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with Dr. Sherr 8/16/84

August 7, 1984

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Document Control Officer
(Attn:) T. O'Bryan)
Information Management Division (TS-793)
Office of Toxic Substances
401 M Street, SW
Washington, DC 20460

Re: Toluene Diisocyanate

Dear Sirs:

As requested in Vol. 5, No. 2 TSCA Chemicals-in-Progress Bulletin (May, 1984), we are enclosing two (2) unpublished toxicological studies we have conducted on toluene diisocyanate. The studies are:

Tox Study 83-40 on 80/20 Toluene Diisocyanate -
A dermal sensitization study in male guinea pigs

Tox Study 83-69 on 80/20 Toluene Diisocyanate -
A study of the sensitization potential of inhaled TDI in guinea pigs

The report on Study 83-69 is in draft form.

Sincerely,

Allan E. Sherr, Ph.D.
Manager, Chemical Petitions and
Regulatory Affairs
Toxicology & Product Safety Dept.

AES:cr

Encl.

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Toxicology Research
Toxicology Evaluation Department

M.T.L. VOLUME 1

TYPE OF REPORT:	Progress	PERIOD COVERED: FROM	1.19.81
PROJECT NUMBER	18750	TO	2.6.81
REPORTED BY	C. Sargent Brunkhorst	REPORT ISSUED	4.6.81
WORK DONE BY	Appendix I	APPROVED BY	

Notebook	Pages
LL 7344	1-138

Vernon C. James
V. C. James, D.V.M., M.S.
Head, Toxicology
Evaluation Department

Study Nos.: 81010
81011

p. 254-265

Title

CL 11,716: Dermal Sensitization Study in Male Guinea Pigs.

Origin and Purpose

The study was designed to assess the irritation and sensitization potential of CL 11,716 when administered topically to guinea pigs. The study was sponsored by the Chemical Research Division, ACCO, Stamford, Ct.

Summary and Conclusion

Five adult male guinea pigs were used in the irritation phase (81010) of these studies. Several concentrations of CL 11,716 (0.025-0.4% in n-butyl ether) or n-butyl ether alone were applied topically to the skin of the back of each guinea pig. Twenty-four and 48 hours after application, the sites of application were scored for erythema, eschar, and edema using the Draize scoring system.[1] Erythema, but no eschar or edema was noted. Mean irritation scores in the irritation phase ranged from 0.6 to 1.0; i.e. barely perceptible to slight erythema.

Twenty male guinea pigs were used in the sensitization phase of the study (81011). Induction doses of 8%, 20%, or 40% CL 11,716, or n-butyl ether alone were applied on Day 0 and scored 24 and 48 hours later. Mean irritation scores, at 24 and 48 hours respectively, were 1.0 and 0.2 for the

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vehicle, 1.4 and 1.6 for 8% CL 11,716, 2.0 and 2.0 for 20% CL 11,716, and 2.0 and 2.0 for 40% CL 11,716. A mean score of 2 indicated slight irritation. Thus, 8% CL 11,716 was slightly less irritating than either 20% or 40% CL 11,716.

Challenge doses of vehicle, or CL 11,716 at 0.025, 0.05, 0.1, 0.2, and 0.4%, were applied topically on days 5 and 14 after induction. The sites of application were scored at 24 and 48 hours after each challenge. There was no mortality in these studies; and except for signs indicative of sensitization no findings of toxicologic significance were noted.

The mean dermal irritation scores of the induction dose increased with the rising concentrations of CL 11,716 in n-butyl ether. The mean dermal irritation scores of the challenge doses increased with both the concentration of the induction doses and concentrations of the challenge doses, though there were essentially no differences between the scores generated from day 5 or 14. The scores from the 24 hours observation period were also generally higher than those from the 48 hour observation period.

Mean irritation scores after challenge with 0.025%- 0.4% were higher than the scores noted in the irritation phase of the study and indicated that sensitization had occurred.

References

1. Draize, J., Woodward, G. and Calvery, H.: J. Pharmacology and Experimental Therapeutics, 82: 377-390 (1944)

[redacted]

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M.T.L. VOLUME 1

I. Materials and Methods

A. Materials

1. Test Substance

a. Identity

CL Number: CL 11,716

b. Batch Information

Source: Dupont Chemical

2. Vehicle

Name: n-Butyl ether

Manufactured by: Production Planning and Inventory Control, Dept. 210, Pearl River

Lot or Control No.: 701583

B. Animals

Young adult guinea pigs*, 5/dose level, were randomly assigned to treatment groups on the basis of pre-dose body weights† and general health.

* Hartley guinea pigs, Camm Breeding Laboratories, Inc., Wayne, N.J.
† LEDTOX Data Acquisition System.

Each guinea pig was assigned a cage number and ear tagged with the last four digits of a Unique Animal Number (UAN) obtained from the Toxicology Research Unique Animal Number File.

C. Animal Maintenance

Guinea pigs were individually housed in stainless steel cages with wire mesh bottoms in temperature and humidity controlled rooms. Twelve hours of continuous fluorescent lighting was provided daily. Feed* and deionized water were available ad libitum.

D. Experimental Design

The experimental design is presented in Table I.

E. Compound Preparation and Administration

The appropriate amounts of test substance (CL 11,716) were measured by volume and incorporated into n-butyl ether to achieve the desired concentrations of 0.025, 0.05, 0.1, 0.2, 0.4, 8, 20, or 40% (v/v). Solutions were prepared fresh on each day of dosing. Dosing volumes were kept constant at 25 mcL/site. Solutions were applied topically by micropipette to areas of clipped skin on the dorsum.

* Certified Guinea Pig Chow® 5026, Ralston Purina Co.

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M.T.L. VOLUME 1

Table I

CL 11,716: Dermal Irritation and Sensitization Study in Male Guinea Pigs

Experimental Design

Group	Study Number	Compound	Concentration % (v/v)	Dose[a] mcL/site	Number of Animals	Computer Animal Number	Unique Animal Number
1	81010	CL 11,716	Vehicle,.025,.05, .1,.2,.4	25	5	1-5	054845-054849
1	81011[b]	CL 11,716	Vehicle	50	5	1-5	054850-054854
2			8	50	5	6-10	054855-054859
3			20	50	5	11-15	054860-054864
4			40	50	5	16-20	054865-054869

a Each animal in Study 81011 received two 25 mcL doses of the test substance on day 0 (1/21/81).

b On day 5, all animals in groups 2, 3 and 4 were challenged with 25 mcL/site of the vehicle; and .025, .05, .1, .2 and .4% solutions of CL 11,716.
On day 14, all animals (including controls) were challenged with the same doses.

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F. Observations and Determinations

All animals were observed twice daily for general condition, behavior, and signs of toxicity. Body weights were recorded on day 0 for all animals and on days 7 and 14 for the animals included in study 81011. Dermal irritaion scores were performed on all animals 24 and 48 hours after each dosing using parameters described in Appendix II. The 5 animals from study 81010 were sacrificed on day 2 of the study and the remaining 20 animals from study 81011 were sacrificed on day 16. No postmortem examinations were performed.

II. Results and Discussion

Mean scores of CL 11,716 in n-butyl ether are summarized in Table IIA and B. The irritation scores of Study 81010 ranged from 0.6 to 1.0 and there was essentially no difference between the concentrations of CL 11,716 in n-butyl ether or the n-butyl ether alone. The mean scores of the induction doses of 8%, 20% and 40% ranged from 1.4 to 2.0 and exhibited a greater response with the higher concentrations. The mean scores of the challenge doses generally increased with both the rising concentrations of the induction and challenge doses. Those scores ranged from 1.6 to 4.6. The 24 hour observation generally noted a greater response than the 48 hour

05B

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Table IIA

CL 11,716: Dermal Irritation and Sensitization Study in Male Guinea Pigs

Dermal (Draize)[a] Irritation Scores

Study	Day of Dose	Dose/Site	24 Hours	48 Hours
81010[b]	0	0.0%	1	0
Irritation		0.025%	1	0.8
Aspect		0.05%	0.6	0
		0.1%	1	1
		0.2%	1	1
		0.4%	1	0.8
81011[c]	0	0.0%	1	0.2
Induction		8.0%	1.4	1.6
Dose		20.0%	2	2
		40.0%	2	2

a Maximum score is 8
b Day 0 was 1/19/81
c Day 0 was 1/21/81

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M.T.L. VOLUME 1

Table IIB

CL 11,716: Dermal Irritation and Sensitization Study in Male Guinea Pigs

Dermal (Draize) Irritation Scores

Study	Day of Dose	Dose/Site	24 Hours Induction Dose				48 Hours Induction Dose			
			0%	8%	20%	40%	0%	8%	20%	40%
81011 Challenge Dose	Day 5	0.0%	-	0.0	0.0	0.0	-	0.0	0.0	0.0
		0.025%	-	2.4	2.0	2.4	-	1.4	1.4	1.6
		0.05%	-	2.0	1.6	2.0	-	1.4	1.6	1.4
		0.1%	-	2.8	2.8	3.4	-	1.4	1.8	1.8
		0.2%	-	2.8	3.2	4.0	-	2.2	3.4	3.2
		0.4%	-	3.4	3.4	4.2	-	2.4	3.0	2.8
81011 Challenge Dose	Day 14	0.0%	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		0.025%	0.5	1.6	1.6	2.0	0.9	1.6	1.8	1.8
		0.05%	0.9	1.8	2.0	2.2	1.0	0.8	1.8	1.4
		0.1%	0.6	2.4	2.8	2.6	0.5	1.6	2.0	2.0
		0.2%	0.0	3.6	4.6	4.2	0.4	3.2	3.4	3.0
		0.4%	0.4	3.2	4.2	4.0	0.5	2.8	3.0	2.8

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observation, while there was no difference between scores generated from the challenge doses of days 5 and 14. Mean irritation scores after challenge with 0.025%-0.4% were greater than the scores noted in the irritation phase of the study and suggested that sensitization had occurred. There were no other signs of clinical or toxicologic effects.

E. J. Burden, Ph.D. Date
Study Director

C. Sargent Brunkhorst Date
Principal Investigator

The raw data of Studies 81010 and 81011, as well as the final report, are located in the Toxicology Research Facility.

This report accurately reflects the data in the study notebooks.

T. Henderson, M.A.
Study Data Verification Group

F. A. Meyer, B.A., Manager
Study Data Verification Group

Appendix I

CL 11,716: Dermal Irritation and Sensitization Study in Male Guinea Pigs

Study Personnel

Responsible Professionals

Study Director:	E. J. Burden, Ph.D.
Principal Investigator:	C. S. Brunkhorst, M.S.
Veterinarian:	C. C. Darrow, D.V.M., M.P.H.
Study Reviewer:	F. A. Meyer, B.S.

Supervisors

Toxicology Information Systems:	R. S. Wasserman, M.S.
Test Substance and Carrier Control:	R. Kudla, Ph.D.
Animal Colony:	J. Torres

Appendix II

CL 11,716: Dermal Irritation and Sensitization Study in Male Guinea Pigs

Dermal Irritation Scores

	Value
Erythema and eschar formation	
No erythema	0
Very slight erythema (barely perceptible)	1
Well defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formations (injuries in depth)	4
Total possible score	4
Edema formation	
No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well defined by definite raising)	2
Moderate edema (raised approximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond the area of exposure	4
Total possible score	4
Total Combined Score - 8	

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Formal Laboratory Report

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PROJECT NUMBER	PROJECT TITLE	VOLUME	YEAR
18750	CL 11,716: Dermal Sensitization Study in Male Guinea Pigs.	MTL 1	1981

SUBTITLE

PAGES 254 TO 265

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C. Sargent-Brunkhorst	973	180	L203	Toxicology Res.	4/6/81

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Toxicology Research
Toxicology Evaluation Department

M.T.L. VOLUME 1

TYPE OF REPORT: Progress
PROJECT NUMBER 18750
REPORTED BY C. Sargent Brunkhorst
WORK DONE BY Appendix I

PERIOD COVERED: FROM 1.19.81
TO 2.6.81
REPORT ISSUED 4.6.81
APPROVED BY

Notebook	Pages
LL 7344	1-138

V. C. James, D.V.M., M.S.
Head, Toxicology
Evaluation Department

Study Nos.: 81010
81011

p. 254-265

Title

CL 11,716: Dermal Sensitization Study in Male Guinea Pigs.

Origin and Purpose

The study was designed to assess the irritation and sensitization potential of CL 11,716 when administered topically to guinea pigs. The study was sponsored by the Chemical Research Division, ACCO, Stamford, Ct.

Summary and Conclusion

Five adult male guinea pigs were used in the irritation phase (81010) of these studies. Several concentrations of CL 11,716 (0.025-0.4% in n-butyl ether) or n-butyl ether alone were applied topically to the skin of the back of each guinea pig. Twenty-four and 48 hours after application, the sites of application were scored for erythema, eschar, and edema using the Draize scoring system.[1] Erythema, but no eschar or edema was noted. Mean irritation scores in the irritation phase ranged from 0.6 to 1.0; i.e. barely perceptible to slight erythema.

Twenty male guinea pigs were used in the sensitization phase of the study (81011). Induction doses of 8%, 20%, or 40% CL 11,716, or n-butyl ether alone were applied on Day 0 and scored 24 and 48 hours later. Mean irritation scores, at 24 and 48 hours respectively, were 1.0 and 0.2 for the

vehicle, 1.4 and 1.6 for 8% CL 11,716, 2.0 and 2.0 for 20% CL 11,716, and 2.0 and 2.0 for 40% CL 11,716. A mean score of 2 indicated slight irritation. Thus, 8% CL 11,716 was slightly less irritating than either 20% or 40% CL 11,716.

Challenge doses of vehicle, or CL 11,716 at 0.025, 0.05, 0.1, 0.2, and 0.4%, were applied topically on days 5 and 14 after induction. The sites of application were scored at 24 and 48 hours after each challenge. There was no mortality in these studies; and except for signs indicative of sensitization no findings of toxicologic significance were noted.

The mean dermal irritation scores of the induction dose increased with the rising concentrations of CL 11,716 in n-butyl ether. The mean dermal irritation scores of the challenge doses increased with both the concentration of the induction doses and concentrations of the challenge doses, though there were essentially no differences between the scores generated from day 5 or 14. The scores from the 24 hours observation period were also generally higher than those from the 48 hour observation period.

Mean irritation scores after challenge with 0.025%- 0.4% were higher than the scores noted in the irritation phase of the study and indicated that sensitization had occurred.

References

1. Draize, J., Woodward, G. and Calvery, H.: J. Pharmacology and Experimental Therapeutics, 82: 377-390 (1944)

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I. Materials and Methods

A. Materials

1. Test Substance

a. Identity

CL Number: CL 11,716

b. Batch Information

Source: Dupont Chemical

2. Vehicle

Name: n-Butyl ether

Manufactured by: Production Planning and Inventory Control, Dept. 210, Pearl River

Lot or Control No.: 701583

B. Animals

Young adult guinea pigs*, 5/dose level, were randomly assigned to treatment groups on the basis of pre-dose body weights† and general health.

* Hartley guinea pigs, Camm Breeding Laboratories, Inc., Wayne, N.J.
† LEDTOX Data Acquisition System.

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Each guinea pig was assigned a cage number and ear tagged with the last four digits of a Unique Animal Number (UAN) obtained from the Toxicology Research Unique Animal Number File.

C. Animal Maintenance

Guinea pigs were individually housed in stainless steel cages with wire mesh bottoms in temperature and humidity controlled rooms. Twelve hours of continuous fluorescent lighting was provided daily. Feed* and deionized water were available ad libitum.

D. Experimental Design

The experimental design is presented in Table I.

E. Compound Preparation and Administration

The appropriate amounts of test substance (CL 11,716) were measured by volume and incorporated into n-butyl ether to achieve the desired concentrations of 0.025, 0.05, 0.1, 0.2, 0.4, 8, 20, or 40% (v/v). Solutions were prepared fresh on each day of dosing. Dosing volumes were kept constant at 25 mcL/site. Solutions were applied topically by micropipette to areas of clipped skin on the dorsum.

* Certified Guinea Pig Chow® 5026, Ralston Purina Co.

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Pearl River, N.Y. 10965

Table I

CL 11,716: Dermal Irritation and Sensitization Study in Male Guinea Pigs

Experimental Design

Group	Study Number	Compound	Concentration % (v/v)	Dose[a] mcL/site	Number of Animals	Computer Animal Number	Unique Animal Number
1	81010	CL 11,716	Vehicle,.025,.05, .1,.2,.4	25	5	1-5	054845-054849
1	81011[b]	CL 11,716	Vehicle	50	5	1-5	054850-054854
2			8	50	5	6-10	054855-054859
3			20	50	5	11-15	054860-054864
4			40	50	5	16-20	054865-054869

a Each animal in Study 81011 received two 25 mcL doses of the test substance on day 0 (1/21/81).

b On day 5, all animals in groups 2, 3 and 4 were challenged with 25 mcL/site of the vehicle; and .025, .05, .1, .2 and .4% solutions of CL 11,716.
On day 14, all animals (including controls) were challenged with the same doses.

F. Observations and Determinations

All animals were observed twice daily for general condition, behavior, and signs of toxicity. Body weights were recorded on day 0 for all animals and on days 7 and 14 for the animals included in study 81011. Dermal irritaion scores were performed on all animals 24 and 48 hours after each dosing using parameters described in Appendix II. The 5 animals from study 81010 were sacrificed on day 2 of the study and the remaining 20 animals from study 81011 were sacrificed on day 16. No postmortem examinations were performed.

