

Glyoxal
(Purified Crystal) CBOCBO

FVI-0704-001235

Single Oral Dose, LD₅₀ as 10% in Water (Spec. Rpt. 2-24-40)
Rat 2.02 (1.63 to 2.52) gm./kg.
G. Pig 0.76 (0.55 to 1.04) "

Single Skin Absorption by G. Pigs, 4-day Poultice (Spec. Rpt. 9-24-40)
LD₅₀ 6.6 gm./kg. R.P. as 40% in water

Stain on Skin (Monthly Rpt. 3-31-44)

There was no difference in skin staining between the crude and the crystal grades at the same concentration

9-1-53



FVI-94-001235
INIT 87/26/94

IR-424

American Cyanamid

3345
(Replaces B-368)



8494800294

Contains No CBI

Glyoxal (purified crystal)

Glyoxal, 30% solution
CBOCBO

Single Oral Dose to Standard Rats (Report 19-132; 1956)

LD₅₀ 4.29 (3.07 to 5.98) ml./kg. as sold, equivalent to 1.29 gm./kg.
on contained aldehyde

Single Inhalation by Rats, Vapors Saturated at Room Temp. (Monthly Rpt. 6-30-52)
8 hours killed 0/6

Primary Irritation, Rabbit Belly Vesicant Test (no report)

Grade 1. Undiluted gave no irritation

Eye Injury from Fluid to Rabbits (Monthly Rpt. 10-31-43)

Grade 4. 15% aldehyde in water severe, 5% minor injury

Cause of Death (Report 18-48; 1955)

Pharmacological Screening: a parasympathomimetic acting on medullary areas of the central nervous system. Death is due to respiratory failure followed by cardiac failure. Toxicologically speaking, death is due to shock of G.I. irritation, with kidney injury when shock does not kill at once.

12-15-56

4786

Replaces 4430

Glyoxal, 30% solution

RECEIVED
COPY SENT
94 JUL 26 PM 3:55

Confidential
Report 18-48

Re 3-27-55

SPB
3/30/55

MELLON INSTITUTE OF INDUSTRIAL RESEARCH
UNIVERSITY OF PITTSBURGH

PROGRESS REPORT for the month ended March 31, 1955

Glyoxal

We were asked to state the cause of death from glyoxal poisoning. From large single doses rats die in about one day, apparently chiefly from shock due to GI irritation. From slightly smaller doses there is considerable kidney injury evident, but not sufficient to explain death from a single dose.

In a pharmacodynamic sense death was due initially to respiratory failure followed within 5 minutes by cardiac failure, and occurred in the following sequence:-

1. 0.3 cc./kg. of Glyoxal (30%) was administered to a dog intravenously.
2. There was a brief, temporary cessation of respiration, accompanied by an abrupt drop in blood pressure.
3. This was promptly followed by an increase in respiratory rate and a slight decrease in respiratory volume as well as a state of hyperventilation was noted. At the same time, the blood pressure rapidly returned to its pre-injection level, and a moderate degree of elevation followed.
4. Then there followed a prolonged period of gradual decrease in respiratory rate and volume till eventual cessation. This was accompanied by a similar gradual decrease in blood pressure to an eventual zero reading after respiration had ceased completely.

Several non-lethal doses were administered to a total of two dogs, and Glyoxal can be labeled as a parasympathomimetic, an antispasmodic (although only briefly), a severe respiratory stimulant, a central nervous system stimulant, a diuretic, and there is an indication that it is not cumulative but rather a degree of refractivity to its pharmacological activities was noted. It does not produce these effects by the release of histamine and likely acts chiefly in the medullary areas of the central nervous system and on the parasympathomimetic effector cells of the autonomic nervous system. It is felt that the autonomic effects precede the central effects since the initial decrease in blood pressure followed by a brief increase and then a prolonged decrease can best be explained by this analysis.

Report 21-74

6-17-58

T-17-58

MELLON INSTITUTE OF INDUSTRIAL RESEARCH

UNIVERSITY OF PITTSBURGH

SPECIAL REPORT

on

Range Finding Tests on High Purity Glyoxal 29.2% SolutionUnion Carbide Chemicals Co., U.C.C.Industrial Fellowship No. 274-21Summary

The high purity glyoxal is about as toxic by mouth as the previous samples of crystal, about half as toxic as the crude sample tested in 1940 and 1943. The LD₅₀ for the 29.2% high purity solution, as received is 7.5 (5.4 to 10.4) ml./kg. or 2.2 gm./kg. on the basis of contained glyoxal. The crystal sample material had an LD₅₀ of 2.0 gm./kg., and the crude 1.1 gm./kg.

One of 4 rabbits succumbed to 20 ml./kg. of the solution as received. This is the highest dosage that can be administered in this test with a fair degree of reliability.

Concentrated vapor generated at room temperature caused no mortality in a group of 6 rats that inhaled this atmosphere for 8 hours.

This solution caused erythema on one of 5 rabbits while 4 were unreactive. Rabbit eyes were severely burned by 0.5 ml. and moderately by 0.1 ml. undiluted. Grade 3.

Sample

On 6-17-58 we received 16 oz. of high purity 29.2% glyoxal solution under code 325 RD 10. This solution was tested instead of the solid hydrate of glyoxal because none of the original material was available at Research. The pure hydrate is said to contain 80% available glyoxal, 1% oxalic acid and 19% water by weight. (For our use this was made up as a 29.2% glyoxal solution). The present product defined by our specifications is as follows:

30 - 30.5% glyoxal, 3% formic acid, 5% formaldehyde and 18% ethylene glycol by weight. The last three percentages are maximal.

Single Oral Dose

The LD₅₀ for undiluted high purity 29.2% solution of glyoxal, as received, is 7.46 (5.35 to 10.41) ml./kg.

