effects were seen in these rats. No corneal, iritic or conjunctival effects were seen in the control rats at any time.

Summary: No significant ocular effects were seen in rat eyes when examined after the fifth and ninth exposures to [redacted]

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Approved by: Gerald L. Kennedy
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DFE:acg
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Date Issued: June 25, 1979

TABLE 1 - Control (0.0 mg/L) H-12,037

Rat Number		1 days 1/1 L	1 days 1/1 R	7 days 1/1 L	7 days 1/1 R
[illegible]	Cornea				
	opacity	0	0	0	0
	area	0	0	0	0
	Iris	0	0	0	0
	Conjunctiva				
	redness	0	0	0	0
	chemosis	0	0	0	0
	discharge	0	0	0	0
	Fluor-1-strip[1]	0	0	0	0
	Stain of cornea	neg	neg	neg	neg
		L	R	L	R
[illegible]	Cornea				
	opacity	0	0	0	0
	area	0	0	0	0
	Iris	0	0	0	0
	Conjunctiva				
	redness	0	0	0	0
	chemosis	0	0	0	0
	discharge	0	0	0	0
	Fluor-1-strip[1]	0	0	0	0
	Stain of cornea	neg	neg	-	neg
		L	R	L	R
[illegible]	Cornea				
	opacity	0	0	0	0
	area	0	0	0	0
	Iris	0	0	0	0
	Conjunctiva				
	redness	0	0	0	0
	chemosis	0	0	0	0
	discharge	0	0	0	0
	Fluor-1-strip[1]	0	0	-	0
	Stain of cornea	neg	neg	-	neg
		L	R	L	R
[illegible]	Cornea				
	opacity	0	0	0	0
	area	0	0	0	0
	Iris	0	0	0	0
	Conjunctiva				
	redness	0	0	0	0
	chemosis	0	0	0	0
	discharge	0	0	0	0
	Fluor-1-strip[1]	-	0	-	0
	Stain of cornea	-	neg	-	neg
		L	R	L	R
[illegible]	Cornea				
	opacity	0	0	0	0
	area	0	0	0	0
	Iris	0	0	0	0
	Conjunctiva				
	redness	0	0	0	0
	chemosis	0	0	0	0
	discharge	0	0	0	0
	Fluor-1-strip[1]	-	0	-	0
	Stain of cornea	-	neg	-	neg

Rat Number		1 days 1/1 L	1 days 1/1 R	7 days 1/1 L	7 days 1/1 R
336383	Cornea				
	opacity	0	0	0	0
	area	0	0	0	0
	Iris	0	0	0	0
	Conjunctiva				
	redness	0	0	0	0
	chemosis	0	0	0	0
	discharge	0	0	0	0
	Fluor-1-strip[1]	-	0	-	0
	Stain of cornea	-	neg	-	neg
		L	R	L	R
336384	Cornea				
	opacity	0	0	0	0
	area	0	0	0	0
	Iris	0	0	0	0
	Conjunctiva				
	redness	0	0	0	0
	chemosis	0	0	0	0
	discharge	0	0	0	0
	Fluor-1-strip[1]	-	0	-	0
	Stain of cornea	-	neg	-	neg
		L	R	L	R
336385	Cornea				
	opacity	0	0	0	0
	area	0	0	0	0
	Iris	0	0	0	0
	Conjunctiva				
	redness	0	0	0	0
	chemosis	0	0	0	0
	discharge	0	0	0	0
	Fluor-1-strip[1]	-	0	-	0
	Stain of cornea	-	neg	-	neg
		L	R	L	R
336386	Cornea				
	opacity	0	0	0	0
	area	0	0	0	0
	Iris	0	0	0	0
	Conjunctiva				
	redness	0	0	0	0
	chemosis	0	0	0	0
	discharge	0	0	0	0
	Fluor-1-strip[1]	-	0	-	0
	Stain of cornea	-	neg	-	neg
		L	R	L	R
336387	Cornea				
	opacity	0	0	0	0
	area	0	0	0	0
	Iris	0	0	0	0
	Conjunctiva				
	redness	0	0	0	0
	chemosis	0	0	0	0
	discharge	0	0	0	0
	Fluor-1-strip[1]	-	0	-	0
	Stain of cornea	neg	neg	-	neg