II. Results and Discussion

Mean scores of CL 11,716 in n-butyl ether are summarized in Table IIA and B. The irritation scores of Study 81010 ranged from 0.6 to 1.0 and there was essentially no difference between the concentrations of CL 11,716 in n-butyl ether or the n-butyl ether alone. The mean scores of the induction doses of 8%, 20% and 40% ranged from 1.4 to 2.0 and exhibited a greater response with the higher concentrations. The mean scores of the challenge doses generally increased with both the rising concentrations of the induction and challenge doses. Those scores ranged from 1.6 to 4.6. The 24 hour observation generally noted a greater response than the 48 hour

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M.T.L. VOLUME 1

Table IIA

CL 11,716: Dermal Irritation and Sensitization Study in Male Guinea Pigs

Dermal (Draize)[a] Irritation Scores

Study	Day of Dose	Dose/Site	24 Hours	48 Hours
81010[b] Irritation Aspect	0	0.0%	1	0
		0.025%	1	0.8
		0.05%	0.6	0
		0.1%	1	1
		0.2%	1	1
		0.4%	1	0.8
81011[c] Induction Dose	0	0.0%	1	0.2
		8.0%	1.4	1.6
		20.0%	2	2
		40.0%	2	2

a Maximum score is 8
b Day 0 was 1/19/81
c Day 0 was 1/21/81

CSB

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Table IIB

CL 11,716: Dermal Irritation and Sensitization Study in Male Guinea Pigs

Dermal (Draize) Irritation Scores

Study	Day of Dose	Dose/Site	24 Hours Induction Dose 0%	8%	20%	40%	48 Hours Induction Dose 0%	8%	20%	40%
81011 Challenge Dose	Day 5	0.0%	-	0.0	0.0	0.0	-	0.0	0.0	0.0
		0.025%	-	2.4	2.0	2.4	-	1.4	1.4	1.6
		0.05%	-	2.0	1.6	2.0	-	1.4	1.6	1.4
		0.1%	-	2.8	2.8	3.4	-	1.4	1.8	1.8
		0.2%	-	2.8	3.2	4.0	-	2.2	3.4	3.2
		0.4%	-	3.4	3.4	4.2	-	2.4	3.0	2.8
81011 Challenge Dose	Day 14	0.0%	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		0.025%	0.5	1.6	1.6	2.0	0.9	1.6	1.8	1.8
		0.05%	0.9	1.8	2.0	2.2	1.0	0.8	1.8	1.4
		0.1%	0.6	2.4	2.8	2.6	0.5	1.6	2.0	2.0
		0.2%	0.0	3.6	4.6	4.2	0.4	3.2	3.4	3.0
		0.4%	0.4	3.2	4.2	4.0	0.5	2.8	3.0	2.8

LPR 3035C - CONTINUOUS 12/80

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observation, while there was no difference between scores generated from the challenge doses of days 5 and 14. Mean irritation scores after challenge with 0.025%-0.4% were greater than the scores noted in the irritation phase of the study and suggested that sensitization had occurred. There were no other signs of clinical or toxicologic effects.

E. J. Burden, Ph.D. Date 4/9/81
Study Director

C. Sargent Brunkhorst Date 4/8/81
Principal Investigator

The raw data of Studies 81010 and 81011, as well as the final report, are located in the Toxicology Research Facility.

This report accurately reflects the data in the study notebooks.

T. Henderson, M.A. 4/9/81
Study Data Verification Group

F. A. Meyer, B.A., Manager 4/9/81
Study Data Verification Group

Appendix I

CL 11,716: Dermal Irritation and Sensitization Study in Male Guinea Pigs

Study Personnel

Responsible Professionals

Study Director:	E. J. Burden, Ph.D.
Principal Investigator:	C. S. Brunkhorst, M.S.
Veterinarian:	C. C. Darrow, D.V.M., M.P.H.
Study Reviewer:	F. A. Meyer, B.S.

Supervisors

Toxicology Information Systems:	R. S. Wasserman, M.S.
Test Substance and Carrier Control:	R. Kudla, Ph.D.
Animal Colony:	J. Torres

Appendix II

CL 11,716: Dermal Irritation and Sensitization Study in Male Guinea Pigs

Dermal Irritation Scores

	Value
Erythema and eschar formation	
No erythema	0
Very slight erythema (barely perceptible)	1
Well defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formations (injuries in depth)	4
Total possible score	4
Edema formation	
No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well defined by definite raising)	2
Moderate edema (raised approximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond the area of exposure	4
Total possible score	4

Total Combined Score - 8

American Cyanamid Company
Medical Research Division
Wilbur G. Malcolm Toxicology Laboratories
Pearl River, NY 10965
(914) 735-5000

CL 11,716: Dermal Sensitization Study in Male Guinea Pigs

CYANAMID *** ANIMAL WEIGHTS(G)/OBSERVATIONS - RAW DATA FOR ARCHIVES *** STUDY NUMBER : 81011 PAGE 1
WILBUR G. MALCOLM TOXICOLOGY LABS. TECHNICIAN : JWH JWH 1/21/81
PEARL RIVER, NEW YORK TIME PERIOD : 0
CMPD: 11,716 SPECIES: GUINEA PIG STUDY TYPE: SENSITIZATION DATE DATA COLLECTED : 21-JAN-81

SAN	UAN	DOSE GROUP	BODY WEIGHT	OLD JAR	NEW JAR	TIME	CATEGORY	GRADE	OBSERVATIONS
TARE WEIGHT = 0.4									
CALIBRATION WEIGHT= 500.2									
1	54850	1	637			08:18			
2	54851	1	628			08:18			
3	54852	1	591			08:18			
4	54853	1	644			08:18			
5	54854	1	659			08:19			
6	54855	2	627			08:19			
7	54856	2	651			08:19			
8	54857	2	606			08:19			
9	54858	2	582			08:19			
10	54859	2	540			08:20			
TARE WEIGHT = 0.5									
CALIBRATION WEIGHT= 499.8									
11	54860	3	594			08:21			
12	54861	3	608			08:21			
13	54862	3	624			08:22			
14	54863	3	582			08:22			
15	54864	3	652			08:22			
16	54865	4	559			08:22			
17	54866	4	634			08:22			
18	54867	4	658			08:23			
19	54868	4	595			08:23			
20	54869	4	609			08:23			

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AN#	BODY WEIGHT
1	757
2	720
3	691
4	789
5	786
6	740
7	719
8	682
9	662
10	614
11	661
12	697
13	740
14	656
15	744
16	606
17	692
18	775
19	647
20	670

TOTAL NUMBER OF ANIMALS IN FILE = 20
TOTAL NUMBER OF ANIMALS WITH NON-ZERO WEIGHT = 20
MEAN = 702.27
STANDARD DEVIATION = 54.07

CSB 3/13/81

CYANAMID *** ANIMAL WEIGHTS(G)/OBSERVATIONS - RAW DATA FOR ARCHIVES *** STUDY NUMBER : B1011 PAGE 1
WILBUR G. MALCOLM TOXICOLOGY LABS. TECHNICIAN : JWH JWH
PEARL RIVER, NEW YORK TIME PERIOD : 0 1/21/81
CMPD: 11,716 SPECIES: GUINEA PIG STUDY TYPE: SENSITIZATION DATE DATA COLLECTED : 21-JAN-81

SAN	UAN	DOSE GROUP	BODY WEIGHT	OLD JAR	NEW JAR	TIME	CATEGORY	GRADE	OBSERVATIONS
1	54850	1				See next page JWH 1/21/81			
2	54851	1				15: 0	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
3	54852	1				See next page JWH 1/21/81			
4	54853	1				15: 0	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
5	54854	1				See next page JWH 1/21/81			
6	54855	2				15: 0	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
7	54856	2				See next page JWH 1/21/81			
8	54857	2				15: 0	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
9	54858	2				15: 0	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
10	54859	2				15: 0	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
11	54860	3				15: 0	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
12	54861	3				15: 1	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
13	54862	3				15: 1	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
14	54863	3				15: 1	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
15	54864	3				15: 1	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
16	54865	4				15: 1	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
17	54866	4				15: 1	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
18	54867	4				15: 1	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
19	54868	4				15: 1	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
20	54869	4				15: 1	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS

3/16/81

CYANAMID *** ANIMAL WEIGHTS(G)/OBSERVATIONS - RAW DATA FOR ARCHIVES *** STUDY NUMBER : 81011 PAGE 1
WILBUR G. MALCOLM TOXICOLOGY LABS. TECHNICIAN : JWH JWH
PEARL RIVER, NEW YORK TIME PERIOD : 0 1/2/81
CMPD: 11,716 SPECIES: GUINEA PIG STUDY TYPE: SENSITIZATION DATE DATA COLLECTED : 21-JAN-81

SAN	UAN	DOSE GROUP	BODY WEIGHT	OLD JAR	NEW JAR	TIME	CATEGORY	GRADE	OBSERVATIONS
1	54850	1				15: 3	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
3	54852	1				15: 3	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
5	54854	1				15: 3	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
7	54856	2				15: 3	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS

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SAN	UAN	DOSE GROUP	BODY WEIGHT	OLD JAR	NEW JAR	TIME	CATEGORY	GRADE	OBSERVATIONS
1	54850	1				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
2	54851	1				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
3	54852	1				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
4	54853	1				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
5	54854	1				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
6	54855	2				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
7	54856	2				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
8	54857	2				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
9	54858	2				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
10	54859	2				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
11	54860	3				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
12	54861	3				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
13	54862	3				8: 0	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
14	54863	3				8: 0	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
15	54864	3				8: 0	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
16	54865	4				8: 0	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
17	54866	4				8: 0	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
18	54867	4				8: 0	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
19	54868	4				8: 0	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
20	54869	4				8: 0	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS

3/16/81

1/22/81

CYANAMID *** ANIMAL WEIGHTS(G)/OBSERVATIONS - RAW DATA FOR ARCHIVES *** STUDY NUMBER : 81011 PAGE 1
WILBUR G. MALCOLM TOXICOLOGY LABS. TECHNICIAN : JWH
PEARL RIVER, NEW YORK TIME PERIOD : 2
CMPD: 11,716 SPECIES: GUINEA PIG STUDY TYPE: SENSITIZATION DATE DATA COLLECTED : 23-JAN-81

SAN	UAN	DOSE GROUP	BODY WEIGHT	OLD JAR	NEW JAR	TIME	CATEGORY	GRADE	OBSERVATIONS
1	54850	1				8:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
2	54851	1				8:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
3	54852	1				8:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
4	54853	1				8:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
5	54854	1				8:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
6	54855	2				8:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
7	54856	2				8:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
8	54857	2				8:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
9	54858	2				8:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
10	54859	2				8:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
11	54860	3				8:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
12	54861	3				8:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
13	54862	3				8:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
14	54863	3				8:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
15	54864	3				8:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
16	54865	4				8:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
17	54866	4				8:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
18	54867	4				8:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
19	54868	4				8:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
20	54869	4				8:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS

CYANAMID *** ANIMAL WEIGHTS(G)/OBSERVATIONS - RAW DATA FOR ARCHIVES *** STUDY NUMBER : 81011 PAGE 1
WILBUR G. MALCOLM TOXICOLOGY LABS. TECHNICIAN : JWH JWH
PEARL RIVER, NEW YORK TIME PERIOD : 1 1/2-1/81
CMPD: 11,716 SPECIES: GUINEA PIG STUDY TYPE: SENSITIZATION DATE DATA COLLECTED : 22-JAN-81

SAN	UAN	DOSE GROUP	BODY WEIGHT	OLD JAR	NEW JAR	TIME	CATEGORY	GRADE	OBSERVATIONS
1	54850	1				14:49	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
2	54851	1				14:49	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
3	54852	1				14:49	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
4	54853	1				14:49	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
5	54854	1				14:49	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
6	54855	2				14:49	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
7	54856	2				14:49	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
8	54857	2				14:49	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
9	54858	2				14:49	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
10	54859	2				14:49	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
11	54860	3				14:49	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
12	54861	3				14:49	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
13	54862	3				14:49	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
14	54863	3				14:49	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
15	54864	3				14:49	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
16	54865	4				14:49	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
17	54866	4				14:49	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
18	54867	4				14:49	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
19	54868	4				14:50	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
20	54869	4				14:50	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS

OSB 1/23/81

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CYANAMID *** ANIMAL WEIGHTS(G)/OBSERVATIONS - RAW DATA FOR ARCHIVES *** STUDY NUMBER : 81011 PAGE 1
WILBUR G. MALCOLM TOXICOLOGY LABS. TECHNICIAN : JWH JWH
PEARL RIVER, NEW YORK TIME PERIOD : 2 1/23/81
CMPD: 11,716 SPECIES: GUINEA PIG STUDY TYPE: SENSITIZATION DATE DATA COLLECTED : 23-JAN-81

SAN	UAN	DOSE GROUP	BODY WEIGHT	OLD JAR	NEW JAR	TIME	CATEGORY	GRADE	OBSERVATIONS
1	54850	1				15:26	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
2	54851	1				15:26	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
3	54852	1				15:26	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
4	54853	1				15:26	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
5	54854	1				15:26	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
6	54855	2				15:26	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
7	54856	2				15:26	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
8	54857	2				15:26	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
9	54858	2				15:26	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
10	54859	2				15:26	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
11	54860	3				15:26	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
12	54861	3				15:26	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
13	54862	3				15:26	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
14	54863	3				15:26	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
15	54864	3				15:26	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
16	54865	4				15:26	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
17	54866	4				15:26	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
18	54867	4				15:27	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
19	54868	4				15:27	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
20	54869	4				15:27	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS

3/16/81

CYANAMID *** ANIMAL WEIGHTS(G)/OBSERVATIONS - RAW DATA FOR ARCHIVES *** STUDY NUMBER : 81011 PAGE 1
WILBUR G. MALCOLM TOXICOLOGY LABS. TECHNICIAN : JWH JWH
PEARL RIVER, NEW YORK TIME PERIOD : 3 1/24/81
CMPD: 11,716 SPECIES: GUINEA PIG STUDY TYPE: SENSITIZATION DATE DATA COLLECTED : 24-JAN-81

SAN	UAN	DOSE GROUP	BODY WEIGHT	OLD JAR	NEW JAR	TIME	CATEGORY	GRADE	OBSERVATIONS
1	54850	1				8: 1	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
2	54851	1				8: 1	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
3	54852	1				8: 1	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
4	54853	1				8: 1	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
5	54854	1				8: 1	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
6	54855	2				8: 1	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
7	54856	2				8: 1	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
8	54857	2				8: 1	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
9	54858	2				8: 1	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
10	54859	2				8: 1	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
11	54860	3				8: 2	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
12	54861	3				8: 2	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
13	54862	3				8: 2	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
14	54863	3				8: 2	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
15	54864	3				8: 2	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
16	54865	4				8: 2	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
17	54866	4				8: 2	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
18	54867	4				8: 2	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
19	54868	4				8: 2	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
20	54869	4				8: 2	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS

CSB 1/26/81

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CYANAMID *** ANIMAL WEIGHTS(G)/OBSERVATIONS - RAW DATA FOR ARCHIVES *** STUDY NUMBER : 81011 PAGE 1
WILBUR G. MALCOLM TOXICOLOGY LABS. TECHNICIAN : JWH JWH
PEARL RIVER, NEW YORK TIME PERIOD : 3 1/24/81
CMPD: 11,716 SPECIES: GUINEA PIG STUDY TYPE: SENSITIZATION DATE DATA COLLECTED : 24-JAN-81

SAN	UAN	DOSE GROUP	BODY WEIGHT	OLD JAR	NEW JAR	TIME	CATEGORY	GRADE	OBSERVATIONS
1	54850	1				10:42	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
2	54851	1				10:42	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
3	54852	1				10:42	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
4	54853	1				10:42	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
5	54854	1				10:42	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
6	54855	2				10:42	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
7	54856	2				10:42	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
8	54857	2				10:42	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
9	54858	2				10:42	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
10	54859	2				10:43	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
11	54860	3				10:43	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
12	54861	3				10:43	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
13	54862	3				10:43	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
14	54863	3				10:43	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
15	54864	3				10:43	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
16	54865	4				10:43	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
17	54866	4				10:43	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
18	54867	4				10:43	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
19	54868	4				10:43	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
20	54869	4				10:43	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS

CBB 1/26/81

CYANAMID *** ANIMAL WEIGHTS(G)/OBSERVATIONS - RAW DATA FOR ARCHIVES *** STUDY NUMBER : 81011 PAGE 1
WILBUR G. MALCOLM TOXICOLOGY LABS. TECHNICIAN : JWH JWH
PEARL RIVER, NEW YORK TIME PERIOD : 4
CMPD: 11,716 SPECIES: GUINEA PIG STUDY TYPE: SENSITIZATION DATE DATA COLLECTED : 25-JAN-81 1/25/81

SAN	UAN	DOSE GROUP	BODY WEIGHT	OLD JAR	NEW JAR	TIME	CATEGORY	GRADE	OBSERVATIONS
1	54850	1			.	7:33	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
2	54851	1				7:33	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
3	54852	1				7:33	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
4	54853	1				7:33	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
5	54854	1				7:33	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
6	54855	2				7:33	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
7	54856	2				7:33	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
8	54857	2				7:33	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
9	54858	2				7:33	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
10	54859	2				7:33	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
11	54860	3				7:33	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
12	54861	3				7:33	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
13	54862	3				7:33	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
14	54863	3				7:33	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
15	54864	3				7:33	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
16	54865	4				7:33	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
17	54866	4				7:33	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
18	54867	4				7:33	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
19	54868	4				7:33	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
20	54869	4				7:33	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS

GOB 1/26/81

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CYANAMID *** ANIMAL WEIGHTS(G)/OBSERVATIONS - RAW DATA FOR ARCHIVES *** STUDY NUMBER : 81011 PAGE 1
WILBUR G. MALCOLM TOXICOLOGY LABS. TECHNICIAN : JWH JWH
PEARL RIVER, NEW YORK TIME PERIOD : 4
CMPD: 11,716 SPECIES: GUINEA PIG STUDY TYPE: SENSITIZATION DATE DATA COLLECTED : 25-JAN-81 1/25/81

SAN	UAN	DOSE GROUP	BODY WEIGHT	OLD JAR	NEW JAR	TIME	CATEGORY	GRADE	OBSERVATIONS
1	54850	1				10:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
2	54851	1				10:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
3	54852	1				10:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
4	54853	1				10:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
5	54854	1				10:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
6	54855	2				10:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
7	54856	2				10:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
8	54857	2				10:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
9	54858	2				10:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
10	54859	2				10:37	NORMAL	1.	NO SIGNIFICANT CLINICAL OBSERVATIONS
11	54860	3				10:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
12	54861	3				10:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
13	54862	3				10:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
14	54863	3				10:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
15	54864	3				10:37	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
16	54865	4				10:38	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
17	54866	4				10:38	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
18	54867	4				10:38	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
19	54868	4				10:38	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
20	54869	4				10:38	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS

KSD 1/26/81

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CYANAMID *** ANIMAL WEIGHTS(G)/OBSERVATIONS - RAW DATA FOR ARCHIVES *** STUDY NUMBER : 81011 PAGE 1
WILBUR G. MALCOLM TOXICOLOGY LABS. TECHNICIAN : JWH JWH
PEARL RIVER, NEW YORK TIME PERIOD : 5
CMPD: 11,716 SPECIES: GUINEA PIG STUDY TYPE: SENSITIZATION DATE DATA COLLECTED : 26-JAN-81 1/26/81

SAN	UAN	DOSE GROUP	BODY WEIGHT	OLD JAR	NEW JAR	TIME	CATEGORY	GRADE	OBSERVATIONS
1	54850	1				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
2	54851	1				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
3	54852	1				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
4	54853	1				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
5	54854	1				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
6	54855	2				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
7	54856	2				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
8	54857	2				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
9	54858	2				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
10	54859	2				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
11	54860	3				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
12	54861	3				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
13	54862	3				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
14	54863	3				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
15	54864	3				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
16	54865	4				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
17	54866	4				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
18	54867	4				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
19	54868	4				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
20	54869	4				7:59	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS

OSM 1/26/81

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CYANAMID *** ANIMAL WEIGHTS(G)/OBSERVATIONS - RAW DATA FOR ARCHIVES *** STUDY NUMBER : 81011 PAGE 1
WILBUR G. MALCOLM TOXICOLOGY LABS. TECHNICIAN : JWH JWH
PEARL RIVER, NEW YORK TIME PERIOD : 5 1/26/81
CMPD: 11,716 SPECIES: GUINEA PIG STUDY TYPE: SENSITIZATION DATE DATA COLLECTED : 26-JAN-81

SAN	UAN	DOSE GROUP	BODY WEIGHT	OLD JAR	NEW JAR	TIME	CATEGORY	GRADE	OBSERVATIONS
1	54850	1				14:49	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
2	54851	1				14:50	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
3	54852	1				14:50	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
4	54853	1				14:50	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
5	54854	1				14:50	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
6	54855	2				14:50	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
7	54856	2				14:50	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
8	54857	2				14:50	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
9	54858	2				14:50	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
10	54859	2				14:50	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
11	54860	3				14:50	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
12	54861	3				14:50	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
13	54862	3				14:50	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
14	54863	3				14:50	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
15	54864	3				14:50	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
16	54865	4				14:50	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
17	54866	4				14:50	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
18	54867	4				14:50	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
19	54868	4				14:50	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
20	54869	4				14:50	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS

CSB 1/26/81

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SAN	UAN	DOSE GROUP	BODY WEIGHT	OLD JAR	NEW JAR	TIME	CATEGORY	GRADE	OBSERVATIONS
1	54850	1				7:55	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
2	54851	1				7:55	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
3	54852	1				7:55	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
4	54853	1				7:55	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
5	54854	1				7:55	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
6	54855	2				7:55	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
7	54856	2				7:55	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
8	54857	2				7:55	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
9	54858	2				7:56	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
10	54859	2				7:56	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
11	54860	3				7:56	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
12	54861	3				7:56	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
13	54862	3				7:56	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
14	54863	3				7:56	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
15	54864	3				7:56	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
16	54865	4				7:56	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
17	54866	4				7:56	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
18	54867	4				7:56	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
19	54868	4				7:56	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
20	54869	4				7:56	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS

CKB 1/27/81

CYANAMID *** ANIMAL WEIGHTS(G)/OBSERVATIONS - RAW DATA FOR ARCHIVES *** STUDY NUMBER : 81011 PAGE 1
WILBUR G. MALCOLM TOXICOLOGY LABS. TECHNICIAN : JWH JWH
PEARL RIVER, NEW YORK TIME PERIOD : 6
CMPD: 11,716 SPECIES: GUINEA PIG STUDY TYPE: SENSITIZATION DATE DATA COLLECTED : 27-JAN-81 1/27/81

SAN	UAN	DOSE GROUP	BODY WEIGHT	OLD JAR	NEW JAR	TIME	CATEGORY	GRADE	OBSERVATIONS
1	54850	1				14:57	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
2	54851	1				14:57	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
3	54852	1				14:57	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
4	54853	1				14:57	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
5	54854	1				14:57	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
6	54855	2				14:57	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
7	54856	2				14:58	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
8	54857	2				14:58	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
9	54858	2				14:58	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
10	54859	2				14:58	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
11	54860	3				14:58	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
12	54861	3				14:58	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
13	54862	3				14:58	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
14	54863	3				14:58	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
15	54864	3				14:58	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
16	54865	4				14:58	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
17	54866	4				14:58	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
18	54867	4				14:58	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
19	54868	4				14:58	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
20	54869	4				14:58	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS

1/27/81

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CYANAMID *** ANIMAL WEIGHTS(G)/OBSERVATIONS - RAW DATA FOR ARCHIVES *** STUDY NUMBER : 81011 PAGE 1
WILBUR G. MALCOLM TOXICOLOGY LABS. TECHNICIAN : JWH JWH
PEARL RIVER, NEW YORK TIME PERIOD : 7 1/28/81
CMPD: 11,716 SPECIES: GUINEA PIG STUDY TYPE: SENSITIZATION DATE DATA COLLECTED : 28-JAN-81

SAN	UAN	DOSE GROUP	BODY WEIGHT	OLD JAR	NEW JAR	TIME	CATEGORY	GRADE	OBSERVATIONS
1	54850	1				7:36	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
2	54851	1				7:36	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
3	54852	1				7:36	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
4	54853	1				7:36	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
5	54854	1				7:36	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
6	54855	2				7:36	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
7	54856	2				7:36	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
8	54857	2				7:36	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
9	54858	2				7:36	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
10	54859	2				7:36	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
11	54860	3				7:36	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
12	54861	3				7:36	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
13	54862	3				7:36	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
14	54863	3				7:36	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
15	54864	3				7:36	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
16	54865	4				7:36	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
17	54866	4				7:36	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
18	54867	4				7:36	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
19	54868	4				7:36	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
20	54869	4				7:36	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS

CSP 1/28/81

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CYANAMID *** ANIMAL WEIGHTS(G)/OBSERVATIONS - RAW DATA FOR ARCHIVES *** STUDY NUMBER : 81011 PAGE 1
WILBUR G. MALCOLM TOXICOLOGY LABS. TECHNICIAN : JWH JWH 1/28/81
PEARL RIVER, NEW YORK TIME PERIOD : 7
CMPD: 11,716 SPECIES: GUINEA PIG STUDY TYPE: SENSITIZATION DATE DATA COLLECTED : 28-JAN-81

SAN	UAN	DOSE GROUP	BODY WEIGHT	OLD JAR	NEW JAR	TIME	CATEGORY	GRADE	OBSERVATIONS
1	54850	1				15:35	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
2	54851	1				15:35	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
3	54852	1				15:35	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
4	54853	1				15:35	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
5	54854	1				15:35	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
6	54855	2				15:35	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
7	54856	2				15:35	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
8	54857	2				15:35	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
9	54858	2				15:35	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
10	54859	2				15:35	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
11	54860	3				15:35	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
12	54861	3				15:35	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
13	54862	3				15:35	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
14	54863	3				15:35	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
15	54864	3				15:35	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
16	54865	4				15:35	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
17	54866	4				15:36	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
18	54867	4				15:36	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
19	54868	4				15:36	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
20	54869	4				15:36	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS

CSB 1/28/81

CYANAMID-MEDICAL RESEARCH DIV. *** ANIMAL WEIGHTS(6)/OBSERVATIONS - RAW DATA FOR ARCHIVES *** STUDY NUMBER : 81031 PAGE 1
TOXICOLOGY RESEARCH SECTION TECHNICIAN : JWH JWH
LEDERLE LABS - PEARL RIVER NY TIME PERIOD : B 1/23/81
CMPD: 11,716 SPECIES: GUINEA PIG STUDY TYPE: SENSITIZATION DATE DATA COLLECTED : 29-JAN-81

SAN	UAN	DOSE GROUP	BODY WEIGHT	OLD JAR	NEW JAR	TIME	CATEGORY	GRADE	OBSERVATIONS
1	54850	1				8:51	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
2	54851	1				8:52	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
3	54852	1				8:52	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
4	54853	1				8:52	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
5	54854	1				8:52	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
6	54855	2				8:52	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
7	54856	2				8:52	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
8	54857	2				8:52	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
9	54858	2				8:52	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
10	54859	2				8:52	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
11	54860	3				8:52	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
12	54861	3				8:52	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
13	54862	3				8:52	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
14	54863	3				8:52	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
15	54864	3				8:52	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
16	54865	4				8:52	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
17	54866	4				8:52	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
18	54867	4				8:52	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
19	54868	4				8:52	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
20	54869	4				8:52	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS

CSB 2/3/81

PEARL RIVER, NEW YORK
CMPD: 11,716

SPECIES: GUINEA PIG

STUDY TYPE: SENSITIZATION

DATE DATA COLLECTED : 30 JAN 81 - 7

SAN	UAN	DOSE GROUP	BODY WEIGHT	OLD JAR	NEW JAR	TIME	CATEGORY	GRADE	OBSERVATIONS
1	54850	1				9:44	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
2	54851	1				9:44	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
3	54852	1				9:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
4	54853	1				9:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
5	54854	1				9:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
6	54855	2				9:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
7	54856	2				9:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
8	54857	2				9:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
9	54858	2				9:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
10	54859	2				9:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
11	54860	3				9:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
12	54861	3				9:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
13	54862	3				9:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
14	54863	3				9:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
15	54864	3				9:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
16	54865	4				9:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
17	54866	4				9:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
18	54867	4				9:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
19	54868	4				9:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
20	54869	4				9:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS

CSB 2/3/81

WILBUR G. MALCOLM TOXICOLOGY LABS.
PEARL RIVER, NEW YORK

TIME PERIOD : 10
CMPD: 11,716 SPECIES: GUINEA PIG STUDY TYPE: SENSITIZATION DATE DATA COLLECTED : 31-JAN-81

SAN	UAN	DOSE GROUP	BODY WEIGHT	OLD JAR	NEW JAR	TIME	CATEGORY	GRADE	OBSERVATIONS
1	54850	1				7:42	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
2	54851	1				7:42	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
3	54852	1				7:42	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
4	54853	1				7:42	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
5	54854	1				7:42	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
6	54855	2				7:42	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
7	54856	2				7:43	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
8	54857	2				7:43	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
9	54858	2				7:43	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
10	54859	2				7:43	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
11	54860	3				7:43	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
12	54861	3				7:43	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
13	54862	3				7:43	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
14	54863	3				7:43	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
15	54864	3				7:43	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
16	54865	4				7:43	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
17	54866	4				7:43	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
18	54867	4				7:43	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
19	54868	4				7:43	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
20	54869	4				7:43	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS

CSD 2/4/81

CYANAMID-MEDICAL RESEARCH DIV. *** ANIMAL WEIGHTS(G)/OBSERVATIONS (KEYED) - RAW DATA FOR ARCHIVES **STUDY NUMBER : 81011 PAGE 1
TOXICOLOGY RESEARCH SECTION TECHNICIAN : PVD
LEDERLE LABS - PEARL RIVER NY DATE DATA ENTERED: 03-FEB-81 TIME PERIOD : 11
CNPD: 11,716 SPECIES: GUINEA PIG STUDY TYPE: SENSITIZATION DATE DATA COLLECTED : 1-FEB-81

NO.	BODY WEIGHT	OLD JAR	NEW JAR	CATEGORY	GRADE	OBSERVATIONS
1				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
2				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
3				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
4				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
5				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
6				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
7				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
8				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
9				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
10				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
11				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
12				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
13				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
14				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
15				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
16				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
17				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
18				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
19				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
20				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS

PVD

EB
2/6/81

2-1-81

TOXICOLOGY RESEARCH SECTION
LEDERLE LABS - PEARL RIVER NY
CMPD: 11,716

SPECIES: GUINEA PIG

STUDY TYPE: SENSITIZATION

NO.	BODY WEIGHT	OLD JAR	NEW JAR	CATEGORY	GRADE	OBSERVATIONS
1				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
2				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
3				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
4				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
5				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
6				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
7				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
8				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
9				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
10				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
11				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
12				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
13				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
14				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
15				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
16				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
17				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
18				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
19				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
20						

PJD

2-1-81

RB 2/5/81

CYANAMID-MEDICAL RESEARCH DIV. *** ANIMAL WEIGHTS/OBSERVATIONS ENTERED/ NEW DATA FOR ARCHIVES

TOXICOLOGY RESEARCH SECTION
LEDERLE LABS - PEARL RIVER NY

TECHNICIAN : JWH JWH
TIME PERIOD : 12 2/2/81
DATE DATA ENTERED: 2-FEB-81
DATE DATA COLLECTED : 2-FEB-81

CMPD: 11,716 SPECIES: GUINEA PIG STUDY TYPE: SENSITIZATION

NO.	BODY WEIGHT	OLD JAR	NEW JAR	CATEGORY	GRADE	OBSERVATIONS
1				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
2				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
3				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
4				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
5				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
6				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
7				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
8				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
9				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
10				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
11				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
12				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
13				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
14				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
15				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
16				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
17				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
18				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
19				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
20				NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS

CLP 2/4/81

99

CYANAMID-MEDICAL RESEARCH DIV. *** ANIMAL WEIGHTS(G)/OBSERVATIONS - RAW DATA FOR ARCHIVES *** STUDY NUMBER : 81011 PAGE 1
TOXICOLOGY RESEARCH SECTION TECHNICIAN : JWH 2/04/81
LEDERLE LABS - PEARL RIVER NY TIME PERIOD : 14
CMPD: 11,716 SPECIES: GUINEA PIG STUDY TYPE: SENSITIZATION DATE DATA COLLECTED : 04-FEB-81

SAN	UAN	DOSE GROUP	BODY WEIGHT	OLD JAR	NEW JAR	TIME	CATEGORY	GRADE	OBSERVATIONS
1	54850	1				7:44	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
2	54851	1				7:44	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
3	54852	1				7:44	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
4	54853	1				7:44	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
5	54854	1				7:44	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
6	54855	2				7:44	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
7	54856	2				7:44	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
8	54857	2				7:44	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
9	54858	2				7:44	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
10	54859	2				7:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
11	54860	3				7:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
12	54861	3				7:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
13	54862	3				7:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
14	54863	3				7:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
15	54864	3				7:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
16	54865	4				7:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
17	54866	4				7:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
18	54867	4				7:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
19	54868	4				7:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
20	54869	4				7:45	NORMAL	1	NO SIGNIFICANT CLINICAL OBSERVATIONS