0005

Carworth Farms-Nelson, non-fasted rats, 5 to 6 weeks of age and 90-120 grams in weight were dosed at levels differing by a factor of 2.0 in a geometric series. The rats were reared in our own colony and maintained from time of weaning on Rockland rat diet (complete). The method of moving average for calculating the median-effective dose (LD₅₀) was applied to the 14-day mortality data.

Autopsy of rats that died on the 8.0 ml./kg. level revealed slightly congested lungs, mottled livers, congested gastrointestinal tracts, pale kidneys and slightly congested adrenals.

Skin Penetration

The maximum dosage that can be applied to the clipped skin of the rabbit trunk is 20.0 ml./kg. One of 4 rabbits succumbed at this level. Two rabbits survived on 10 and 2 on 5 ml./kg. which helps to verify the low toxicity by the percutaneous route.

Male albino New Zealand strain rabbits, 3 to 5 months of age and averaging 2.5 kg. in weight were immobilized during the 24-hour skin contact period. Thereafter, the VINYLITE sheeting used to retain the dose in contact with the clipped skin of the trunk was removed and the animals were caged for the remainder of the 14-day observation period. The rabbits were procured locally and maintained on Rockland rabbit ration. The moving average method of calculating the LD₅₀ was used.

Glyoxal, high purity causes erythema on most rabbits and slight orange to brown staining on the skin which blanches to a yellow stain later on. Autopsy findings on the rabbit that died were meager - only lung congestion and a pale liver.

Inhalation

Concentrated vapor, generated at room temperature by passing air at 2.5 liters/minute through a fritted glass disc immersed in 50 ml. of the glyoxal solution caused no mortality among 6 female rats exposed for 8 hours and observed subsequently for a total of 14 days.

Irritation

One rabbit of 5 dosed with 0.01 ml. undiluted had marked erythema and the other 4 showed no response to the uncovered applications. Grade 2.

Instillation of 0.5 ml. undiluted caused severe corneal burns of the rabbit eye while 0.1 ml. produced moderate burns. Grade 3.

Charles P. Carpenter


ASSISTANT ADMINISTRATIVE YELLOW

Typed: August 12, 1958 - ccf

Table 21-139

Glyoxal (29.2%) High Purity

Single Doses to Male Albino Rats by Mouth

Fed Undiluted by Stomach Tube

Rat Number	1958 Date Dosed	Grams Wt.	Weight Change in 14 Days	Dosage; Ml. per kilo	Dose in Ml.	Days to Death
61404	7-22	94	-	16.0	1.5	0
61408	7-22	105	-	16.0	1.7	0
61308	7-22	92	-	16.0	1.5	0
61377	7-22	90	-	16.0	1.4	0
61379	7-22	92	-	16.0	1.5	1
60609	7-15	107	-	8.0	0.86	1
60621	7-15	111	-	8.0	0.89	2
60603	7-15	120	-	8.0	0.96	2
60626	7-15	96	+ 58	8.0	0.77	-
60625	7-15	106	+ 66	8.0	0.85	-
60638	7-15	113	+ 76	4.0	0.45	-
60639	7-15	98	+ 32	4.0	0.39	-
60634	7-15	107	+ 55	4.0	0.43	-
61045	7-15	95	+ 73	4.0	0.38	-
61041	7-15	103	+ 70	4.0	0.41	-
61042	7-15	91	+ 74	2.0	0.18	-
61034	7-15	92	+ 76	2.0	0.18	-
61046	7-15	103	+ 37	2.0	0.21	-
61066	7-15	115	+ 78	2.0	0.23	-
61064	7-15	96	+ 69	2.0	0.19	-

LD₅₀ = 7.46 (5.35 to 10.4) ml./kg.

Confidential

Report 28-103

R: 8-2-65

1-8
9-5-65

MELLON INSTITUTE

Special Report

Range Finding Tests on Glyoxal, 40%

Chemicals Division, Union Carbide Corporation Industrial Fellowship 274-28

Summary

Stomach Intubation, rat - LD₅₀ = 7.07 ml./kg. as received (males)
6.16 ml./kg. as received (females)
Skin Penetration, rabbit - LD₅₀ = 10.0 ml./kg. as received; necrosis
Inhalation, rat -
Substantially saturated vapor evolved under static
conditions at approximately 22°C.
8 hours killed 0 of 6

Uncovered Skin Irritation, rabbit - minor, Grade 4.
Eye Injury, rabbit - trace, Grade 2.
Intraperitoneal Injection, rat - LD₅₀ = 0.49 ml./kg. as received.

Interpretation

Glyoxal, 40%, manifests slight acute toxicity by both the peroral and skin penetration routes and presents no hazard by infrequent inhalation under normal handling conditions. Rabbit skin and eyes were irritated to only a minor degree by contact with the "as received" material while moderately high toxicity resulted from intraperitoneal injection to rats.

In 1958, a high purity sample (approximately 30% concentration) of glyoxal was studied by this laboratory (Rpt. 21-74). This earlier sample appears to be somewhat less toxic by the skin penetration route than the present material. A dosage level of 20 ml./kg. of the earlier 30% concentration sample killed only 1 of 4 rabbits.

Sample

Quantity: 5 gallon Date Received: 6-8-65 M. I. Sample No.: 28-152
Submitted by: F. W. Stone Division: Chemicals, Research & Development
South Charleston, West Virginia
Identification: S-754795; 23-DS-2-4
sample meets current manufacturing specifications;
contains no ethylene glycol and little if any formic acid.

Peroral, Single Dose to Rats

LD₅₀ - males - 7.07 (4.82 to 10.4) ml./kg. as received.
- females - 6.16 (4.69 to 8.06) ml./kg. as received.
Conditions - standard.