[1]dried reddish brown
[2]brown

TABLE II - (0.01 mg/L) H-12,037

Rabbit Number		5 days 1/1 L	5 days 1/1 R	7 days 1/15 L	7 days 1/15 R
116368	Cornea				
	opacity	0	0	0	0
	area	0	0	0	0
	Iris	0	0	0	0
	Conjunctiva				
	redness	0	0	0	0
	chemosis	0	0	0	0
	discharge	0'	0'	0'	0'
	Fluor-i-escrip®	0	0	0	0
	Sicals of cornea	neg	neg	-	neg
		L	R	L	R
116369	Cornea				
	opacity	0	0	0	0
	area	0	0	0	0
	Iris	0	0	0	0
	Conjunctiva				
	redness	0	0	0	0
	chemosis	0	0	0	0
	discharge	0'	0'	0'	0'
	Fluor-i-escrip®	-	0	-	0
	Sicals of cornea	-	neg	-	neg
		L	R	L	R
116370	Cornea				
	opacity	0	0	0	0
	area	0	0	0	0
	Iris	0	0	0	0
	Conjunctiva				
	redness	0	0	0	0
	chemosis	0	0	0	0
	discharge	0	0	0	0
	Fluor-i-escrip®	-	0	0	0
	Sicals of cornea	-	neg	0	neg
		L	R	L	R
116371	Cornea				
	opacity	0	0	0	0
	area	0	0	0	0
	Iris	0	0	0	0
	Conjunctiva				
	redness	0	0	0	0
	chemosis	0	0	0	0
	discharge	0	0	0	0
	Fluor-i-escrip®	-		-	0
	Sicals of cornea	-	neg	-	neg
		L	R	L	R
116372	Cornea				
	opacity	0	0	0	0
	area	0	0	0	0
	Iris	0	0	0	0
	Conjunctiva				
	redness	0	0	0	0
	chemosis	0	0	0	0
	discharge	0	0	0	0
	Fluor-i-escrip®	-	0	-	0
	Sicals of cornea	-	neg	-	neg

Rabbit Number		5 days 1/1 L	5 days 1/1 R	7 days 1/15 L	7 days 1/15 R
116373	Cornea				
	opacity	0	0	0	0
	area	0	0	0	0
	Iris	0	0	0	0
	Conjunctiva				
	redness	0	0	0	0
	chemosis	0	0	0	0
	discharge	0	0	0	0
	Fluor-i-escrip®	-	0	-	0
	Sicals of cornea	-	neg	-	neg
		L	R	L	R
116374	Cornea				
	opacity	0	0	0	0
	area	0	0	0	0
	Iris	0	0	0	0
	Conjunctiva				
	redness	0	0	0	0
	chemosis	0	0	0	0
	discharge	0	0	0'	0
	Fluor-i-escrip®	-	0	-	0
	Sicals of cornea	-	neg	-	neg
		L	R	L	R
116375	Cornea				
	opacity	0	0	0	0
	area	0	0	0	0
	Iris	0	0	0	0
	Conjunctiva				
	redness	0	0	0	0
	chemosis	0	0	0	0
	discharge	0	0	0	0
	Fluor-i-escrip®	-	0	-	0
	Sicals of cornea	-	neg	-	neg
		L	R	L	R
116376	Cornea				
	opacity	0	0	0	0
	area	0	0	0	0
	Iris	0	0	0	0
	Conjunctiva				
	redness	0	0	0	0
	chemosis	0	0	0	0
	discharge	0	0	0'	0
	Fluor-i-escrip®	-	0	-	0
	Sicals of cornea	-	neg	-	neg
		L	R	L	R
116377	Cornea				
	opacity	0	0	0	0
	area	0	0	0	0
	Iris	0	0	0	0
	Conjunctiva				
	redness	0	0	0	0
	chemosis	0	0	0	0
	discharge	0	0	0	0
	Fluor-i-escrip®	-	0	-	0
	Sicals of cornea	-	neg	-	neg

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TABLE III - (0.08 mg/L) H-12,037

Rat Number		5 days 3/1 L	5 days 3/1 R	7 days 3/10 L	7 days 3/10 R
336389	Cornea				
	opacity	0	0	0	0
	area	0	0	0	0
	Iris	0	0	0	0
	Conjunctiva				
	redness	0	0	0	0
	chemosis	0	0	0	0
	discharge	0[1]	0[1]	1[1]	1[1]
	Fluor-i-strip[a]	0	0	0	0
	Blemis of cornea	neg	neg	neg	neg
336390	Cornea				
	opacity	0	0	0	0
	area	0	0	0	0
	Iris	0	0	0	0
	Conjunctiva				
	redness	0	0	0	0
	chemosis	0	0	0	0
	discharge	0	0	1[1]	1[1]
	Fluor-i-strip[a]	-	0	-	0
	Blemis of cornea	-	neg	-	neg
336390	Cornea				
	opacity	0	0	0	0
	area	0	0	0	0
	Iris	0	0	0	0
	Conjunctiva				
	redness	0	0	0	0
	chemosis	0	0	0	0
	discharge	0	0	0	0
	Fluor-i-strip[a]	-	0	-	0
	Blemis of cornea	-	neg	-	neg
336391	Cornea				
	opacity	0	0	0	0
	area	0	0	0	0
	Iris	0	0	0	0
	Conjunctiva				
	redness	0	0	0	0
	chemosis	0	0	0	0
	discharge	0[1]	0[1]	1[1]	1[1]
	Fluor-i-strip[a]	-	0	-	0
	Blemis of cornea	-	neg	-	neg
336392	Cornea				
	opacity	0	0	0	0
	area	0	0	0	0
	Iris	0	0	0	0
	Conjunctiva				
	redness	0	0	0	0
	chemosis	0	0	0	0
	discharge	0	0	1[1]	1[1]
	Fluor-i-strip[a]	-	0	-	0
	Blemis of cornea	-	neg	-	neg