3/6/81

2/11/81 JWH

** INDIVIDUAL PHYSICAL EXAMINATON FINDINGS 2/ 4/81- 2/ 4/81 **

DOSE GROUP	NO.	CATEGORY	DATE	TIME	OBSERVATIONS
1	1	NORMAL	2- 4-81	7:44	NO SIGNIFICANT CLINICAL OBSERVATIONS
			2- 4-81	15:30	NO SIGNIFICANT CLINICAL OBSERVATIONS
1	2	NORMAL	2- 4-81	7:44	NO SIGNIFICANT CLINICAL OBSERVATIONS
			2- 4-81	15:30	NO SIGNIFICANT CLINICAL OBSERVATIONS
1	3	NORMAL	2- 4-81	7:44	NO SIGNIFICANT CLINICAL OBSERVATIONS
			2- 4-81	15:30	NO SIGNIFICANT CLINICAL OBSERVATIONS
1	4	NORMAL	2- 4-81	7:44	NO SIGNIFICANT CLINICAL OBSERVATIONS
			2- 4-81	15:30	NO SIGNIFICANT CLINICAL OBSERVATIONS
1	5	NORMAL	2- 4-81	7:44	NO SIGNIFICANT CLINICAL OBSERVATIONS
			2- 4-81	15:30	NO SIGNIFICANT CLINICAL OBSERVATIONS
2	6	NORMAL	2- 4-81	7:44	NO SIGNIFICANT CLINICAL OBSERVATIONS
			2- 4-81	15:30	NO SIGNIFICANT CLINICAL OBSERVATIONS
2	7	NORMAL	2- 4-81	7:44	NO SIGNIFICANT CLINICAL OBSERVATIONS
			2- 4-81	15:30	NO SIGNIFICANT CLINICAL OBSERVATIONS
2	8	NORMAL	2- 4-81	7:44	NO SIGNIFICANT CLINICAL OBSERVATIONS
			2- 4-81	15:30	NO SIGNIFICANT CLINICAL OBSERVATIONS
2	9	NORMAL	2- 4-81	7:44	NO SIGNIFICANT CLINICAL OBSERVATIONS
			2- 4-81	15:30	NO SIGNIFICANT CLINICAL OBSERVATIONS
2	10	NORMAL	2- 4-81	7:45	NO SIGNIFICANT CLINICAL OBSERVATIONS
			2- 4-81	15:30	NO SIGNIFICANT CLINICAL OBSERVATIONS
3	11	NORMAL	2- 4-81	7:45	NO SIGNIFICANT CLINICAL OBSERVATIONS
			2- 4-81	15:30	NO SIGNIFICANT CLINICAL OBSERVATIONS
3	12	NORMAL	2- 4-81	7:45	NO SIGNIFICANT CLINICAL OBSERVATIONS
			2- 4-81	15:30	NO SIGNIFICANT CLINICAL OBSERVATIONS
3	13	NORMAL	2- 4-81	7:45	NO SIGNIFICANT CLINICAL OBSERVATIONS
			2- 4-81	15:30	NO SIGNIFICANT CLINICAL OBSERVATIONS
3	14	NORMAL	2- 4-81	7:45	NO SIGNIFICANT CLINICAL OBSERVATIONS
			2- 4-81	15:30	NO SIGNIFICANT CLINICAL OBSERVATIONS
3	15	NORMAL	2- 4-81	7:45	NO SIGNIFICANT CLINICAL OBSERVATIONS

P.M. Observation.
Replacement JWH

3/4/81

2/11/81 JWH

** INDIVIDUAL PHYSICAL EXAMINATON FINDINGS 2/ 4/81- 2/ 4/81 **

DOSE GROUP	NO.	CATEGORY	DATE	TIME	OBSERVATIONS
3	15	NORMAL	2- 4-81	15:30	NO SIGNIFICANT CLINICAL OBSERVATIONS
4	16	NORMAL	2- 4-81	7:45	NO SIGNIFICANT CLINICAL OBSERVATIONS
			2- 4-81	15:30	NO SIGNIFICANT CLINICAL OBSERVATIONS
4	17	NORMAL	2- 4-81	7:45	NO SIGNIFICANT CLINICAL OBSERVATIONS
			2- 4-81	15:30	NO SIGNIFICANT CLINICAL OBSERVATIONS
4	18	NORMAL	2- 4-81	7:45	NO SIGNIFICANT CLINICAL OBSERVATIONS
			2- 4-81	15:30	NO SIGNIFICANT CLINICAL OBSERVATIONS
4	19	NORMAL	2- 4-81	7:45	NO SIGNIFICANT CLINICAL OBSERVATIONS
			2- 4-81	15:30	NO SIGNIFICANT CLINICAL OBSERVATIONS
4	20	NORMAL	2- 4-81	7:45	NO SIGNIFICANT CLINICAL OBSERVATIONS
			2- 4-81	15:31	NO SIGNIFICANT CLINICAL OBSERVATIONS

P.M. Observation
Replacement JWH

3/6/81

18

Study 81010

		Day 1	Day 2
Animal 1	site 1	1	0
	2	1	1
	3	0	0
	4	1	1
	5	1	1
	6	1	1
Animal 2	site 1	1	0
	2	1	0
	3	0	0
	4	1	1
	5	1	1
	6	1	1
Animal 3	site 1	1	0
	2	1	1
	3	1	0
	4	1	1
	5	1	1
	6	1	1
Animal 4	site 1	1	0
	2	1	1
	3	0	0
	4	1	1
	5	1	1
	6	1	0
Animal 5	site 1	1	0
	2	1	1
	3	1	0
	4	1	1
	5	1	1
	6	1	1

CBB 1/20/81

CBB 1/21/81

CBB 1/21/81

Study 81011 (Induction) Dermal Scores

Site: #1

Animal	Day 1		2		6	8	9	15	16
	eryth.	edema	eryth.	edema	N.A.	N.A.	N.A.	N.A.	N.A.
1	1	0	0	0					
2	1	0	0	0					
3	1	0	0	0					
4	1	0	1	0					
5	1	0	0	0					
6	1+	0	1	1					
7	1+	0	1	0					
8	1+	1	1	1					
9	1	0	1	1					
10	1	1	1	0					
11	1	1	1	1					
12	1+	1+	1	1					
13	2	1+	1	1					
14	1	0	1	1					
15	1	1	1	1					
16	1	1	1	1					
17	1	1	1	1					
18	1	1+	1	1					
19	1	1+	1	1					
20	1	1+	1	1					
	CMB 1/22/81	CMB 1/22/81	CMB 1/22/81	CMB 1/22/81					

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CMB 3/4/81

81011

Dermal Scores

0.0 - vehicle

Day	1	2	6		7		8		9		15		16	
			ER	Ed	ER	Ed	ER	Ed	ER	Ed	ER	ED	ER	ED
	N.A.	N.A.	1	0	0	0					0	0	0	0
1			1	0	0	0					0	0	0	0
2			1	0	0	0					0	0	0	0
3			1	0	1	0					0	0	0	0
4			1	0	1	0					0	0	0	0
5			0	0	0	0					0	0	0	0
6			0	0	0	0					1	0	0	0
7			0	0	0	0					1	0	0	0
8			0	0	0	0					1	0	0	0
9			0	0	0	0					0	0	0	0
10			0	0	0	0					0	0	0	0
11			0	0	0	0					1	0	0	0
12			0	0	0	0					0	0	0	0
13			0	0	0	0					0	0	0	0
14			0	0	0	0					0	0	0	0
15			0	0	0	0					0	0	0	0
16			0	0	0	0					0	0	0	0
17			0	0	0	0					0	0	0	0
18			0	0	0	0					0	0	0	0
19			0	0	0	0					0	0	0	0
20			0	0	0	0					0	0	0	0

CSB 1/27/81 CSB 2/2/81 CSB 2/5/81 CSB 2/6/81 CSB 3/4/81

R 6603A - 1/77

81011

Mean Score[+] after Exposure to

Induction [TDI]	Response on Day	Challenge Dose Concentration* %					
		0	0.025	0.05	0.1	0.2	0.4
0*	1	.8	—	—	—	—	—
	2	.2	—	—	—	—	—
	6	.8	—	—	—	—	—
	7	.4	—	—	—	—	—
	15	0	.6	0	.6	.4	1.4
	16	0	.8	.6	.8	1.4	1.6
8	1	1.4	—	—	—	—	—
	2	1.6	—	—	—	—	—
	6	0	2.4	2	2.8	2.8	3.4
	7	0	1.4	1.4	1.4	2.2	2.4
	15	.6	1.6	1.8	2.4	3.6	3.2
	16	0	1.6	.8	1.6	3.2	2.8
20	1	2	—	—	—	—	—
	2	2	—	—	—	—	—
	6	0	2	1.6	2.8	3.2	3.4
	7	0	1.4	1.6	1.8	3.4	3
	15	2	1.6	2	2.8	4.6	4.2
	16	0	1.8	1.8	2	3.4	3
40	1	2	—	—	—	—	—
	2	2	—	—	—	—	—
	6	0	2.4	2	3.4	4	4.2
	7	0	1.6	1.4	1.8	3.2	2.8
	15	0	2	2.2	2.6	4.2	4
	16	0	1.8	1.4	2	3	2.8

+ MAXIMUM = 4 FOR ERY + ESC + 4 FOR EDEMA.

— NOT DONE

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3/16

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DRAFT CONFIDENTIAL RESEARCH REPORT

SENSITIZATION POTENTIAL OF INHALED TDI IN GUINEA PIGS

by

C. J. Collins, B.Tech.
C. Breckenridge, Ph.D.
P. Tellier, D.V.M., Dip.Path.
C. B. Bier, Ph.D.
B. E. Osborne, B.Sc., M.I.Biol., Ph.D.
B. G. Procter, D.V.M., M.Sc.
P. J. Araujo, B.Sc.

For: Cyanamid Canada Inc.
2255 Sheppard Avenue East
Willowdale, Ontario
M2J 4Y5

Project No.: 81194

Date: September 13, 1983

MONTREAL
87 Senneville Rd., Senneville, Quebec H9X 3R3, Canada
Tel: (514) 457-2280 Telex: 05-821582
Cable: BIOCAN

BIO-RESEARCH LABORATORIES LTD.

Please complete this form and return to
Mrs. B. J. Patterson
Bio-Research Laboratories Ltd.

THIS WILL ACKNOWLEDGE RECEIPT OF REPORT ENTITLED

SENSITIZATION POTENTIAL OF INHALED TDI IN GUINEA PIGS

Project No.: 81194

Report No.: _____

Date: September 13, 1983

Signed: _____

Date: _____

For: _____

MONTREAL
87 Senneville Rd., Senneville, Quebec H9X 3R3. Canada
Tel: (514) 457-2280 Telex: 05-821582
Cable: BIOCAN

BIO-RESEARCH LABORATORIES LTD.

PROJECT NO. 81194

SENSITIZATION POTENTIAL OF INHALED TDI IN GUINEA PIGS

This research was conducted at Bio-Research Laboratories under the direction of:

C. J. Collins, B.Tech.
Study Director

Date

With the participation of the following:

C. Breckenridge, Ph.D.
Head, Inhalation and Reproduction Toxicology

Date

P. Tellier, D.V.M., Dip.Path.
Staff Pathologist

Date

C. B. Bier, Ph.D.
Clinical Pathologist

Date

MONTREAL
87 Senneville Rd., Senneville, Quebec H9X 3R3, Canada
Tel: (514) 457-2280 Telex: 05-821582
Cable: BIOCAN

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PROJECT NO. 81194

SENSITIZATION POTENTIAL OF INHALED TDI IN GUINEA PIGS

B. E. Osborne, B.Sc., M.I.Biol., Ph.D.
Director of Toxicology Operations

Date

B. G. Procter, D.V.M., M.Sc.
Director of Toxicology Services

Date

P. J. Araujo, B.Sc.
Analytical Chemist

Date

MONTREAL
87 Senneville Rd., Senneville, Quebec H9X 3R3, Canada
Tel. (514) 457-2280 Telex: 05-821582
Cable: BIOCAN

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SUMMARY AND CONCLUSION

A group of 8 female English smooth-haired guinea pigs was exposed to TDI for 5 successive days, 3 h/day by inhalation at a target concentration of 4.23 ug/L of air. A control group was exposed to air alone.

The animals in both groups were challenged by inhalation during a 1-h exposure on days 18 and 19 of the study with TDI at a target concentration of 0.423 ug/L and again on days 25 to 27 with TDI-guinea pig serum albumin (TDI-GPSA) at a target concentration of 0.015 to 0.020 mg/L. The pulmonary response of the animals to challenge was monitored by recording respiratory rates during and following challenge.

The animals were challenged topically with TDI and TDI-GPSA on day 28 and the skin response was assessed after 24 and 48 hours.

Clinical signs and body weights were recorded during the study, and necropsies were conducted on animals that died or were sacrificed. Blood samples were taken at intervals for the measurement of antibody titers and for the preparation of differential blood smears.

Evidence of skin sensitization, as demonstrated by an erythemal response to intradermal TDI-GPSA, was observed in 7 animals in the TDI group. There was evidence of skin sensitization in 1 control animal.

Evidence of pulmonary sensitization, as demonstrated by an increase in respiratory rate following challenge with TDI-GPSA, was observed in 3 animals in the TDI group.

The evidence of sensitization in the TDI group correlated with the presence of serum antibody in the test but not the control group.

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INTRODUCTION

This study was performed in order to assess the sensitization potential of TDI (toluene diisocyanate) when administered by the inhalation route and challenged by the inhalation and topical routes in the guinea pig.

The study was performed at Bio-Research Laboratories Ltd., Senneville, Quebec. The first exposure to TDI took place on June 19, 1983, and the last necropsy was conducted on July 21, 1983. Data, the final report and any specimens or samples are retained in the scientific archives of Bio-Research Laboratories Ltd.

EXPERIMENTAL PROCEDURES

1. Test Article

The test article was received from American Cyanamid Co., Stamford, Connecticut, on April 22, 1983. Approximately 1 quart of test article was received in 2 1-pint glass containers. An additional 2 L of test article were received in 4 1-pint glass containers on June 10, 1983. The latter sample was used in the main study and was labeled 80/20 TDI (Toluene Diisocyanate) Poison B. UN 2078 and was a pale yellow liquid.

The test article was stored at room temperature, out of direct light.

2. Test System

Thirty-six female English smooth-haired guinea pigs (Cavia porcellus) approximately 4-5 weeks old, ordered in the weight range 250-300 g, were received from Hilltop Laboratory Animals, Scottdale, Pennsylvania, on April 22, 1983. Subsequent to arrival, the animals were examined by a veterinary aide.

Eight animals were randomly allocated to each test group, permanently identified by ear mark and housed individually in shoebox-type cages. Laboratory guinea pig diet (Purina Guinea Pig Chow No. 5025) and tap water were provided ad libitum except during the inhalation exposure. None of the contaminants known to be present in either the food or the water was present in quantities which could reasonably be expected to interfere with the purpose or quality of this research.

Two groups of females were identified and treated as follows:

Group		Target Chamber Concentrations	Antigenic Challenges Target Chamber Concentrations I (days 18 and 19)	II (days 25 to 27)	Animal Nos.
1	Air control	-	TDI, 0.06 ppm 0.423 ug/L	TDI-GPSA 0.015-0.020 mg/L	151-158
2	TDI	TDI, 0.6 ppm, 4.23 ug/L	TDI, 0.06 ppm 0.423 ug/L	TDI-GPSA 0.015-0.020 mg/L	251-258

3. Inhalation Exposure Equipment

Individual 4-L metal and glass exposure chambers were used for the sensitization exposures and for the challenge exposures on days 18 and 19.

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Airflow through each 4-L whole-body chamber was maintained at 10 L/min by adjusting the needle valve between the exposure chamber and the generation system, which was maintained at positive pressure. The high ventilation rate was used because unstable chamber concentrations had been observed previously at lower ventilation rates.

On study days 18 and 19, the 6 mm I.D. tube on the outlet of the chamber was replaced by a tube approximately 30 cm long and 3 mm I.D. The increased resistance provided by this tube permitted the pressure fluctuations generated by each animal to be monitored and, incidentally, increased the small positive pressure within each chamber.

A single nose-only rodent exposure unit with overall dimensions of 40 cm high, 30 cm wide and 12 cm deep (chamber volume equal to approximately 10 L) was utilized in the challenge exposures on days 25 to 27. This chamber was designed such that 4 plexiglas cones (approximately 3-inch diameter) could be inserted into the exposure manifold. The cones which served to restrain the individual guinea pigs were constructed so as to allow the animals to breathe the atmosphere containing the test article within the chamber without otherwise coming into contact with the material.

Airflow through the 10-L chamber was set at 17 L/min and was measured in the exhaust line by means of a ball-type flowmeter. A slight negative pressure within the chamber with respect to the room atmosphere was maintained.

Temperature and relative humidity in the exposure chambers were monitored at intervals during exposures by means of sensors located inside the chamber. Decontamination of chamber air was accomplished by passing the air through an activated charcoal filter prior to eliminating it from the facility.

Generation of Test Atmospheres

Vapors of TDI were generated on study days 1 to 5, 18 and 19 using a glass bubbler containing approximately 100 mL of TDI and fitted with a sintered glass frit. Predried compressed air was further dessicated by passage through a column containing Drierite^{R} prior to passage through the generator. The output from the generator was diluted with at least 40 L/min predried compressed air prior to passing into a manifold supplying the 4-L chambers. Chamber concentration could be adjusted by changing the airflow through the bubbler.

Aerosols of TDI-GPSA were generated using a Pitt No. 1 glass nebulizer. Compressed air to operate the atomizer was supplied by a Sihi air compressor, and the air was pre-dried in Hankinson's refrigerated air dryers prior to passage through the aerosol generator.

An aerosol of the TDI-GPSA complex was generated vertically into the chamber using a 1% solution of TDI-GPSA in distilled water. A drop of pH 7.5 phosphate buffer was added to the mixture in order to ensure that the TDI-GPSA dissolved. The concentration of test article was controlled by adjusting the rate of liquid flow of test article which was delivered by a syringe pump to the nebulizer. Make-up air not provided by the compressed air line was conditioned room air.

5. Sensitization Procedures

Each guinea pig in Groups 1 and 2 was exposed for 3 h on study days 1 to 5 to a vapor of TDI at target concentrations of 4.23 ug/L.

The group size (8 animals) exceeded the number of animals which could be monitored simultaneously using the respiratory monitoring equipment. Each group of animals was therefore divided into 2 subgroups, Subgroup A and Subgroup B, each consisting of 4 animals. The start of the study was offset for the 2 subgroups across 3 days, but each animal received the same number of exposures on the appropriate study days.

6. Challenge Procedures

On days 18 and 19 of the study, animals in both groups were exposed to a vapor of TDI (antigenic challenge I) at a target concentration of 0.423 ug/L for a 75-min period.