Male Rats

Dosage ml./kg.	Dead Dosed	Days to Death	Weight Change	Signs and/or Symptoms
20.0	5/5	0, 1	—	None reported.
10.0	4/5	1	+	
5.0	1/5	1	++++	
2.5	0/5	—	+++++	

Gross Pathology - congestion throughout the thoracic and the abdominal viscera;
some intestinal hemorrhage.

Conclusions - slight acute peroral toxicity to male rats.

Female Rats

Dosage ml./kg.	Dead Dosed	Days to Death	Weight Change	Signs and/or Symptoms
10.0	5/5	1	—	None reported.
5.0	1/5	1	++++	
2.5	0/5	—	+++++	

Gross Pathology - no autopsies done.

Conclusions - slight acute peroral toxicity to female rats.

Skin Penetration, Single Dose to RabbitsLD₅₀ - 10.0 (6.76 to 14.8) ml./kg. as received.

Conditions - standard; under VINYLITE covering.

Dosage Ml./Kg.	Dead Dosed	Days to Death	Weight Change	Skin Irritation	Signs and/or Symptoms
20.0	4/4	1	---	Necrosis.	Sluggish.
10.0	2/4	2, 3	++	"	
5.0	0/4	---	+++	"	

Gross Pathology - congestion and some hemorrhage of the lungs; congested livers and kidneys.

Conclusions - slight acute dermal toxicity by covered skin application; necrosis of the skin.

Inhalation, Single, by Rats

Conditions - standard procedure B; at approximately 22°C.

Proce- dure	Time	Concen- tration	Dead Dosed	Days to Death	Weight Change	Signs and/or Symptoms
B	8 hrs.	---	0/6	---	+++++	None.

Gross Pathology - nothing remarkable.

Conclusions - not hazardous to life by infrequent inhalation of vapor evolved under normal handling conditions.

Skin Irritation, Rabbit

Conditions - standard.
Applied as received.

Conclusions - moderate erythema on 3 animals and marked capillary injection on 2 others. Grade 4.

Eye Irritation, Rabbit

Conditions - standard.
Instilled as received.

Conclusions - an excess (0.5 ml.) caused traces of diffuse corneal necrosis in 5 eyes. Grade 2.

Parenteral, Single Dose to Rats

Intraperitoneal injection
LD₅₀ - 0.49 (0.38 to 0.65) ml./kg. as received.

Conditions - female albino, 90 to 120 gram rats.

Dosage Ml./Kg.	Dead Dosed	Days to Death	Weight Change	Signs and/or Symptoms
1.6	5/5	0	—	None reported.
0.8	5/5	1	—	
0.4	1/5	1	++++	
0.2	0/5	—	++++	

Gross Pathology - no autopsies done.

Conclusions - high acute toxicity by intraperitoneal injection to rats.

Approved:

Charles P. Conroy
Charles P. Conroy, Ph.D.
Assistant Administrative Fellow

Jean S. West
Jean S. West, B.S.
Junior Fellow

Acknowledgments

Skin Penetration, Irritation Tests - Naomi I. Condra, B.S., Junior Fellow
Inhalation Studies - Edwin R. Kinkead, B.S., Research Associate

Typed: August 4, 1953 - md

Confidential

R: 1-3-66

Report 29-1

20 Pages

MELLON INSTITUTE

Special Report

Results of Feeding Glyoxal in the Diet
of Rats and of Dogs for Three Months

Chemicals Division, Union Carbide Corporation Industrial Fellowship 274-29

Table of Contents

	<u>Page</u>
Summary	1
Sample	1
<u>Three-Month Feeding to Rats</u>	
Animal Management, Procedure and Statistics' Treatment of Data	2
Results	3
<u>Three-Month Feeding to Dogs</u>	
Animal Management and Procedure	3
Results	5
Conclusions	9
<u>Appendix</u>	
<u>Three-Month Feeding to Rats</u>	
Table 29-1 Summary of Results	10
Table 29-2 Mean Body Weight Changes	11
Table 29-3 Synopsis of Micro- and Gross-Pathology, Rats	12
Figure 1 Mean Body Weight Changes	4
<u>Three-Month Feeding to Dogs</u>	
Table 29-4 Vital Statistics and Organ Weights	14
Table 29-5 Mean Body Weight	15
Table 29-6 Mean Diet Consumption and Dosage	15
Table 29-7 Individual and Mean Biochemical and Hematological Results	16
Table 29-8 Individual and Mean Results of Differential Count	18
Table 29-9 Synopsis of Micro- and Gross-Pathology, Dogs	19
Figure 2 Body Weights of Dogs Receiving 0.417 or 0.208% Glyoxal	6
Figure 3 Body Weights of Dogs Receiving 0.104 or 0.000% Glyoxal	7
Figure 4 Mean Body Weight Changes	8

Summary

Glyoxal was incorporated in the diet of Harlan-Wistar albino rats for three months. The following criteria of effect were examined:

mortality
appetite
liver and kidney weights
gross- and micro-pathology
mean body weight changes

In dogs fed glyoxal for 90 days the following criteria of effect were added to those mentioned above:

blood urea nitrogen
alkaline phosphatase
bromsulfalein retention
complete blood count

The body weight gain of the male rats at 0.25 gm./kg. was less than that for the controls. Liver weight, as percentage of body weight, was increased at this dosage level. None of the criteria examined were significantly altered at 0.125 gm./kg. for the rats, or at 0.417% in the diet of the dogs which is equivalent to 0.125 gm./kg./day. Therefore, the dosage level of glyoxal that was without significant effect when included in the diet of rats or dogs for three months is 0.12 gm./kg./day

Sample

Fifty pounds of glyoxal, 40%, received 7-6-65 from South Charleston, West Virginia were identified by the Passed No. S 757968 and code 23-DS-28-3. While this sample was a 40% aqueous solution, all of the dosages in this report are on the basis of grams of glyoxal (active agent) per kilogram body weight.