Rat Number		5 days 3/1 L	5 days 3/1 R	7 days 3/10 L
336393	Cornea			
	opacity	0	0	0
	area	0	0	0
	Iris	0	0	0
	Conjunctiva			
	redness	0	0	0
	chemosis	0	0	0
	discharge	0	0	1[1]
	Fluor-i-strip[a]	-	0	-
	Blemis of cornea	-	neg	-
336394	Cornea			
	opacity	0	0	0
	area	0	0	0
	Iris	0	0	0
	Conjunctiva			
	redness		0	0
	chemosis	0	0	0
	discharge	0	0	0[1]
	Fluor-i-strip[a]	-	0	-
	Blemis of cornea	-	neg	-
336395	Cornea			
	opacity	0	0	0
	area	0	0	0
	Iris	0	0	0
	Conjunctiva			
	redness	0	0	0
	chemosis	0	0	0
	discharge	0	0	0
	Fluor-i-strip[a]	-	0	-
	Blemis of cornea	-	neg	-
336396	Cornea			
	opacity	0	0	0
	area	0	0	0
	Iris	0	0	0
	Conjunctiva			
	redness	0	0	0
	chemosis	0	0	0
	discharge	0[1]	0[1]	0[1]
	Fluor-i-strip[a]	-	0	-
	Blemis of cornea	-	neg	-
336397	Cornea			
	opacity	0	0	0
	area	0	0	0
	Iris	0	0	0
	Conjunctiva			
	redness	0	0	0
	chemosis	0	0	0
	discharge	0	0	0
	Fluor-i-strip[a]	-	0	-
	Blemis of cornea	-	neg	-

[a] Fluorescein stain

500026

E. I. du Pont de Nemours and Company
Haskell Laboratory for Toxicology and Industrial Medicine

HASKELL LABORATORY REPORT NO. 160-69

Material Tested: [redacted]

Haskell No.: 6001

Other Codes: [redacted]

ACUTE INHALATION DUST TOXICITY

Procedure: Two different types of dust generators were used to generate [redacted] aerosols.

(1) DeVilbiss Dust Generator: A heavy dust cloud was generated by blowing ~ 30 L/minute of air through a high velocity Cu-tubing jet submerged in a mechanically stirred reservoir of the test material. The air carried the dust particles into an 8-liter exposure chamber. Suitable diluting air was introduced between the generator and the chamber to achieve lower concentrations. This generator did not fractionate the dust and all particle sizes, large and small, were delivered into the exposure chamber.

(2) Fornberger Dust Generator: This generator was used for low atmospheric dust concentrations. With this generator, a falling stream of dust particles from a stirred reservoir impinged on a pneumatic jet. The air stream from this jet carried the particles to a cyclone head where the larger ones were returned to the reservoir. This generator achieved some particle size fractionation and the rats received mainly particles $\leq 5\ \mu$ mass median diameter. As with the DeVilbiss generator, the generator itself was run under constant conditions and dust concentrations were lowered by diluting the stream with air between the generator and the exposure chamber.

Six rats of 250-270 grams body weight were used per exposure. Only their heads were exposed. All exposures were four hours. The eyes were stained with fluorescein immediately after exposure to check on eye damage by the test material. Rats were sacrificed for histopathologic examination at 1, 7, 14, 27, and 42 days post-exposure. Tissues from two rats dying during exposure were also examined microscopically.

In both methods, the airborne solids were measured in the exposure chamber by collecting the solids in a known air volume on a filter of known pore size. The concentration was determined five times during each four-hour exposure. At the mid-point of each exposure, a particle size distribution measurement was made with a Monsanto Cascade Impactor.