On study days 25-27, animals in both groups were exposed to an aerosol of TDI-GPSA complex (antigenic challenge II) at a target gravimetric concentration of 0.015 to 0.020 mg/L for a 20-min period. This exposure was, however, preceded by a 20-min exposure to GPSA alone at the same concentration and followed by a 15-min clearance period. This exposure was to ensure the animals did not respond to GPSA alone.

7. Exposure Procedure

On study days 1 to 5, the animals were loaded individually into the 4-L chambers together with a small quantity of bedding to absorb urine and feces.

Pressure changes in the cone due to animal respiration were amplified with a Grass DC amplifier and recorded on the chart of a 4-channel polygraph.

On study days 25 to 27 the respiratory rate was measured for each guinea pig for each minute during the last 10 minutes pre-exposure and during each exposure. Mean and standard deviation values were calculated. Additionally, for each minute of each exposure on days 25 to 27, 3-min moving averages of the respiratory rates were calculated as percentages of the pre-exposure mean value for each animal. The pre-exposure mean value was calculated from the 5 values (minute minus 6 to minute minus 2) pre-exposure. The value at minute minus 1 pre-exposure was excluded in order to avoid any disturbances associated with the start of exposure.

13. Skin Sensitization Studies

On study day 28 the following procedures were carried out for all animals.

(a) Preparation of Test System

Prior to test article application, the hair on the dorsal surface of all animals was removed by shaving.

(b) Test Article Preparation

TDI was mixed with acetone on a weight/volume basis to give either a 0.1% or a 0.01% concentration. Acetone was used as the vehicle control.

TDI-GPSA was dissolved in sterile saline on a weight/volume basis to give either a 0.1% or a 0.01% concentration. A drop of phosphate buffer pH 7.5 had been added to the mixture to ensure that the TDI-GPSA dissolved. GPSA alone, dissolved in the same way, at a concentration of 0.1% was used as the vehicle control.

(c) Dosing (Challenge)

The dose volume was 100 u' administered topically in the case of TDI onto 2.5 cm diameter nonoccluded sites and intradermally in the case of TDI-GPSA.

(d) Dose Frequency

Each animal received 1 challenge dose at each concentration.

(e) Route of Administration

The dermal route was selected in keeping with the purpose of the research.

(f) Test System Observations Following Test Article Administration

Approximately 1 h after removing the hair by shaving, the animals were challenged with topical application of 2 doses of TDI and 1 vehicle control dose of acetone and an intradermal injection of 2 doses of TDI-GPSA and 1 of GPSA. Each dose was administered at a different site.

Observations of irritation were made according to the method of Draize, J.H., et al., J. Pharmacol. Exp. Ther. 83:377, 1944, at 24 and 48 hours following the application.

Individual scoring results are listed in Tables 16 and 17.

14. Gross Pathology

All surviving animals were killed on day 30 of the study. They were then subjected to necropsy, and lungs were weighed and preserved by infusion with the fixative. The skin including the topical sites was preserved in 10% neutral buffered formalin.

RESULTS

1. Preliminary Particle Size Analysis of Ovalbumin Atmospheres

The particle size analysis of an ovalbumin atmosphere (of similar molecular weight to the TDI-GPSA used in the study), generated under the same experimental conditions, gave the following distribution:

Effective Cut-off Diameter (um)	Cumulative Percentage Mass Less Than Size Range
9.0	95.4
5.8	89.8
4.7	78.9
3.3	67.4
2.1	42.1
1.1	24.6
0.7	5.6
0.4	0.0

The mass median diameter and its geometric standard deviation were calculated to be 1.5 um and 2.8 respectively.

2. Chamber Conditions

The nominal and analytical concentrations are presented in Tables 2 to 5 for the exposures to TDI and in Tables 6 and 7 for the challenge exposures to TDI-GPSA.

Chamber concentrations during the exposure of Group 2 to TDI on study days 1-5 were considered to be satisfactory in view of the chemical instability of TDI vapor in the presence of water vapor. A tendency towards low concentration on the first day of exposure was observed. Higher concentrations were observed on subsequent days, and reductions in air flow through the TDI generator were necessary in order to maintain the concentration within satisfactory limits.

Chamber concentrations for subgroups 1A and 2A were below the target concentration on study day 18 but were satisfactory on study day 19. Chamber concentrations for subgroups 1B and 2B on study days 18 and 19 were deliberately increased above the original target concentrations in order to achieve the maximum concentration which did not produce marked respiratory depression.

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Marked variability in nominal concentration was observed and was considered to be attributable to the error in measuring the small weight losses from the relatively heavy generation system.

Chamber concentrations during the GPSA and TDI-GPSA challenges of Groups 1 and 2 were generally close to the target range, although occasional low values were observed. A low value for the TDI-GPSA exposure of subgroup 2A on study day 25 was observed but not considered to be necessarily representative of the chamber concentration as this exposure had been preceded by other exposures that day, under the same generator conditions, in which satisfactory gravimetric concentrations had been demonstrated.

Chamber temperature and humidity data during the exposures are presented in Appendices 2 to 5 and were within acceptable ranges. The low observed relative humidity during exposure to TDI was to be anticipated as all the air supply was predried compressed air.

3. Clinical Signs

Loss of condition was observed in animal 155 beginning during the second week of the study. This change was considered unlikely to be related to the experimental procedures.

Lethargy and apparently slightly depressed respiration were observed during the exposures to TDI on study days 1 to 5, 18 and 19. Coughing was occasionally observed on study days 4 and 5 in animal 251.

There were no other treatment-related clinical abnormalities.

4. Body Weights

Individual and group mean body weights are presented in Tables 8 and 9.

Animal 155 was the lightest of all the animals and showed a marked body weight loss between days 15 and 22. These changes were considered unlikely to be related to the experimental procedures (see Clinical Signs).

Body weight gains in the remaining animals were satisfactory.

5. Respiratory Rates

The results of the measurement on study days 25-27 of respiratory rates of individual animals for each minute of exposure, and for 10 minutes pre-exposure, are presented in Appendices 6 to 11. The 3-minute moving averages presented as percentages of the pre-exposure mean values are presented in Tables 10 to 15.

There were no changes in respiratory rate on study days 18 and 19 suggestive of a sensitization response. Respiratory rate data for these days have not therefore been presented.

Increases in respiratory rate indicative of a sensitization response during challenge with TDI-GPSA were observed in animals 251 and 252 (Group 2 - TDI) on study days 25 and 26 and in animal 257 on study day 25 (Tables 13 and 14). Animal 251 had shown a transient increase in respiratory rate during challenge with GPSA alone on day 25. Animal 257 showed a similar transient increase with GPSA alone on day 27 (Table 15).

The only other increase in respiratory rate worthy of comment was a sustained increase in animal 153 (air control) on day 27 during challenge with GPSA, and with TDI-GPSA (Table 12). This animal had a low pre-exposure respiratory rate on that day, resulting in the numerically large size of the increases observed. This animal did not exhibit similar changes on days 25 and 26.

6. Skin Sensitization Studies

The individual skin scores are presented in Tables 16 and 17.

The animals sensitized were as follows:

Group No.	Animals Sensitized	Percentage Sensitized	Allergenic Potential
1	158	13	Mild
2	251, 252, 253, 254, 255, 257, 258	88	Extreme

7. Differential White Cell Counts

The results of the differential white cell counts are presented in Tables 18 to 21.

There were no treatment-related changes.

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8. Gross Pathology

The results of the gross pathology examinations are presented in Appendix 14. The pathologist's report is presented in Appendix 15.

There were no treatment-related changes.

9. Lung Weights

Individual absolute and relative lung weights are presented in Appendices 12 and 13. Group mean values are presented in Tables 22 and 23.

There were no treatment-related effects revealed in the lung weight data.

DISCUSSION

Unpublished studies in this laboratory and the published work of Karol et al. (References 2-4) have indicated that a pulmonary response in sensitized guinea pigs typically consists of an increase in respiratory rate and, in highly sensitized animals, is often accompanied by characteristic changes in breathing pattern. The work of Karol et al. indicates that the response to an isocyanate-protein complex is rapid, occurring almost immediately after the start of challenge, and an incidence of 40% responders following a suitable regime of sensitization exposure to TDI has been reported.

The incidence of responders (3/8) in this study was similar to that of Karol et al. The response was, however, less intense.

Animals 251, 252 and 257, which showed a pulmonary response, were also positive for the skin sensitization and serum antibody studies. Animals 253 and 255 were positive for both skin sensitization and serum antibody. Animals 254 and 258 were positive for skin alone. Animal 256 was positive for antibody alone.

REFERENCES

1. NIOSH Manual of Analytical Methods, Vol. 1, Second Edition.

2. Karol, M.H., Dixon, C., Brady, M., and Alarie, Y. (1980). Immunologic Sensitization and Pulmonary Hypersensitivity by Repeated Inhalation of Aromatic Isocyanates. Toxicol. Appl. Pharmacol. 53, 260-270.

3. Karol, M.H. (1983). Concentration-Dependent Immunological Response to Toluene Diisocyanate (TDI) Following Inhalation Exposure. Toxicol. Appl. Pharmacol. 68.

4. Karol, M.H., and Magreni, C. (1982). Extensive Skin Sensitization with Minimal Antibody Production in Guinea Pigs as a Result of Exposure to Dicyclohexylmethane-4,4'-diisocyanate. Toxicol. Appl. Pharmacol. 65, 291-301.

TABLE NO. 1 TIME NOTATION SYSTEM PROJECT NO. 81194

Event	Subgroup A Calendar Date	Subgroup B Calendar Date
Study Day 1 First Day of Inhalation Sensitization Exposure	June 19	June 22
Study Day 5 Day 5 of Inhalation Sensitization Exposures	June 23	June 26
Study Day 18 First Challenge Exposure to TDI	July 6	July 9
Study Day 19 Last Challenge Exposure to TDI	July 7	July 10
Study Day 25 First Challenge Exposure to TDI-GPSA	July 13	July 16
Study Day 27 Last Challenge Exposure to TDI-GPSA	July 15	July 18
Study Day 28 Topical Skin Challenge	July 16	July 19
Study Day 30 Terminal Necropsy	July 18	July 21

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TABLE NO. 2 TDI CHAMBER CONCENTRATIONS (UG/L) PROJECT NO. 81194

GROUP 1A

EXPOSURE DAY	TREATMENT TIME (MINUTES) 50	100	150	170	MEAN	S.D.	NOMINAL CONCENTRATION (UG/L)
18	0.35	0.16	0.26	0.32	0.27	0.08	6.7
19	0.38	0.24	0.32	*	0.31	0.07	6.6

* Sampling error suspected - value excluded

TABLE NO. 3 TDI CHAMBER CONCENTRATIONS (UG/L) PROJECT NO. 81194

GROUP 1B

EXPOSURE DAY	TREATMENT TIME (MINUTES) 50	100	150	170	MEAN	S.D.	NOMINAL CONCENTRATION (UG/L)
18	0.85	0.84	0.40#	0.79	0.83	0.03	3.3
19	.93	1.00	1.02	0.65	0.90	0.17	16.3

Sampling problem - excluded from mean

#2

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TABLE NO. 4 TDI CHAMBER CONCENTRATIONS (UG/L) PROJECT NO. 81194

GROUP 2A

STUDY DAY	TREATMENT TIME (MINUTES) 50	100	150	170	MEAN	S.D.	NOMINAL CONCENTRATION (UG/L)
1	2.34	2.93	3.18	2.34	2.70	0.43	10.53
2	3.65	3.80	4.40	4.03	3.97	0.33	13.1
3	4.30	4.85	5.55	7.45	5.54	1.37	13.03
4	4.28	4.13	4.08	4.10	4.15	0.09	13.16
5	4.58	4.88	4.60	*	4.69	0.17	13.16
18	0.39	0.21	0.19	0.09	0.22	0.12	6.8
19	0.43	0.20	0.48	0.33	0.36	0.12	6.6

* Missing observation

TABLE NO. 5 TDI CHAMBER CONCENTRATIONS (UG/L) PROJECT NO. 81194

GROUP 2B

STUDY DAY	TREATMENT TIME (MINUTES) 50	100	150	170	MEAN	S.D.	NOMINAL CONCENTRATION (UG/L)
1	3.73	4.00	3.98	3.40	3.78	0.28	14.41
2	5.23	4.90	5.90	4.78	5.20	0.50	10.53
3	6.45	4.13	5.65	5.43	5.42	0.96	18.43
4	6.20	5.25	6.08	6.95	6.12	0.70	10.56
5	5.28	6.64	6.48	7.03	6.36	0.75	11.88
18	0.97	0.94	1.15	0.77	0.96	0.16	3.3
19	1.02	1.13	1.26	0.91	1.08	0.15	3.3

#2

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TABLE NO. 6

GPSA AND TDI-GPSA EXPOSURE CONCENTRATIONS (MG/L) - GROUP 1

PROJECT NO. 81194

STUDY DAY	TEST ARTICLE	SUBGROUP A CONCENTRATION GRAVIMETRIC 1	GRAVIMETRIC 2	NOMINAL*	SUBGROUP B CONCENTRATION GRAVIMETRIC 1	GRAVIMETRIC 2	NOMINAL*
25	GPSA	0.018	0.013	5.26	**	0.018	6.21
	TDI-GPSA	0.017	0.014	**	0.017	0.017	8.32
26	GPSA	0.025	0.018	5.53	0.018	0.018	7.18
	TDI-GPSA	0.024	0.022	5.29	0.018	0.018	6.74
27	GPSA	0.020	0.020	6.79	0.017	0.019	6.88
	TDI-GPSA	0.018	0.022	6.94	0.018	0.018	7.00

*Expressed in terms of the formulated 1% solution used
**Missing observation

TABLE NO. 7

GPSA AND TDI-GPSA EXPOSURE CONCENTRATIONS (MG/L) - GROUP 2

PROJECT NO. 81194

STUDY DAY	TEST ARTICLE	SUBGROUP A CONCENTRATION GRAVIMETRIC 1	SUBGROUP A CONCENTRATION GRAVIMETRIC 2	SUBGROUP A CONCENTRATION NOMINAL*	SUBGROUP B CONCENTRATION GRAVIMETRIC 1	SUBGROUP B CONCENTRATION GRAVIMETRIC 2	SUBGROUP B CONCENTRATION NOMINAL*
25	GPSA	0.017	0.013	5.85	0.017	0.020	7.15
	TDI-GPSA	0.007	**	4.06	0.010	0.020	6.44
26	GPSA	0.023	0.010	6.79	0.023	0.020	7.41
	TDI-GPSA	0.019	0.022	6.59	0.020	0.018	7.38
27	GPSA	0.021	0.023	8.35	0.018	0.019	5.76
	TDI-GPSA	0.020	0.021	7.09	0.020	0.018	7.68

*Expressed in terms of the formulated 1% solution used
**Missing observation

#2

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TABLE NO. 8 INDIVIDUAL BODY WEIGHTS (G)
PROJECT NO.: 81194

ANIMAL NO. / STUDY DAY	1	8	15	22	29
FEMALES GROUP 1 AIR CONTROL					
151	563	571	634	641	645
152	520	547	591	626	622
153	464	500	511	537	537
154	586	601	649	654	665
155	404	445	462	408	430
156	510	538	571	590	572
157	543	582	588	603	585
158	482	529	546	563	537
MEAN	509.0	539.1	569.0	578.8	574.1
S.D.	58.4	49.6	61.9	79.2	74.9
N	8	8	8	8	8

Evaporate toluene to dryness
HPLC. Methylene chloride.
linear sorbent programme.

Analytical Chemistry 48(3) 497 March 76
TDI .02 ppb in 20 L sample.