Three-Month Feeding to Rats

Animal Management, Procedure and Statistical Treatment of Data

Harlan-Wistar rats from our breeding colony, originally established and currently maintained with rats purchased from Harlan Industries, Cumberland, Indiana, were used in this study. The rats were identified at 24 days of age and weighed at least once a week until 45 days of age, when doses were started.

0013

At the time of randomization, only rats whose body weights were within plus or minus two standard deviations from the mean weight of rats of their sex were accepted for the study. Any rat that lost weight or that had poor tone during the preliminary observation period was rejected. The range of weights on the first day the rats ate their glyoxal diets was 135 to 186 grams for the females, 171 to 238 grams for the males. The males and females were randomized separately.

Individual food and water containers were used for each pair of rats and were never used for any others unless washed and sterilized beforehand. Rats of the same sex were housed, two to a cage, in wire-bottom and front metal cages. Diet was provided in eight- or twelve-ounce opal glass feeder jars. The diet for each group of two or four rats was stored in a separate glass stock feeder jar provided with a screw cap. These jars were weighed when full, at the start of each period, and at biweekly periods thereafter to determine the amount of diet consumed. Three stock jars were used for each dosage group of ten rats, thus providing three independent measurements. Water was available to the rats at all times in nonfouling siphon water bottles equipped with stainless steel tips.

Ten males and 10 females were started on glyoxal at dosage levels of 0.25, 0.125, 0.03125 or 0.000 gm./kg. on 7-16-65. One week later, on 7-23-65, an additional group was started (from the same lot of rats randomized on 7-16) at 0.0625 gm./kg. The rats were weighed twice during the first week of doses and weekly thereafter until they had eaten the diet for approximately three months. The rats were observed daily for signs of any abnormality. At the conclusion of the three months, on October 14, 1965 for the males and October 15 for the females, the rats were killed by sectioning the cervical cord and the neck vessels without disturbing the trachea. To accomplish maximum exsanguination they were suspended until heart action had ceased. Thoracic and abdominal organs were examined in the gross and suitable portions taken for micro-pathological examination. Liver and kidneys of each rat were removed and weighed.

The basic diet in which glyoxal was incorporated, by means of a vertical mixer, was ground PURINA laboratory chow. The percentage of the chemical in the diet was adjusted at two-week intervals to maintain a relatively constant dosage throughout the three-month period. Information on the amount of diet consumed during the previous period and on the projected body weight of the rats, based on their previous rate of weight gain, was used in this estimation (see formula in Table 29-1). The mean dosage is indicated in Table 29-1. The majority of the time the dosages were within 10% of the preset goals.

The results of each quantitative continuous variable were intercompared for the four dosage groups and the control by use of the following tests:

- (a) Bartlett's homogeneity of variance
- (b) analysis of variance
- (c) Duncan's multiple range

The latter was used, if F for analysis of variance was significantly high, to delineate which groups differed from the control. If Bartlett's test indicated heterogeneous variances, the F-test was used for each group versus the control. If these individual F-tests were not significant, Student's t-test was used; if significant, the means were compared by the Cochran t-test. The fiducial limit of 0.25 was employed as the practical level of difference not believed to be produced by chance.

For growth effects, the means for each sex were calculated and compared after adjustment of the individual weights of each rat to a gain in weight over their weight on 7-16-65.

Results

The results of the various criteria of stress are summarized in Table 29-1. The mean body weight changes at 6 intervals are presented in Table 29-2 and in Figure 1.

There was no mortality or diet consumption alteration in any of the groups. In fact, none of the criteria of effect were significantly changed by the inclusion of glyoxal in the diets of the female rats. While the body weight gains of the males at 0.25 gm./kg. were statistically significantly depressed for the first two weeks, the differences from the controls were not significant thereafter. However, inspection of Figure 1 indicates this difference. While liver weight, per se, was similar in all groups of males, the weight of these organs as a percentage of body weight basis was increased at 0.25 and, to a minor extent, at 0.0625 (but not significantly at 0.125 gm./kg.). Kidney weights, as percentages of body weights, were similar. No significant gross or micropathological changes were seen in the organs examined; Table 29-3.