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Results:

Generator	Average Dust Concentration (mg/L)	Mortality Ratio	Mass Median Diameter (μ)	Clinical Observations: During Exposure	Clinical Observations: Post-Exposure
1	5.7	6/6	5.4 ± 3.2	Gasping, irregular breathing, red discharge around eyes and nose, salivation, death (1/6)	Death from 15 minutes to 48 hours (5/6)
	4.8	6/6	16 ± 3.4	Same as above, but no deaths	Some rupture of eyes, all other eyes opaque; all dead in 48 hours
	2.3[1]	6/6	7.6 ± 3.8	Same as above	Same as above; fluorescein stain confirmed external eye damage
2	0.93[1]	1/6	1.8 ± 2.5	Gasping, irregular breathing, red discharge around eyes and nose	Severe weight loss first day, mild loss the next day; normal growth thereafter; > 80% of rats have opaque and corroded appearing eyes; external damage confirmed with fluorescein stain; one death 2nd night
	0.81[2]	2/6	1.8 ± 2.8	Same as above except one death	Same as above; eyes appeared normal after 20 days
	0.38	1/6[3]	2.4 ± 2.4	Same as above	Severe weight losses first day; normal growth thereafter

1 Acute daily control exposure.

2 Sacrificed at 1, 7 and 14 days.

3 Sacrificed at 37 and 42 days.

4 Death due related to test material.

Pathology: Rats dying during exposure had hyperinflated lungs. Some of the test material was present in the stomach. They also had a fluffy white exudate in the trachea. The ratio of liver weight to body weight was at the high end of the normal range one day after exposure. It increased to a maximum (two times normal) at 7-14 days after exposure and then decreased to the high end of the normal range at the last sacrifice, 42 days post-exposure.

Pathology (Cont'd.):

Microscopic tissue examination[4] indicated that acute pulmonary edema developed promptly but disappeared in about [illegible] with leaving no residual injury. No dust particles were seen in the lungs microscopically. There was irritation of the stomach which cleared in two weeks and irritation of the eyes which was still present when the last pair of rats was sacrificed 42 days after exposure. The liver tissue appeared microscopically normal at all times and the mechanism of enlargement was not apparent.

Discussion: The time pattern and magnitude of rat liver enlargement caused by inhalation of [redacted] were similar to those caused by inhalation of 3-(1H,1H,2H,2H-polyfluoroalkoxy)propane sulfonic acid, sodium salt (Surfactant TLF-2654; Haskell Laboratory Report No. 254-68). Inhalation of Surfactant TLF-2654 caused changes in liver cell morphology (Haskell Laboratory Report No. 254-68) but inhalation of [redacted] did not. However, the exposures to the two materials were not highly comparable, since exposure to Surfactant TLF-2654 was whole body, whereas exposure to [redacted] was head only. This effective from the TLF-2654 exposures would reflect ingestion of greater amounts of material than grooming. No strict [illegible] can be made for liver enlargement caused by inhalation of [redacted] versus ingestion since comparable [illegible] studies have not been carried out after ingestion of [redacted]. However, 14 days after inhalation of a fractionally [illegible] dose of [redacted], liver to body weight ratio was two times normal. Fourteen days after ingestion of the highest [illegible] oral dose, liver to body weight ratio was < 1.5 times normal (Haskell Laboratory Report No. 55-61).

A study of rat liver enlargement versus time after ingestion has been carried out for the ammonium salt of 3,5-dioxo-2,5-di(trifluoromethyl)-undecafluorocyclohexanesulfonic acid (AHF; Haskell Laboratory Report No. 70-61). In this study, the ratio of liver weight to body weight reached a maximum 5-10 days after ingestion of 1/5 of the Approximate Lethal Dose (which dose was 12 mg/kg) and stayed relatively constant for the rest of the study (last sacrifice 56 days after treatment).

[redacted] would be considered highly toxic by inhalation administration as judged by four-hour rat inhalation. Orally, it would be considered to have only moderate acute toxicity.

Summary: The Approximate Lethal Concentration (ALC) of [redacted] is 0.8 mg/L for a four-hour rat exposure. It is considered highly toxic by inhalation. Only the rat heads were exposed to minimize complicating the study by inhaling the test material. Inhalation of the test material caused liver enlargement which reached a maximum (two to three times normal) 7-14 days after exposure. Liver weights returned to the normal range 42 days after exposure. No changes in liver cell morphology were observed. The small amount ingested caused irritation of the stomach which repaired normally. The material also caused corneal opacity and ulceration which were still microscopically evident 42 days after exposure.

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[4] Lungs, liver, trachea, gastrointestinal tract were the only tissues examined microscopically.

Summary (Cont'd.):

[redacted] should be handled with at least the same care as ANT. Ingestion and inhalation should be avoided and any spillage on the skin or eyes should be washed off immediately. There should be medical follow-up of any known eye exposure.

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Approved by: _____
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Director

Distribution
Date: March 12, 1969

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