Now .6 ppm v/v TDI = 4.23 ug/L air.
UV - visible

Wallace 502-588-5351

TDI	pre	15	22	30
151	IGG1 2			
2	–			
3				
4		Within	control	
5		.1		
6				
7				
8				

probably respiratory

Skin ~~IGG~~ neither topical TDI

.2 is +ve

251	.09	.11	.4	.2	.35	.27	.8	
2	.11	.13	.43	.26	.48	.19	.39	
3	.08	.21	.25	.21	.31	.22	.33	
4	.09	.14	low					
5	.10	.12	.35	.18	.57	.15	.61	
6	.1	.12	.16	.14	.38	.13	.32	
7	.08	.14	.41	*	.68	.25	.55	
8	.09	.13	.11	.08	.16	.07	.13	

Skin neither
10 cellular
T-cell

* missing

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TABLE NO. 9
PROJECT NO.: 81194

INDIVIDUAL BODY WEIGHTS (G)

ANIMAL NO. / STUDY DAY	1	8	15	22	29
FEMALES GROUP 2 TDI					
251	553	484	503	601	594
252	455	565	555	513	516
253	476	493	489	519	515
254	623	659	668	675	667
255	488	533	550	554	534
256	532	571	595	570	605
257	495	505	541	546	545
258	485	542	549	571	575
MEAN	513.4	544.0	556.3	568.6	568.9
S.D.	54.2	56.4	55.6	51.6	52.2
N	8	8	8	8	8

TABLE NO. 10 RESPIRATORY RATE PROJECT NO. 81194
(3-MINUTE MOVING AVERAGE AS % OF PRE-EXPOSURE MEAN)

GROUP 1 - AIR CONTROL
STUDY DAY 25

TIME AFTER START OF EXPOSURE (MINUTES)		ANIMAL NO. 151	152	153	154	155	156	157	158
Exposure to GPSA	2	107	96	106	102	101	92	90	95
	3	105	98	108	104	101	89	91	104
	4	97	98	112	100	91	88	92	108
	5	99	98	112	100	97	91	85	111
	6	101	98	117	102	97	100	80	102
	7	113	101	111	107	95	105	79	101
	8	110	101	113	109	95	104	82	105
	9	119	104	111	112	96	101	78	107
	10	110	96	111	112	102	103	78	*
	11	116	94	108	112	103	108	79	*
	12	107	86	108	107	101	106	83	*
	13	109	88	108	102	96	106	91	104
	14	104	91	108	102	90	103	89	104
	15	104	93	106	105	92	107	87	104
	16	107	99	103	107	91	104	77	106
	17	109	99	99	107	92	102	75	106
	18	112	101	99	107	89	100	72	111
	19	109	98	99	107	92	101	73	110
Exposure to TDI-GPSA	2	110	96	110	115	92	110	97	113
	3	102	96	110	117	90	107	102	102
	4	107	93	116	119	89	107	100	105
	5	107	90	99	102	89	108	98	107
	6	115	90	103	104	97	105	93	108
	7	118	90	112	104	108	104	98	107
	8	115	88	114	110	110	108	100	112
	9	115	88	117	107	102	111	100	111
	10	112	91	111	110	89	112	97	109
	11	112	93	108	104	89	107	91	101
	12	109	93	103	107	95	104	95	101
	13	112	93	103	102	99	101	95	100
	14	112	96	101	105	103	101	96	99
	15	107	96	101	102	*	104	95	103
	16	104	93	97	107	*	107	92	102
	17	104	90	101	102	*	107	85	101
	18	109	88	110	97	*	108	86	94
	19	106	88	114	94	89	108	91	96
Pre-exposure mean respiratory rate used to calculate the above percentages		106	127	99	98	104	122	128	114

*Not calculable
#5

TABLE NO. 11 RESPIRATORY RATE PROJECT NO. 81194
(3-MINUTE MOVING AVERAGE AS % OF PRE-EXPOSURE MEAN)

GROUP 1 - AIR CONTROL
STUDY DAY 26

TIME AFTER START OF EXPOSURE (MINUTES)		ANIMAL NO. 151	152	153	154	155	156	157	158
Exposure to GPSA	2	111	101	88	115	99	103	110	117
	3	113	102	90	117	94	102	111	109
	4	112	101	91	120	95	103	113	106
	5	108	100	92	122	95	102	116	106
	6	106	97	93	118	101	106	118	114
	7	105	100	97	115	102	109	127	115
	8	106	101	100	115	102	111	139	122
	9	114	102	103	115	100	113	136	119
	10	113	102	99	116	100	113	130	118
	11	114	101	93	115	103	114	122	115
	12	108	101	91	113	109	114	122	114
	13	109	100	90	110	108	116	119	112
	14	105	100	88	110	108	120	115	106
	15	102	100	92	110	105	118	110	106
	16	100	100	89	112	108	116	131	112
	17	101	98	93	110	106	114	129	111
	18	102	100	87	110	110	113	137	113
	19	104	103	88	109	109	107	128	106
Exposure to TDI-GPSA	2	111	104	93	109	*	102	116	108
	3	118	111	96	103	110	106	114	103
	4	121	108	95	109	104	105	111	103
	5	124	110	99	109	119	103	108	101
	6	117	101	110	109	123	103	111	102
	7	115	100	110	109	119	103	114	101
	8	118	98	105	106	101	103	116	103
	9	121	98	96	110	95	100	120	101
	10	117	100	96	108	93	108	124	104
	11	118	100	95	106	92	113	124	108
	12	110	101	91	102	94	118	124	115
	13	107	102	92	103	*	123	122	117
	14	99	102	96	104	*	125	125	118
	15	101	104	95	107	*	121	119	114
	16	101	105	93	109	*	107	113	108
	17	116	105	92	109	97	99	106	102
	18	116	107	95	107	108	99	107	101
	19	116	107	94	110	113	103	106	108
Pre-exposure mean respiratory rate used to calculate the above percentages		104	127	127	110	102	123	111	110

*Not calculable
#5

TABLE NO. 12 RESPIRATORY RATE PROJECT NO. 81194
(3-MINUTE MOVING AVERAGE AS % OF PRE-EXPOSURE MEAN)

GROUP 1 - AIR CONTROL
STUDY DAY 27

TIME AFTER START OF EXPOSURE (MINUTES)		ANIMAL NO. 151	152	153	154	155	156	157	158
Exposure to GPSA	2	118	121	115	111	90	105	124	112
	3	123	137	125	112	95	102	119	109
	4	121	131	124	114	101	107	118	106
	5	120	126	127	115	105	113	116	103
	6	124	112	139	115	101	116	123	103
	7	125	113	154	115	98	108	122	102
	8	127	119	172	120	94	107	114	105
	9	125	128	172	130	94	108	114	103
	10	117	132	154	127	92	112	125	107
	11	117	132	141	122	92	109	134	103
	12	108	121	131	114	93	113	126	106
	13	108	116	139	115	99	125	119	104
	14	104	110	139	115	99	136	109	107
	15	104	117	143	115	105	132	103	106
	16	105	117	139	117	101	116	102	104
	17	96	115	139	119	100	105	109	100
	18	90	115	131	117	94	103	114	100
	19	87	120	131	115	98	103	112	100
Exposure to TDI-GPSA	2	115	113	129	115	111	109	116	108
	3	114	116	135	117	100	111	119	99
	4	108	115	135	117	90	112	116	100
	5	102	113	141	115	96	119	114	97
	6	102	117	139	112	101	119	113	98
	7	100	123	139	112	103	121	113	99
	8	101	130	133	111	100	116	113	103
	9	101	126	121	108	95	121	111	104
	10	110	122	114	107	91	124	117	99
	11	118	116	105	105	83	131	122	99
	12	126	113	110	109	86	124	122	97
	13	126	106	111	108	91	117	115	100
	14	123	105	116	111	94	111	110	98
	15	114	108	118	113	93	112	108	97
	16	107	112	118	119	89	112	112	94
	17	102	113	136	120	85	114	*	92
	18	102	115	147	120	82	110	*	90
	19	108	118	151	115	85	111	*	88
Pre-exposure mean respiratory rate used to calculate the above percentages		104	110	87	105	118	113	105	115

* - Not calculable

BIO

M-TMU came as liquid; now is a solid.

TABLE NO. 13 RESPIRATORY RATE . PROJECT NO. 81194
(3-MINUTE MOVING AVERAGE AS % OF PRE-EXPOSURE MEAN)

GROUP 2 - TDI
STUDY DAY 25

TIME AFTER START OF EXPOSURE (MINUTES)		ANIMAL NO. 251	252	253	254	255	256	257	258
Exposure to GPSA	2	119	93	135	93	109	126	130	101
	3	135	97	141	106	111	122	135	99
	4	135	97	128	107	111	118	127	101
	5	135	93	130	109	111	118	116	101
	6	122	91	121	105	104	116	106	102
	7	135	91	121	108	112	118	111	101
	8	130	92	116	110	114	116	113	92
	9	129	92	117	115	113	116	113	92
	10	114	94	114	109	104	109	108	95
	11	114	95	114	106	106	106	108	97
	12	107	97	110	95	106	106	114	97
	13	108	98	112	95	104	109	111	95
	14	109	101	110	93	*	111	108	93
	15	113	96	102	89	*	114	116	99
	16	111	95	102	91	*	116	119	101
	17	114	92	103	96	105	115	114	100
	18	115	93	111	105	103	109	103	96
	19	115	94	109	110	107	106	99	96
Exposure to TDI-GPSA	2	102	86	120	99	*	105	96	98
	3	107	91	130	100	*	105	100	91
	4	109	103	129	106	*	105	100	94
	5	115	120	125	115	93	108	112	98
	6	121	133	112	115	90	108	122	103
	7	124	140	118	107	98	105	135	104
	8	129	143	123	99	101	102	138	99
	9	133	146	129	102	*	103	140	93
	10	134	149	124	102	*	105	138	91
	11	129	149	128	99	*	105	142	97
	12	125	149	128	96	*	102	142	99
	13	127	149	125	97	*	102	147	102
	14	127	146	115	98	113	107	142	102
	15	135	146	117	95	111	107	140	109
	16	135	136	115	91	105	108	133	108
	17	137	131	115	89	114	106	131	110
	18	133	123	115	91	110	111	133	110
	19	131	128	115	91	114	111	135	113
Pre-exposure mean respiratory rate used to calculate the above percentages		92	126	89	108	107	118	106	125

*Not calculable
#5

BIO

TABLE NO. 14 RESPIRATORY RATE PROJECT NO. 81194
(3-MINUTE MOVING AVERAGE AS % OF PRE-EXPOSURE MEAN)

GROUP 2 - TDI
STUDY DAY 26

TIME AFTER START OF EXPOSURE (MINUTES)		ANIMAL NO. 251	252	253	254	255	256	257	258
Exposure to GPSA	2	118	115	128	110	116	116	119	105
	3	112	107	122	107	116	128	*	109
	4	115	101	119	110	120	128	*	105
	5	124	106	122	112	120	128	*	99
	6	124	110	117	117	126	118	127	98
	7	121	110	117	114	126	120	116	105
	8	110	108	111	112	126	115	107	104
	9	108	108	111	110	124	114	103	105
	10	113	108	105	110	120	111	114	98
	11	115	114	105	110	115	115	123	98
	12	118	109	105	107	113	115	124	98
	13	110	106	109	105	115	115	116	102
	14	112	103	105	105	122	111	113	100
	15	118	111	107	105	120	112	113	100
	16	120	114	107	103	111	111	113	98
	17	118	114	109	105	100	112	109	94
	18	115	108	107	107	91	107	109	91
	19	112	108	112	112	90	107	104	88
Exposure to TDI-GPSA	2	115	100	122	105	102	114	99	95
	3	117	98	117	107	92	109	101	95
	4	117	103	114	107	90	109	101	95
	5	120	106	114	105	87	109	108	94
	6	120	110	122	105	88	109	118	91
	7	120	114	117	110	89	108	123	90
	8	114	117	115	126	95	113	122	93
	9	112	122	105	131	93	113	108	91
	10	112	123	104	131	94	113	104	93
	11	114	125	100	129	95	109	100	94
	12	116	125	106	129	103	112	109	98
	13	123	125	111	134	109	111	109	98
	14	136	131	119	125	103	111	106	98
	15	146	135	117	118	96	111	97	94
	16	140	142	116	112	*	112	98	92
	17	134	144	109	112	*	111	103	85
	18	126	149	109	120	*	109	110	85
	19	136	147	111	120	*	108	107	86
Pre-exposure mean respiratory rate used to calculate the above percentages		89	104	88	89	119	102	105	124

* - Not calculable

#5

TABLE NO. 15 RESPIRATORY RATE PROJECT NO. 81194
(3-MINUTE MOVING AVERAGE AS % OF PRE-EXPOSURE MEAN)

GROUP 2 - TDI
STUDY DAY 27

TIME AFTER START OF EXPOSURE (MINUTES)		ANIMAL NO. 251	252	253	254	255	256	257	258
Exposure to GPSA	2	129	123	117	142	109	118	144	114
	3	129	123	115	136	112	118	132	112
	4	126	127	113	133	112	112	126	106
	5	127	125	111	128	110	114	122	95
	6	124	117	106	121	115	112	127	95
	7	122	114	105	121	120	114	137	99
	8	119	114	103	124	126	116	142	105
	9	120	120	103	124	119	117	144	108
	10	122	123	105	120	110	117	126	105
	11	120	120	103	114	101	111	128	102
	12	114	117	101	112	*	107	126	99
	13	112	114	99	113	*	102	135	102
	14	116	114	98	114	*	105	123	98
	15	122	115	100	130	119	109	110	98
	16	120	117	426	131	108	111	104	95
	17	112	117	*	131	108	118	109	97
	18	108	114	*	116	120	117	107	103
	19	112	122	*	118	123	114	109	106
Exposure to TDI-GPSA	2	120	130	102	122	122	114	125	93
	3	131	120	105	123	113	111	118	93
	4	132	118	108	125	115	111	117	93
	5	135	114	110	130	105	109	106	96
	6	122	114	109	133	111	107	113	100
	7	123	112	107	130	117	108	113	104
	8	125	108	105	125	126	108	116	104
	9	122	108	101	119	132	116	116	100
	10	124	111	102	114	127	113	*	100
	11	122	115	111	109	116	112	*	102
	12	132	120	116	109	106	107	*	105
	13	127	120	117	112	104	109	112	108
	14	125	123	108	124	106	111	112	109
	15	117	122	105	126	103	111	109	109
	16	118	123	107	130	109	113	104	109
	17	114	125	106	118	110	111	101	106
	18	116	129	104	111	114	111	102	108
	19	120	129	98	101	110	107	109	102
Pre-exposure mean respiratory rate used to calculate the above percentages		82	104	93	87	102	114	91	113

*Not calculable
#5

TABLE NO. 16

INDIVIDUAL SKIN IRRITATION (ERYTHEMA/EDEMA) SCORES*
IN GUINEA PIGS

PROJECT NO. 81194

GROUP 1

ANIMAL NO.	INTRADERMAL INJECTION						TOPICAL APPLICATION					
	0.1% TDI-GPSA		0.01% TDI-GPSA		0.1% GPSA		0.1% TDI		0.01% TDI		100% ACETONE	
	24 HR	48 HR	24 HR	48 HR	24 HR	48 HR	24 HR	48 HR	24 HR	48 HR	24 HR	48 HR
151	1/0	0/0	1/0	1/0	1/0	1/0	0/0	0/0	0/0	0/0	0/0	0/0
152	1/0	1/0	1/1	1/0	1/0	1/0	0/0	0/0	0/0	0/0	0/0	0/0
153	1/0	1/0	1/0	1/0	1/0	1/0	0/0	0/0	0/0	0/0	0/0	0/0
154	1/0	1/0	1/0	0/0	1/0	1/0	0/0	0/0	0/0	0/0	0/0	0/0
155	1/0	1/0	1/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
156	1/0	1/0	1/0	1/0	1/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
157	1/0	1/0	1/0	1/0	1/0	1/0	0/0	0/0	0/0	0/0	0/0	0/0
158	1/0	2/0	1/0	1/0	1/0	1/0	0/0	0/0	0/0	0/0	0/0	0/0

* Maximum Erythema = 4
  Maximum Edema = 4

#4

TABLE NO. 17

INDIVIDUAL SKIN IRRITATION (ERYTHEMA/EDEMA) SCORES*
IN GUINEA PIGS

PROJECT NO. 81194

GROUP 2

ANIMAL NO.	INTRADERMAL INJECTION						TOPICAL APPLICATION					
	0.1% TDI-GPSA		0.01% TDI-GPSA		0.1% GPSA		0.1% TDI		0.01% TDI		100% ACETONE	
	24 HR	48 HR	24 HR	48 HR	24 HR	48 HR	24 HR	48 HR	24 HR	48 HR	24 HR	48 HR
251	2/1	2/0	2/0	2/0	1/0	1/0	1/0	0/0	0/0	0/0	0/0	0/0
252	2/1	2/0	2/1	2/0	1/1	1/0	0/0	0/0	0/0	0/0	0/0	0/0
253	2/2	2/1	2/1	2/0	1/0	1/0	0/0	0/0	0/0	0/0	0/0	0/0
254	2/0	2/0	2/0	2/0	1/0	1/0	1/0	0/0	0/0	0/0	0/0	0/0
255	2/1	2/0	1/0	1/0	1/0	1/0	1/0	0/0	0/0	0/0	0/0	0/0
256	1/1	1/0	1/0	1/0	1/0	1/0	0/0	0/0	0/0	0/0	0/0	0/0
257	2/1	2/1	1/0	1/0	1/0	1/0	1/0	1/0	0/0	0/0	0/0	0/0
258	2/1	1/1	1/1	0/0	1/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0

* Maximum Erythema = 4
  Maximum Edema = 4

#4

TABLE NO. 18

INDIVIDUAL BLOOD SMEARS
PREDOSE

PROJECT NO. 81194

	GUINEA PIG NO.	WBC DIFFERENTIAL (%)						COMMENT ON SMEAR
		NEUT.						
		SEG.	NON-SEG.	LYMPH.	MONO.	EOS.	BASO.	
GROUP 1								
AIR CONTROL	151	13	0	82	3	2	0	3 Kurloff corpuscles seen.
	152	12	0	84	2	2	0	10 Kurloff corpuscles seen.
	153	14	0	80	5	1	0	3 Kurloff corpuscles seen.
	154	6	0	90	2	1	1	2 Kurloff corpuscles seen.
	155	19	0	77	3	1	0	-
	156	21	0	77	1	3	1	2 Kurloff corpuscles seen.
	157	10	0	85	1	4	0	2 Kurloff corpuscles seen.
	158	29	0	68	2	0	1	1 Kurloff corpuscle seen.
GROUP 2	251	11	0	89	0	0	0	2 Kurloff corpuscles seen.
TDI	252	41	0	53	4	2	0	2 Kurloff corpuscles seen.
	253	23	0	72	3	2	0	2 Kurloff corpuscles seen.
	254	12	0	80	7	1	0	3 Kurloff corpuscles seen.
	255	20	0	76	3	0	1	2 Kurloff corpuscles seen.
	256	26	0	73	1	0	0	3 Kurloff corpuscles seen.
	257	19	0	78	2	0	1	3 Kurloff corpuscles seen.
	258	14	0	81	4	1	0	2 Kurloff corpuscles seen. Polychromatophilic RBCs seen.