Three Months Feeding to Dogs

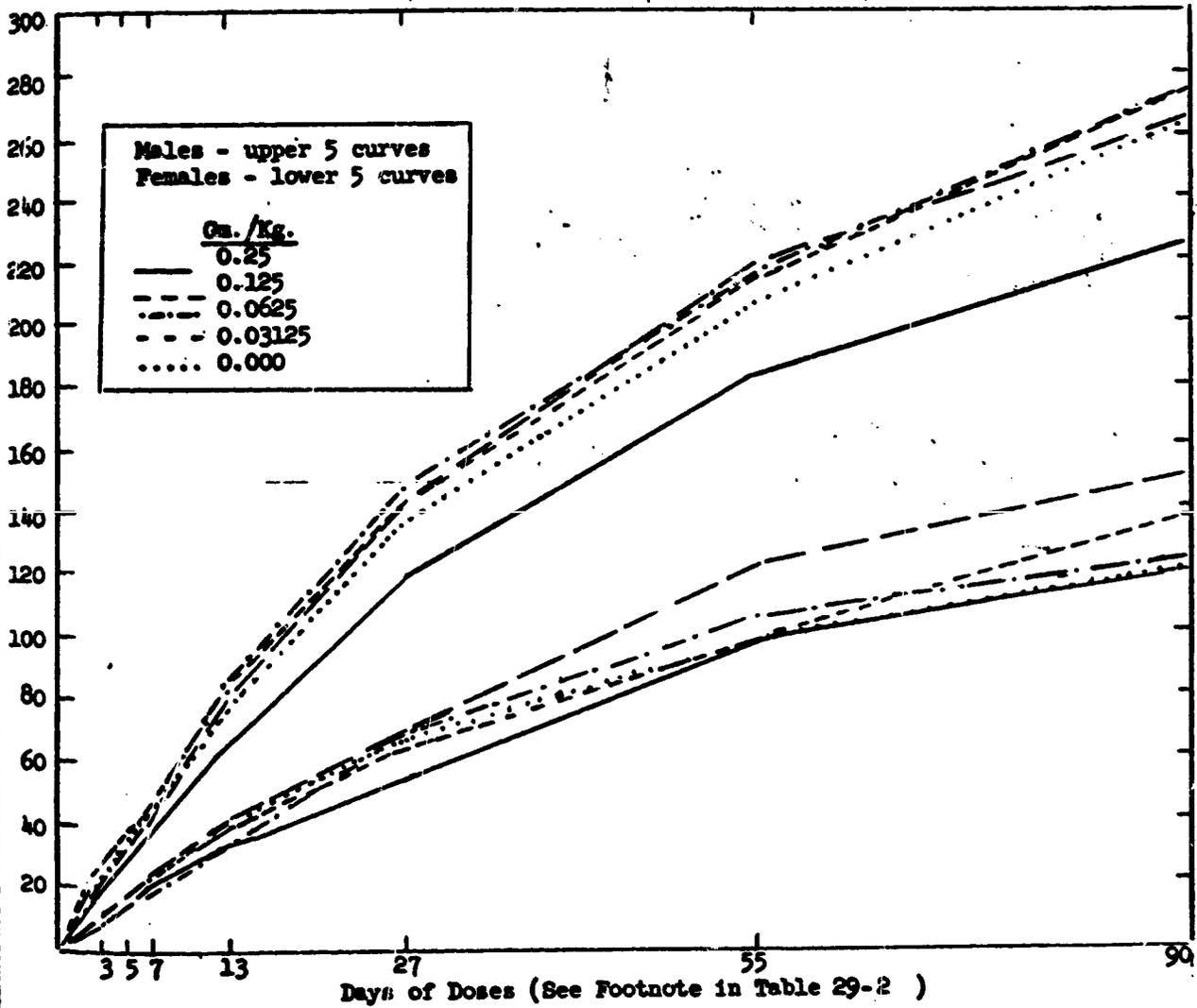
Animal Management and Procedure

The Beagle dogs listed in Table 29-4 were bred in our kennel. They were 15 to 21 months of age on 7-27-65 when they received their first dose of glyoxal in their diets.

The material was mixed into the basic dry diet at concentrations of 0.017, 0.2083, 0.104 or 0.00%. The basic diet of all of the dogs was Friskies Dog Food Meal, a product of Carnation Company, Los Angeles, California. The Friskies, as supplied, consisted of small, hard pellets which were ground in an Abla'000 mill using a 1/4" screen. The dogs received their diet, seven days a week, wetted with a Parlac-water mixture. From 7-27-65 to 8-12-65 to every 10 cups of Parlac (a 28% butterfat powdered whole milk product of Borden Co., New York) was added 60 cups of water. After 8-12-65 the quantity of Parlac was cut in half.

Figure 1

Mean Body Weight Gain of Rats on Diets Containing Glyoxal



To convert the 0.417, 0.2083, 0.104 or 0.00% by weight of glyoxal in the diet to dosage in grams of glyoxal per kilogram of body weight per dog per day, the number of cups of vetted diet eaten by each group of dogs each dosage day was measured. Approximately once a month these dosages were calculated using the data on diet prepared, diet consumed and the mean body weight of the dogs. These mean data are presented in Table 29-6. The weighted mean dosage levels attained for these three groups, respectively, were 0.115, 0.065 and 0.031 grams of glyoxal per kilogram body weight per dog per day.

Before the start of the study the dogs were randomly distributed by sex and birth date, insofar as possible, among the treated and control groups. Furthermore, prior to the first day of inclusion of the glyoxal in the diets, the following were determined:

blood urea nitrogen
serum alkaline phosphatase, and
hematocrit

The above were repeated, along with the following, after 11 weeks of doses:

bromsulfalein percentage retention
hemoglobin
total red and white blood cells by means of a
Coulter counter and differential white
blood cell count.