HEMO

TABLE NO. 19

INDIVIDUAL BLOOD SMEARS
DAY 15

PROJECT NO. 81194

	GUINEA PIG NO.	WBC DIFFERENTIAL (%)						COMMENT ON SMEAR
		NEUT.						
		SEG.	NON-SEG.	LYMPH.	MONO.	EOS.	BASO.	
GROUP 1 AIR CONTROL	155	15	0	82	2	1	0	1 Kurloff corpuscle seen.
	156	11	0	85	3	0	1	-
	157	10	0	85	2	3	0	5 Kurloff corpuscles seen.
	158	25	0	70	5	0	0	3 Kurloff corpuscles seen.
GROUP 2 TDI	255	9	0	91	0	0	0	1 erythroblast seen.
	256	30	0	63	5	1	1	2 Kurloff corpuscles seen.
	257	11	0	88	0	0	1	6 Kurloff corpuscles seen.
	258	13	0	81	6	0	0	1 Kurloff corpuscle seen. polychromatophilic RBCs seen.

HEMO.1

TABLE NO. 20

INDIVIDUAL BLOOD SMEARS
DAY 22

PROJECT NO. 81194

	GUINEA PIG NO.	WBC DIFFERENTIAL (%)						COMMENT ON SMEAR
		NEUT. SEG.	NEUT. NON-SEG.	LYMPH.	MONO.	EOS.	BASO.	
GROUP 1 AIR CONTROL	155	48	0	49	2	1	0	1 Kurloff corpuscle seen.
	156	19	0	76	1	4	0	3 Kurloff corpuscles seen.
	157	11	0	86	2	1	0	1 Kurloff corpuscle seen.
	158	14	0	85	0	1	0	-
GROUP 2 TDI	255	15	0	77	5	3	0	5 Kurloff corpuscles seen. Polychromatophilic RBCs seen.
	256	6	0	92	1	0	1	1 Kurloff corpuscle seen. Polychromatophilic RBCs seen.
	257	11	0	83	4	1	1	6 Kurloff corpuscles seen.
	258	8	0	88	1	3	0	3 Kurloff corpuscles seen.

HEMO. 2

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TABLE NO. 21

INDIVIDUAL BLOOD SMEARS
DAY 30

PROJECT NO. 81194

	GUINEA PIG NO.	WBC DIFFERENTIAL (%)						COMMENT ON SMEAR
		NEUT						
		SEG.	NON-SEG.	LYMPH.	MONO.	EOS.	BASO	
GROUP 1 AIR CONTROL	151	36	0	56	4	1	3	-
	152	5	0	94	1	0	0	-
	153	6	0	93	1	0	0	1 Poychromatophilic RBCs seen.
	154	35	0	64	0	1	0	1 Kurloff corpuscle seen. Polychromatophilic RBCs seen.
GROUP 2 TDI	251	9	0	87	1	3	0	3 Kurloff corpuscles seen.
	252	56	0	41	0	3	0	6 Kurloff corpuscles seen. Polychromatophilic RBCs seen.
	253	47	0	48	2	2	1	1 Kurloff corpuscle seen.
	254	11	0	87	2	0	0	1 Kurloff corpuscle seen.

HEMO. 3

TABLE NO. 22 GROUP MEAN (S.D.) ABSOLUTE ORGAN WEIGHTS (G) PROJECT NO :81194

FEMALES

	TERMINAL BODY WEIGHT (G)	LUNGS
GROUP 1 AIR CONTROL	521.6 69.32	3.452 .3501
GROUP 2 TDI	571.8 52.05	3.602 .1933

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TABLE NO. 23 GROUP MEAN (S.D.) RELATIVE ORGAN WEIGHTS (G%) PROJECT NO :81194

FEMALES

	TERMINAL BODY WEIGHT (G)	LUNGS
GROUP 1	571.6	.60?
AIR CONTROL	69.32	.0530
GROUP 2	571.8	.634
TDI	52.05	.0602

BIO-RESEARCH LABORATORIES LTD.

Standard Procedure

APPENDIX NO. 1

subject.	no: C-20-45 WP 143(A)
DETERMINATION OF 2-4-TOLUENEDIISOCYANATE (TDI) BY THE MARCALI METHOD	date effective. May 16, 1983
	supersedes.
prepared by. D. Carbonneau / approved by.	page 1 of 2

Basic Instrumentation:

Unicam scanning spectrophotometer or equivalent

Spectrophotometric Conditions:

Detector wavelength	550 nm
Path length	1 cm, 2 cm

Reageants:

- Absorber solution: Transfer 600 mL of distilled water in one liter volumetric flask. Add 35 mL of HCL conc. and 22 mL of glacial acetic acid conc., then dilute with distilled water to the mark. Prepare as needed.

- Sulfamic Acid Solution: 10 g of sulfamic acid in 100 mL of distilled water.

- Sodium Nitrite Solution: Dissolve 3 grams of sodium nitrite and 5 grams of sodium bromide in 80 mL of distilled water. Adjust the volume to 100 mL.

- N-(1-Naphthyl)-ethylenediamine Solution: Dissolves 50 mg of the N-(1-Naphthyl)-ethylenediamine dihydrochloride in 25 mL of distilled water. Add 1 mL of HCL conc. and dilute to 50 mL with distilled water. Stable 4 days.

- Glacial Acetic Acid 6N: Dilute 1 mL of Glacial acetic acid into 29 mL of distilled water.

- HCL 1.2 N: To 1 mL of conc. HCL add 10 mL of distilled water.

Standard A Preparation:

Accurately weigh approximately 140 mg* of 2,4-toluene diamine. Add 660 mL of glacial acetic acid to dissolve the powder then dilute to one liter with distilled water.

Standard Curve Preparation:

Transfer 10 mL of Std. A solution into 27.8 mL of glacial acetic acid. Dilute to one liter with distilled water. This solution contains an equivalent of 2 mcg TDI/mL.

*140 mg of 2-4toluene diamine equivalent to 200 mg of 2,4-toluenediisocyanate (TDI).

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APPENDIX NO. 1 (CONT'D.)

s.p. no. C-20-45 WP 143(A	date effective. May 16, 1983	supersedes.	page 2 of 2

Standard Curve Preparation:

A) Add 5 mL of 1.2N hydrochloric acid to each of eight 25 mL suitable test tubes.

B) To each test tube add the following amounts of Std. B solution: 0.0, 0.5, 1.0, 2.0, 3.0, 4.0, 5.0 and 10 mL.

C) Dilute each solution to 15 mL with .6N acetic acid solution.

D) Add .5 mL of sodium nitrite solution to each test tube. Shake and allow to stand for two minutes.

E) Then add 1 mL of sulfamic acid solution to each test tube. Shake and allow to stand for two minutes.

F) Then add 1 mL of the N-1-naphthylethylenediamine solution to each test tube. Shake and allow to stand 15 minutes.

G) Dilute the contents of each test tube to 20 mL with water.

Read the absorbance of the standards at 550 nm vs the blank (the test tube containing 0.0 mL of standard solution B).

Sample Preparation:

- Accurately measure each sample volume. Transfer 10 mL from each sample into a suitable test tube. Add 5 mL of absorber soln. to each test tube. Repeat steps D through G of the standard curve preparation for each sample. Read the absorbance at 550 nm.

Calculation:

Record the absorbance of the Std. curve. Per linear regression determine the concentration of the samples. The Std. concentration should be expressed in mcg/test tube.

- Per linear regression, we obtain a sample concentration in mcg/test tube so that each concentration should be divided by 10 to have the original sample concentration in mcg/mL.

- Multiply the mcg/mL found by the total volume to obtain the total amount of TDI.

- Some samples will have to be diluted in the absorber solution because of their high TDI concentration.

APPENDIX NO. 2 INHALATION CHAMBER TEMPERATURE (°C) AND RELATIVE HUMIDITY (%) PROJECT NO. 81194

GROUP 1A

STUDY DAY		TREATMENT TIME POST-EXPOSURE
18	TEMPERATURE	21.0
	RELATIVE HUMIDITY	43
19	TEMPERATURE	21.0
	RELATIVE HUMIDITY	45

STUDY DAY		TREATMENT TIME GPSA CHALLENGE	TREATMENT TIME TDI-GPSA CHALLENGE
25	TEMPERATURE	23.0	23.0
	RELATIVE HUMIDITY	45	59
26	TEMPERATURE	*	24.5
	RELATIVE HUMIDITY		54
27	TEMPERATURE	21.5	21.0
	RELATIVE HUMIDITY	44	43

* Missing observation

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APPENDIX NO. 3 INHALATION CHAMBER TEMPERATURE (°C) AND RELATIVE HUMIDITY (%) PROJECT NO. 81194

GROUP 1B

STUDY DAY		TREATMENT TIME POST-EXPOSURE
18	TEMPERATURE	22.0
	RELATIVE HUMIDITY	25
19	TEMPERATURE	22.5
	RELATIVE HUMIDITY	21

		TREATMENT TIME	
		GPSA CHALLENGE	TDI-GPSA CHALLENGE
25	TEMPERATURE	21.0	21.0
	RELATIVE HUMIDITY	43	43
26	TEMPERATURE	21.0	21.0
	RELATIVE HUMIDITY	45	45
27	TEMPERATURE	22.0	20.5
	RELATIVE HUMIDITY	55	50

#2

APPENDIX NO. 4 INHALATION CHAMBER TEMPERATURE (°C) AND RELATIVE HUMIDITY (%) PROJECT NO. 81194

GROUP 2A

STUDY DAY		APPROXIMATE TREATMENT TIME (MINUTES) 50	100	150	170
1	TEMPERATURE	22.0	22.5	22.0	22.0
	RELATIVE HUMIDITY	25	24	23	20
2	TEMPERATURE	22.0	21.0	21.0	22.0
	RELATIVE HUMIDITY	25	24	27	20
3	TEMPERATURE	22.0	22.0	22.0	22.0
	RELATIVE HUMIDITY	20	20	23	23
4	TEMPERATURE	22.0	25.0	27.0	24.0
	RELATIVE HUMIDITY	31	18	21	18
5	TEMPERATURE	23.0	24.0	24.0	23.0
	RELATIVE HUMIDITY	21	26	25	24

STUDY DAY		TREATMENT TIME POST-EXPOSURE
18	TEMPERATURE	21.0
	RELATIVE HUMIDITY	43
19	TEMPERATURE	21.0
	RELATIVE HUMIDITY	43

		TREATMENT TIME GPSA CHALLENGE	TDI-GPSA CHALLENGE
25	TEMPERATURE	23.0	*
	RELATIVE HUMIDITY	47	
26	TEMPERATURE	23.0	24.0
	RELATIVE HUMIDITY	49	53
27	TEMPERATURE	21.5	21.5
	RELATIVE HUMIDITY	44	44

* Missing observation

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APPENDIX NO. 6 (CONT'D) RESPIRATORY RATE (BREATHS/MIN) PROJECT NO. 81194

GROUP 1 - AIR CONTROL
STUDY DAY 25

TIME AFTER START OF EXPOSURE (MINUTES)		ANIMAL NO. 151	152	153	154	155	156	157	158
Exposure to TDI-GPSA	1	125	115	94	94	94	143	111	150
	2	100	125	83	94	100	130	120	115
	3	125	125	150	150	91	130	143	120
	4	100	115	94	100	88	130	130	115
	5	115	115	100	100	97	130	111	125
	6	125	115	100	100	91	136	136	125
	7	125	115	107	107	115	120	111	120
	8	125	115	125	100	130	125	130	120
	9	115	107	107	115	97	150	143	143
	10	125	115	115	100	91	130	111	115
	11	115	125	107	107	88	130	120	115
	12	115	115	100	100	97	130	120	115
	13	115	115	100	107	111	120	125	115
	14	125	125	107	94	100	120	120	111
	15	115	125	94	107	111	130	125	111
	16	100	115	100	100	*	130	120	130
	17	115	115	94	107	*	130	111	107
	18	115	115	107	94	86	130	97	107
	19	115	107	125	83	94	136	125	107
	20	107	115	107	100	97	130	130	115
	Mean	116	117	106	103	99	131	122	119
	S.D.	9	5	15	13	11	7	12	11

*Not calculable

#5

APPENDIX NO. 6 RESPIRATORY RATE (BREATHS/MIN) PROJECT NO. 81194

GROUP 1 - AIR CONTROL
STUDY DAY 25

TIME AFTER START OF EXPOSURE (MINUTES)		ANIMAL NO. 151	152	153	154	155	156	157	158
Pre-exposure	-10	100	115	94	94	107	115	120	115
	-9	107	125	94	94	107	120	158	111
	-8	100	125	107	100	91	130	111	130
	-7	115	125	107	100	103	120	130	107
	-6	115	125	107	94	97	125	130	107
	-5	107	-	100	107	97	115	136	115
	-4	100	136	100	94	103	125	136	111
	-3	100	125	94	88	97	125	120	*
	-2	107	125	94	107	125	120	120	*
	-1	100	136	100	107	103	130	158	136
Mean of minutes -6 to -2		106	127	99	98	104	122	128	114
S.D.		6	5	5	9	12	4	8	10
Exposure to GPSA	1	107	115	94	94	97	115	115	111
	2	125	125	115	107	136	115	100	107
	3	107	125	107	100	83	107	130	107
	4	100	125	100	100	97	103	120	143
	5	100	125	125	94	103	111	103	120
	6	115	125	107	100	103	120	103	115
	7	107	125	115	107	97	136	103	115
	8	136	136	107	107	97	130	100	115
	9	107	125	115	107	103	115	111	130
	10	115	136	107	115	100	125	91	120
	11	107	107	107	107	115	136	97	*
	12	125	115	107	107	107	136	115	125
	13	107	107	107	100	94	115	107	111
	14	115	115	107	94	97	136	130	120
	15	107	125	107	107	88	125	107	125
	16	107	115	100	107	103	130	97	111
	17	125	136	100	100	91	125	94	125
	18	115	125	94	107	91	120	97	125
	19	115	125	100	107	94	120	88	130
	20	115	125	100	100	100	130	97	120
Mean		113	123	106	103	100	123	105	120
S.D.		9	8	8	6	11	10	12	9

*Not calculable

#5

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APPENDIX NO. 7 RESPIRATORY RATE (BREATHS/MIN) PROJECT NO. 81194

GROUP 1 - AIR CONTROL
STUDY DAY 26

TIME AFTER START OF EXPOSURE (MINUTES)		ANIMAL NO. 151	152	153	154	155	156	157	158
Pre-exposure	-10	115	136	107	115	107	150	125	125
	-9	100	136	100	100	107	125	125	125
	-8	94	136	107	94	100	125	125	125
	-7	100	136	107	115	115	125	100	125
	-6	107	125	100	100	125	125	107	115
	-5	100	125	125	100	115	125	115	115
	-4	107	125	136	115	100	125	115	107
	-3	115	125	150	115	94	125	115	88
	-2	100	*	115	115	107	115	115	115
	-1	100	136	107	107	94	125	94	125
Mean of minutes -6 to -2		104	127	127	110	102	123	111	110
S.D.		7	5	17	7	9	4	9	14
Exposure to GPSA	1	107	130	103	136	100	125	125	136
	2	120	125	111	125	100	125	115	130
	3	120	130	120	120	103	130	125	120
	4	115	136	111	143	86	120	130	111
	5	115	120	115	136	103	130	120	120
	6	107	125	125	125	103	125	136	120
	7	111	125	115	130	103	136	136	136
	8	111	130	130	125	107	143	150	125
	9	111	130	136	125	103	130	176	143
	10	136	130	125	130	97	143	125	125
	11	107	130	115	130	107	143	130	120
	12	115	125	115	120	111	136	150	136
	13	115	130	115	125	115	143	125	120
	14	111	125	111	120	103	150	120	115
	15	103	125	107	120	111	150	136	115
	16	107	130	130	125	107	136	111	120
	17	103	125	100	125	111	143	188	136
	18	107	120	125	115	107	143	130	111
	19	111	136	107	125	120	130	136	125
	20	107	136	103	120	107	120	158	115
Mean		112	128	116	126	105	135	136	124
S.D.		7	5	10	7	7	9	20	9

*Not calculable

#5

APPENDIX NO. 7 (CONT'D) RESPIRATORY RATE (BREATHS/MIN) PROJECT NO. 81194

GROUP 1 - AIR CONTROL
STUDY DAY 26

TIME AFTER START OF EXPOSURE (MINUTES)		ANIMAL NO. 151	152	153	154	155	156	157	158
Exposure to TDI-GPSA	1	120	130	115	120	*	120	125	125
	2	120	136	120	136	130	125	130	115
	3	107	130	120	111	103	130	130	115
	4	143	158	125	115	103	136	120	111
	5	130	125	115	115	111	120	120	115
	6	115	136	136	130	150	125	120	107
	7	120	125	167	115	115	136	130	115
	8	125	120	115	115	100	120	130	111
	9	125	130	115	120	94	125	125	115
	10	130	125	136	130	97	125	143	107
	11	111	125	115	107	94	150	143	120
	12	130	130	111	115	91	143	125	130
	13	103	130	120	115	103	143	143	130
	14	103	130	120	111	*	167	136	125
	15	103	130	125	120	*	150	136	136
	16	111	136	115	125	94	130	125	115
	17	103	136	115	115	107	115	115	107
	18	150	130	120	120	97	120	111	115
	19	111	143	125	120	125	130	130	111
	20	103	136	111	125	125	130	111	130
	Mean	118	132	122	119	108	132	127	118
	S.D.	14	8	13	7	16	13	10	9

*Not calculable

#5

APPENDIX NO. 8 RESPIRATORY RATE (BREATHS/MIN) PROJECT NO. 81194

GROUP 1 - AIR CONTROL
STUDY DAY 27

TIME AFTER START OF EXPOSURE (MINUTES)		ANIMAL NO. 151	152	153	154	155	156	157	158
Pre-exposure	-10	100	103	83	103	*	115	107	107
	-9	91	107	83	103	*	125	115	136
	-8	97	103	83	103	*	125	107	100
	-7	100	107	86	103	107	115	100	107
	-6	94	125	86	103	100	115	94	115
	-5	97	120	81	97	94	88	100	107
	-4	100	103	83	115	136	120	130	150
	-3	94	111	97	97	136	125	88	100
	-2	120	107	88	111	103	111	97	111
	-1	111	111	88	107	120	120	111	107
	Mean of minutes -6 to -2	104	110	87	105	118	113	105	115
	S.D.	11	6	6	8	19	15	16	20
Exposure to GPSA	1	115	115	83	115	107	120	136	130
	2	130	143	115	120	100		120	125
	3	125	143	103	115	111	115	136	130
	4	130	167	111	120	125	111	120	120
	5	125	125	111	125	120	136	115	115
	6	120	125	111	120	125	136	130	120
	7	143	120	143	120	111	120	143	120
	8	130	130	150	125	111	111	111	111
	9	125	143	158	136	111	130	107	130
	10	136	150	143	150	111	125	143	115
	11	107	143	103	115	103	125	143	125
	12	125	143	125	120	111	120	136	115
	13	107	115	115	125	115	136	120	125
	14	107	125	125	120	125	167	120	120
	15	111	125	125	120	111	158	103	125
	16	107	136	125	125	136	120	103	120
	17	111	125	115	125	111	115	115	115
	18	83	120	125	125	107	120	125	111
	19	88	136	103	120	115	115	120	120
	20	100	143	115	120	125	115	107	115
	Mean	116	132	120	123	115	126	123	120
	S.D.	15	13	18	8	9	15	13	6

*Not calculable.