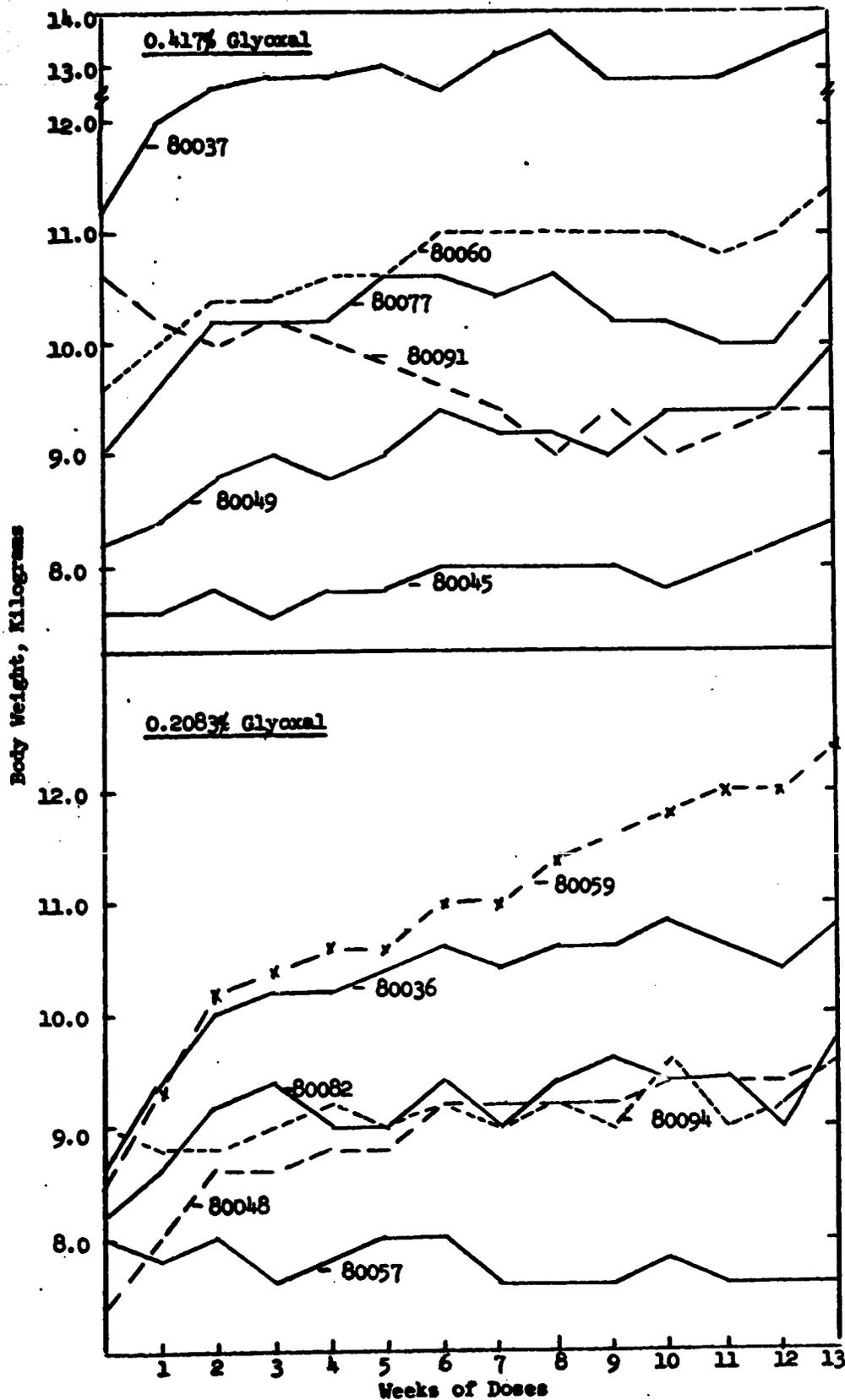
Bromsulfalein retention was determined by withdrawing a blood sample 15 minutes after the dogs received intravenously 5 mg./kg. of the dye. Serum phosphatase and urea nitrogen were expressed as mg./100 ml. The statistical treatment of the data was similar to that described for the data on the rats.

Results

The individual body weights of the dogs are illustrated in Figure 2 and 3. The mean body weight changes, from the weight on the first day of inclusion of glyoxal in the diets, are presented in Figure 4 and in Table 29-5. The mean gains of all groups were statistically similar throughout the study. The highest F, for analysis of variance, was 0.53; after 10 weeks of doses. To be significant for 3 versus 20 degrees of freedom for groups and for error respectively, the F would have had to exceed 3.10 for $P = 0.05$. Therefore, body weight was not affected by the inclusion of 0.417% glyoxal in the diet.

Similarly, the means of the glyoxal-dosed and control dogs were statistically similar in all criteria; namely, hematology, biochemistry, organ weight, and pathology. The individual and mean values for these are presented in Tables 29-4, 29-7, 29-8, and 29-9.