#5

APPENDIX NO. 9 RESPIRATORY RATE (BREATHS/MIN) PROJECT NO. 81194

GROUP 2 - TDI
STUDY DAY 25

TIME AFTER START OF EXPOSURE (MINUTES)		ANIMAL NO. 251	252	253	254	255	256	257	258
Pre-exposure	-10	88	136	88	107	91	120	94	130
	-9	83	150	88	100	136	111	100	150
	-8	88	167	88	100	136	120	111	136
	-7	88	150	88	100	136	120	97	130
	-6	94	167	100	115	120	111	100	120
	-5	83	136	107	107	125	115	88	130
	-4	94	136	94	107	103	120	111	125
	-3	94	107	83	125	94	130	103	115
	-2	94	125	75	100	111	103	115	130
	-1	94	125	88	100	100	120	111	125
Mean of minutes -6 to -2		92	126	89	108	107	118	106	125
S.D.		5	12	12	10	12	10	11	6
Exposure to GPSA	1	107	115	115	94	130	150	120	120
	2	107	111	136	100	111	150	143	115
	3	115	125	111	107	107	143	150	143
	4	150	130	130	136	136	136	136	115
	5	107	111	103	103	111	136	115	120
	6	115	111	115	115	107	143	115	143
	7	115	120	107	120	115	130	107	120
	8	143	111	103	115	136	143	130	115
	9	100	115	100	120	115	136	120	111
	10	111	120	111	136	111	130	107	120
	11	103	120	94	97	107	120	115	125
	12	100	120	100	111	120	125	120	120
	13	91	125	100	100	111	130	125	120
	14	107	125	100	97	103	130	107	115
	15	103	130	94	103	*	130	111	115
	16	100	107	79	88	115	143	150	143
	17	103	120	100	103	111	136	115	120
	18	111	120	97	120	111	125	97	111
	19	103	111	100	115	107	125	115	130
	20	103	125	94	120	125	125	103	120
Mean		110	119	104	110	115	134	120	122
S.D.		14	7	13	13	10	9	15	10

*Not calculable

#5

BIO

APPENDIX NO. 9 (CONT'D) RESPIRATORY RATE (BREATHS/MIN) PROJECT NO. 81194

GROUP 2 - TDI
STUDY DAY 25

TIME AFTER START OF EXPOSURE (MINUTES)		ANIMAL NO. 251	252	253	254	255	256	257	258
Exposure to TDI-GPSA	1	86	107	107	103	*	120	97	136
	2	97	103	107	111	115	130	107	111
	3	97	115	107	107	*	120	100	120
	4	100	125	136	107	107	120	111	111
	5	103	150	103	130	100	130	107	120
	6	115	176	97	136	91	130	136	136
	7	115	176	100	107	97	120	143	130
	8	111	176	120	103	125	120	150	125
	9	130	188	111	111	100	120	143	115
	10	125	188	115	115	*	125	150	107
	11	115	188	107	103	115	125	143	120
	12	115	188	120	103	*	120	158	136
	13	115	188	115	103	120	115	150	115
	14	120	188	100	107	120	125	158	130
	15	115	176	94	107	120	136	143	136
	16	136	188	120	94	115	115	143	143
	17	120	150	94	94	100	130	136	125
	18	120	158	94	100	150	130	136	143
	19	125	158	120	100	103	130	150	143
	20	115	167	94	94	111	130	143	136
	Mean	114	163	108	107	112	125	135	127
	S.D.	12	29	12	11	14	6	19	12

*Not calculable

#5

APPENDIX NO. 10 RESPIRATORY RATE (BREATHS/MIN) PROJECT NO. 81194

GROUP 2 - TDI
STUDY DAY 26

TIME AFTER START OF EXPOSURE (MINUTES)		ANIMAL NO. 251	252	253	254	255	256	257	258
Pre-exposure	-10	94	107	100	94	115	100	94	107
	-9	115	115	88	107	115	100	94	100
	-8	88	107	83	115	125	100	100	107
	-7	83	100	75	94	125	100	94	107
	-6	88	115	88	100	125	94	94	115
	-5	88	100	88	88	100	100	88	136
	-4	88	107	88	94	120	100	103	120
	-3	94	100	88	83	115	120	120	115
	-2	88	107	88	88	136	91	103	136
	-1	88	107	88	94	125	97	111	115
Mean of minutes -6 to -2		89	104	88	89	119	102	105	124
S.D.		3	4	0	5	13	11	12	11
Exposure to GPSA	1	115	125	125	100	136	115	107	111
	2	100	136	107	100	136	120	111	130
	3	100	100	107	94	143	120	158	150
	4	100	100	107	94	136	150	*	125
	5	107	115	100	107	150	120	150	115
	6	125	115	115	100	143	120	130	130
	7	100	115	94	107	158	120	120	120
	8	100	115	100	100	150	125	115	143
	9	94	107	100	94	143	107	103	125
	10	94	115	94	100	150	115	107	125
	11	115	115	83	100	136	115	150	115
	12	100	125	100	94	125	120	130	125
	13	100	100	94	94	143	115	111	125
	14	94	107	94	94	143	115	125	130
	15	107	115	88	94	150	107	120	120
	16	115	125	100	94	136	120	111	125
	17	100	115	94	88	111	111	125	120
	18	100	115	94	100	111	111	107	107
	19	107	107	94	100	103	103	111	111
	20	94	115	107	100	107	111	111	111
Mean		103	114	100	98	136	117	121	123
S.D.		8	9	10	5	16	10	16	11

*Not calculable

#5

BIO

APPENDIX NO. 10 (CONT'D) RESPIRATORY RATE (BREATHS/MIN) PROJECT NO. 81194

GROUP 2 - TDI
STUDY DAY 26

TIME AFTER START OF EXPOSURE (MINUTES)		ANIMAL NO. 251	252	253	254	255	256	257	258
Exposure to TDI-GPSA	1	100	107	107	94	143	120	107	125
	2	100	100	107	94	107	115	103	115
	3	107	107	107	94	115	111	103	115
	4	107	100	94	100	107	107	111	125
	5	100	115	100	94	100	115	103	115
	6	115	115	107	88	103	111	125	111
	7	107	115	115	100	111	107	143	115
	8	100	125	88	107	103	111	120	111
	9	97	125	100	130	125	125	120	120
	10	103	130	88	115	103	107	100	107
	11	100	130	86	107	107	111	107	120
	12	103	130	91	125	130	115	107	125
	13	107	130	103	115	130	115	130	120
	14	120	130	100	120	130	107	107	120
	15	136	150	111	100	107	115	97	125
	16	136	143	97	97	107	115	100	107
	17	103	150	97	103	*	111	111	111
	18	120	158	94	100	*	111	115	100
	19	115	158	97	120	136	111	120	107
	20	130	143	103	103	120	107	103	115
	Mean	110	128	100	105	116	112	112	115
	S.D.	12	18	8	12	13	5	12	7

*Not calculable

#5

APPENDIX NO. 11 RESPIRATORY RATE (BREATHS/MIN) PROJECT NO. 81194

GROUP 2 - TDI
STUDY DAY 27

TIME AFTER START OF EXPOSURE (MINUTES)		ANIMAL NO. 251	252	253	254	255	256	257	258
Pre-exposure	-10	81	107	86	97	125	100	107	107
	-9	88	107	88	136	100	107	107	115
	-8	81	120	81	94	125	115	88	115
	-7	91	100	81	94	136	125	83	115
	-6	100	125	*	77	136	100	88	136
	-5	88	115	100	77	100	107	94	107
	-4	88	115	88	83	107	107	79	100
	-3	77	91	91	97	83	107	88	107
	-2	79	100	94	86	94	125	107	115
	-1	79	100	91	91	125	125	88	136
Mean of minutes -6 to -2		82	104	93	87	102	114	91	113
S.D.		5	11	5	8	16	10	10	14
Exposure to GPSA	1	107	136	115	136	107	130	143	125
	2	107	120	103	115	115	150	130	120
	3	103	130	107	120	111	125	120	143
	4	107	136	111	120	115	130	111	115
	5	100	130	97	107	115	130	115	100
	6	107	125	100	107	107	130	107	107
	7	100	111	97	100	130	125	125	115
	8	94	120	94	107	130	136	143	115
	9	100	125	97	115	125	136	120	125
	10	103	130	97	100	107	130	130	125
	11	97	130	97	97	103	136	94	107
	12	97	115	94	100	97	115	125	115
	13	88	120	91	94	*	115	125	115
	14	91	120	91	100	143	120	120	115
	15	107	115	91	103	125	125	91	103
	16	103	125	97	136	94	130	91	115
	17	86	125	*	103	111	125	103	103
	18	86	115	*	103	125	150	103	111
	19	94	115	*	97	130	125	88	136
	20	97	150	130	107	120	115	107	111
Mean		99	125	101	108	116	129	115	116
S.D.		7	9	10	12	13	10	16	11

*Not calculable

#5

APPENDIX NO. 11 RESPIRATORY RATE (BREATHS/MIN) PROJECT NO. 81194

GROUP 2 - TDI
STUDY DAY 27

TIME AFTER START OF EXPOSURE (MINUTES)		ANIMAL NO. 251	252	253	254	255	256	257	258
Pre-exposure	-10	81	107	86	97	125	100	107	107
	-9	88	107	88	136	100	107	107	115
	-8	81	120	81	94	125	115	88	115
	-7	91	100	81	94	136	125	83	115
	-6	100	125	*	77	136	100	88	136
	-5	88	115	100	77	100	107	94	107
	-4	88	115	88	83	107	107	79	100
	-3	77	91	91	97	83	107	88	107
	-2	79	100	94	86	94	125	107	115
	-1	79	100	91	91	125	125	88	136
Mean of minutes -6 to -2		82	104	93	87	102	114	91	113
S.D.		5	11	5	8	16	10	10	14
Exposure to GPSA	1	107	136	115	136	107	130	143	125
	2	107	120	103	115	115	150	130	120
	3	103	130	107	120	111	125	120	143
	4	107	136	111	120	115	130	111	115
	5	100	130	97	107	115	130	115	100
	6	107	125	100	107	107	130	107	107
	7	100	111	97	100	130	125	125	115
	8	94	120	94	107	130	136	143	115
	9	100	125	97	115	125	136	120	125
	10	103	130	97	100	107	130	130	125
	11	97	130	97	97	103	136	94	107
	12	97	115	94	100	97	115	125	115
	13	88	120	91	94	*	115	125	115
	14	91	120	91	100	143	120	120	115
	15	107	115	91	103	125	125	91	103
	16	103	125	97	136	94	130	91	115
	17	86	125	*	103	111	125	103	103
	18	86	115	*	103	125	150	103	111
	19	94	115	*	97	130	125	88	136
	20	97	150	130	107	120	115	107	111
Mean		99	125	101	108	116	129	115	116
S.D.		7	9	10	12	13	10	16	11

*Not calculable

#5

APPENDIX NO. 11 (CONT'D) RESPIRATORY RATE (BREATHS/MIN) PROJECT NO. 81194

GROUP 2 - TDI
STUDY DAY 27

TIME AFTER START OF EXPOSURE (MINUTES)		ANIMAL NO. 251	252	253	254	255	256	257	258
Exposure to TDI-GPSA	1	100	150	97	100	130	136	107	107
	2	97	125	91	111	107	125	111	107
	3	100	130	97	107	136	130	125	100
	4	125	120	103	103	103	125	88	107
	5	100	120	100	115	111	125	107	107
	6	107	115	103	120	107	125	94	111
	7	94	120	100	111	120	115	107	120
	8	103	115	94	107	130	130	107	120
	9	111	103	97	107	136	125	103	111
	10	88	120	91	97	136	143	107	107
	11	107	125	97	94	115	120	*	120
	12	107	115	120	94	103	120	100	120
	13	111	136	107	97	107	125	103	115
	14	94	125	100	100	107	130	103	130
	15	103	125	94	125	111	125	100	125
	16	91	130	97	103	97	125	94	115
	17	97	130	107	111	125	136	91	130
	18	94	130	91	94	115	120	91	115
	19	94	143	91	83	107	125	97	120
	20	107	130	91	86	115	120	111	111
	Mean	102	125	98	103	116	126	102	115
	S.D.	9	10	7	11	12	7	9	8

*Not calculable
#5

FEMALES

	GUINEA PIG NO.	TERMINAL BODY WEIGHT (G)	LUNGS
GROUP 1	151	645.0	4.183
AIR CONTROL	152	618.0	3.473
	153	536.0	3.385
	154	641.0	3.628
	155	433.0	3.084
	156	568.0	3.180
	157	585.0	3.416
	158	547.0	3.213
GROUP 2	251	589.0	3.761
TDI	252	518.0	3.904
	253	517.0	3.351
	254	669.0	3.692
	255	563.0	3.472
	256	618.0	3.574
	257	541.0	3.378
	258	559.0	3.681

FEMALES

	GUINEA PIG NO.	TERMINAL BODY WEIGHT (G)	LUNGS
GROUP 1 AIR CONTROL	151	645.0	.649
	152	618.0	.562
	153	536.0	.632
	154	641.0	.574
	155	433.0	.712
	156	568.0	.560
	157	585.0	.584
	158	547.0	.587
GROUP 2 TDI	251	589.0	.639
	252	518.0	.754
	253	517.0	.648
	254	669.0	.552
	255	563.0	.617
	256	618.0	.578
	257	541.0	.624
	258	559.0	.658

BIO

APPENDIX NO. 14 GROSS PATHOLOGY FINDINGS FOR INDIVIDUAL FEMALES PROJECT NO. 81194

Group 1 - Air Control

Guinea Pig No. 151

No abnormal findings.

Guinea Pig No. 152

No abnormal findings.

Guinea Pig No. 153

Liver — Multiple white areas present throughout left lobe of liver.

Guinea Pig No. 154

No abnormal findings.

Guinea Pig No. 155

No abnormal findings.

Guinea Pig No. 156

No abnormal findings.

Guinea Pig No. 157

No abnormal findings.

Guinea Pig No. 158

Liver — Several pale well-demarcated areas (pinpoint to 2 X 2 X 1 mm) scattered throughout the right and left lobes.

Group 2 - TDI

Guinea Pig No. 251

Lungs — Mottled area (approximately 15 X 10 mm) present on the edge of the left lobe.

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APPENDIX NO. 14 (CONT'D) | GROSS PATHOLOGY FINDINGS FOR INDIVIDUAL FEMALES | PROJECT NO. 81194

Group 2 - TDI (Cont'd)

Guinea Pig No. 252

Ovaries — Clear fluid-filled cysts (approximately 4 mm in diameter) present on the right ovary.

Guinea Pig No. 253

No abnormal findings.

Guinea Pig No. 254

No abnormal findings.

Guinea Pig No. 255

No abnormal findings.

Guinea Pig No. 256

Liver — Well-demarcated pale area (approximately 3 X 4 mm) on the diaphragmatic surface of the left lobe.

Guinea Pig No. 257

Liver — Well-demarcated pale area (approximately 5 X 5 mm) on the diaphragmatic surface of the left lobe.

Guinea Pig No. 258

No abnormal findings.

APPENDIX NO. 15 PATHOLOGIST'S REPORT PROJECT NO. 81194

Few gross pathological findings were observed in the female guinea pigs exposed to TDI. Two guinea pigs (Nos. 256 and 257) in Group 2 (TDI) and 2 guinea pigs (Nos. 153 and 158) in Group 1 (air control) showed 1 or several pale or white areas on the liver. These findings are suggestive of focal coagulative necrosis, a relatively common background finding in the liver of the guinea pig. Other findings in the treated guinea pigs appeared to be either agonal or incidental.

Exposure of female guinea pigs to TDI appeared to cause no adverse effect.

Pierre Tellier, D.V.M., Dip.Path.
Staff Pathologist

Date

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