Body Weights of Individual Dogs Receiving
0.417 or 0.208% Glyoxal in their Diets



0018

Figure 3

Body Weights of Individual Dogs Receiving
0.10% or 0.00% Glyoxal in their Diets

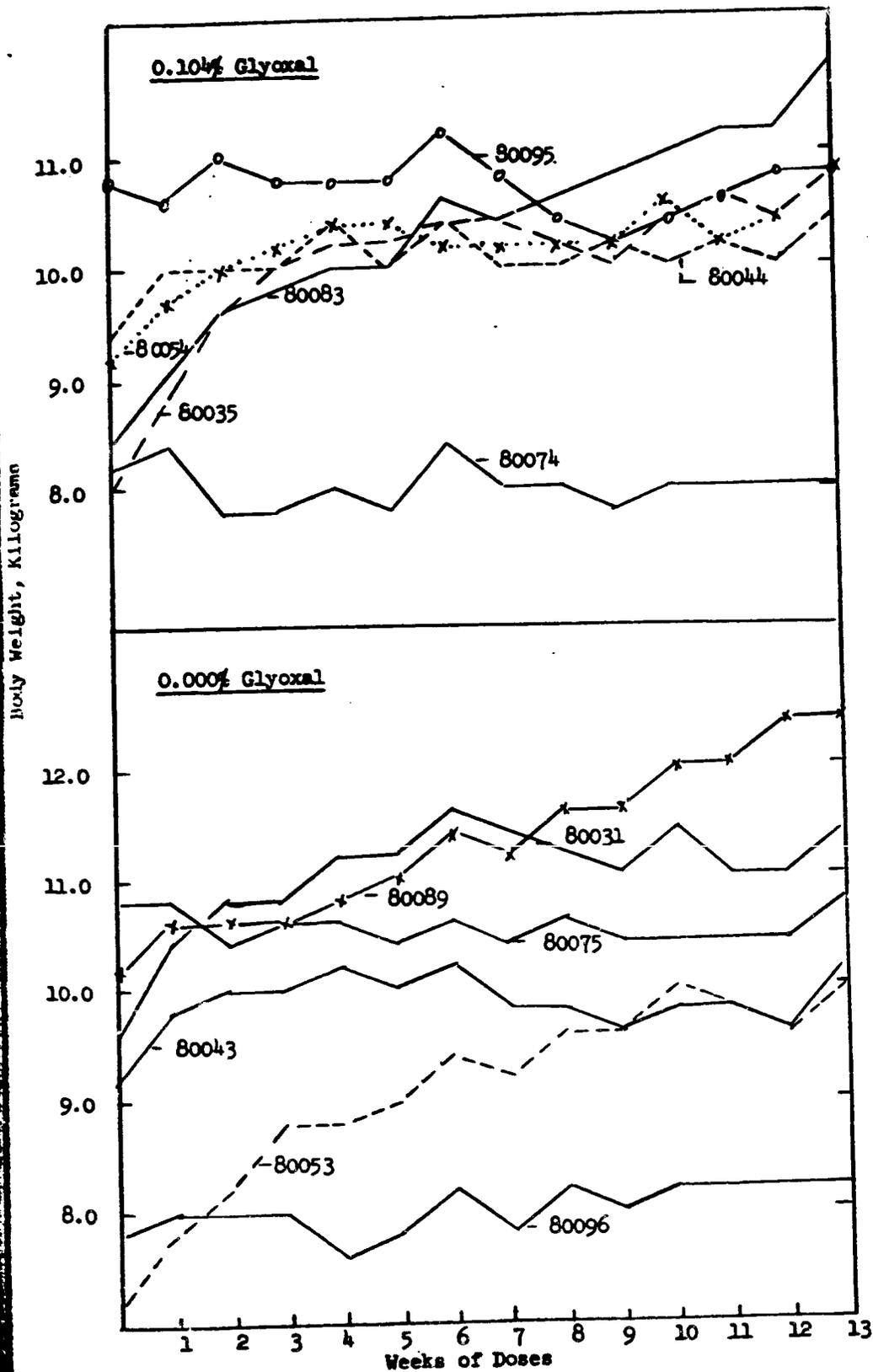
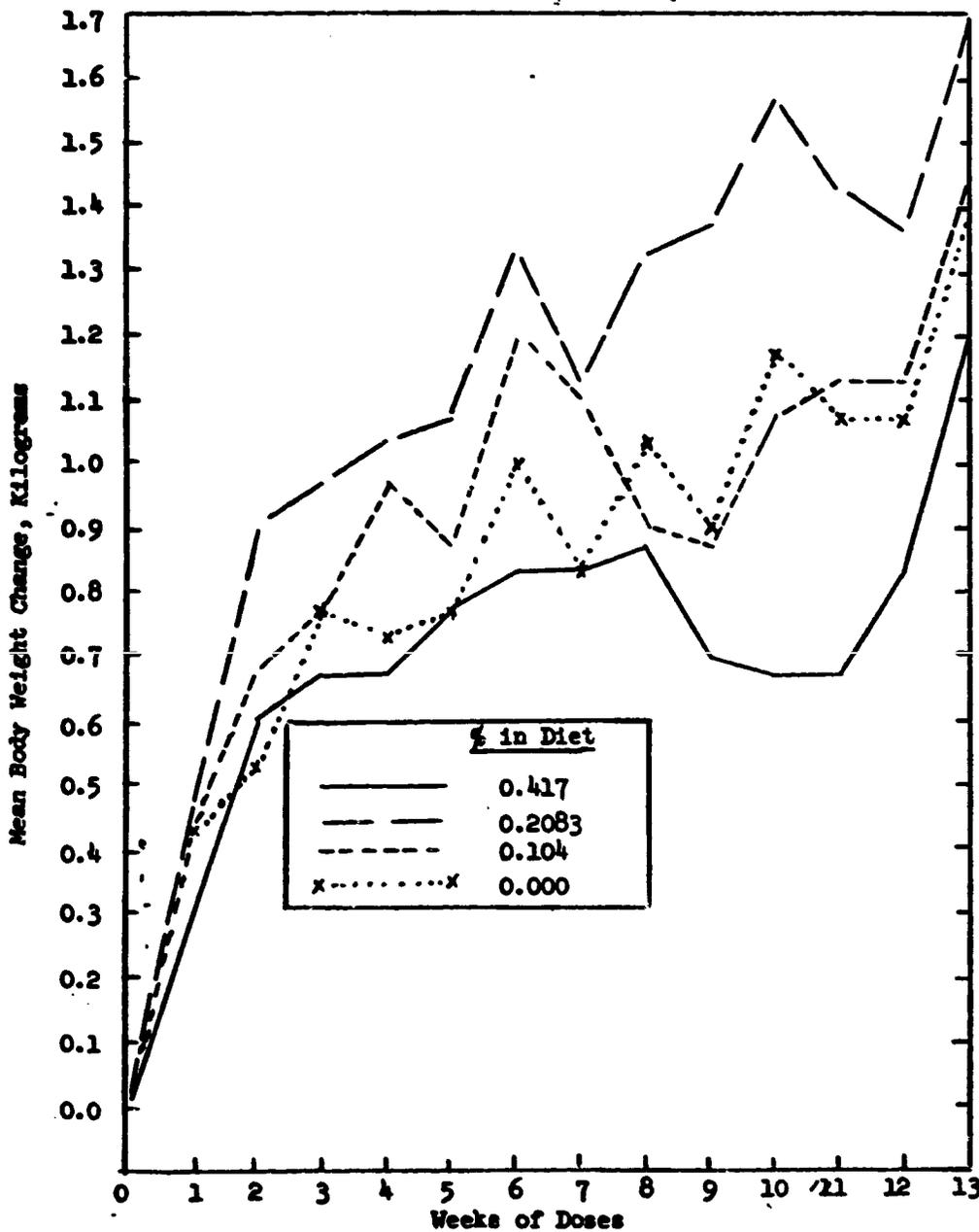


Figure 4
Mean Body Weight Changes of Dogs Receiving
Glyoxal in their Diets



Conclusions

While the changes seen at 0.25 gm./kg. in the rat were minor, none of any significance were seen at 0.125 gm./kg. Similarly, none of the criteria measured were significantly altered at the highest dosage level fed to dogs for 90 days which was 0.417% in the diet, equivalent to 0.115 grams of glyoxal per kilogram body weight per dog per day. Therefore, the dosage level of glyoxal without deleterious effect for rats and dogs for three months is 0.12 gm./kg./day.

Carrol S. Weil

Carrol S. Weil, M.A.
Senior Fellow

Approved:

Charles P. Carpenter

Charles P. Carpenter, Ph.D.
Assistant Administrative Fellow

Acknowledgments:

Diet preparation and consumption,
feeding and weighing of rats

Murray D. Woodside, M.Litt.
Junior Fellow

Jack Bernard, B.S.
Research Associate

Pathological examination,
biochemistry and hematology

John M. King, D.V.M., Ph.D.
Fellow

Typed 1-5-66 - acc

Table 29-1
Summary of Results of Inclusion of Glyoxal in the Diet of Rats

	Male Rats		Female Rats	
	0.25	0.125	0.0625	0.03125
Dosage goal; gm./kg./day	0.253	0.132	0.0632	0.03270
Dosage attained; gm./kg./day	0.253	0.132	0.0632	0.03270
Diet consumption; gm./rat/day	22.32	24.27	23.39	24.23
Body weight gain, grams	225.1	266.3	274.0	274.0
Liver weight, grams	15.65	16.43	16.51	15.61
Liver weight as % of body weight	3.64 ^b	3.42	3.46 ^a	3.31
Kidney weight, grams	2.99	3.36 ^a	3.31 ^a	3.10
Kidney weight as % of body weight	0.70	0.70	0.70	0.65
Mortality	0	0	0	0

a. $0.05 > P > 0.01$ b. $0.01 > P > 0.001$
To convert dosage to percentage in the diet, one may use:

$$X = 100 \frac{KW}{G} \text{ where:}$$

- X = percentage in the diet
- K = dosage in grams/kilogram/day
- W = body weight in kilograms
- G = diet consumption in grams/animal/day

Table 29-2

Mean Body Weight - Rats

Days of Doses x	Doseage; Gm./Kg. Glyoxal in Diet												Homogeneity of Variance, Chi Square	Analysis of Variance, F
	0.25		0.125		0.0625		0.03125		0.000		Mean	Standard Deviation		
	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation				
0	205.3	19.9	212.9	16.4	204.9	18.0	197.6	17.7	200.0	15.2	0.76	1.13		
	Male Rats													
	Body Weight, Grams													
	Body Weight Change, Gms.													
3	15.9	4.7	18.6	4.4	"	"	21.6	4.2	18.5	4.4	0.09	2.75		
5	28.0a	4.6	31.8	6.4	"	"	35.9	5.6	33.3	3.8	2.74	4.03a		
7	28.7a	8.0	46.1	8.5	"	"	47.8	7.6	45.9	5.3	2.14	2.94a		
13	65.0a	10.2	79.5	15.7	83.7	10.8	84.2	11.6	77.6	10.7	2.45	4.21b		
27	119.4	20.1	141.3	30.7	141.4	21.8	146.2	19.1	135.4	23.4	1.26	2.00		
55	183.6	33.2	219.3	51.5	213.8	34.1	215.3	25.7	206.4	45.2	5.42	1.33		
90	225.1	27.4	266.3	58.1	274.0	37.9	274.0	24.9	264.0	58.5	10.52	2.16		
	Female Rats													
	Body Weight, Grams													
	Body Weight Change, Gms.													
0	169.8	12.7	156.5	15.8	159.9	15.6	163.5	17.2	162.4	13.3	1.15	1.07		
3	9.5	4.5	10.8	2.7	"	"	9.9	5.9	9.6	3.7	5.47	0.18		
5	14.4	4.4	17.6	4.1	"	"	18.8	5.4	14.2	4.3	0.80	2.44		
7	20.4	5.1	24.1	5.7	"	"	23.3	8.4	19.7	4.0	5.41	1.28		
13	33.4	6.5	41.3	7.6	33.9	10.0	37.8	12.8	33.4	7.3	5.74	1.47		
27	65.3	10.9	79.1	14.0	63.9	13.5	67.7	19.0	65.9	11.9	3.51	1.88		
55	98.3	15.8	120.6a	20.8	97.5	15.2	105.4	28.8	97.0	13.7	7.16	2.60a		
90	119.8	20.6	149.9	28.4	122.3	16.0	137.0	37.0	120.2	24.5	7.09	2.55		

x Rats on 0.0625 gm./kg. started on diet 7 days after other dosed groups. Therefore, subtract 7 from days of doses in this column for 0.0625 gm./kg. rats

a. 0.05 > P > 0.01 b. 0.01 > P > 0.001

Table 29-4

Vital Statistics and Organ Weights

Dog Number	Sex	Birth Date	Body Wt. at Start of Study, Kg.	At Three Months of Doses				
				Body Weight, Kg.	Liver Weight, Grams	Liver Wt. as % of Body Wt.	Kidney Weight, Grams	Kidney Wt. as % of Body Wt.
0.417% Glyoxal in Diet								
80045	F	1-7-64	7.6	8.4	271	3.23	42	0.50
80037	M	11-27-63	11.2	13.6	425	3.12	66	0.48
80077	F	3-4-64	9.0	10.8	360	3.33	44	0.41
80049	M	1-7-64	8.2	10.0	333	3.33	44	0.44
80091	F	4-6-64	10.6	9.2	211	2.29	40	0.43
80060	M	2-20-64	9.6	11.4	294	2.58	50	0.44
Mean	-	-	9.4	10.6	316	2.98	48	0.45
0.2083% Glyoxal in Diet								
80057	F	2-18-64	8.0	7.4	201	2.72	32	0.43
80036	M	11-27-63	8.6	10.8	353	3.27	52	0.48
80082	F	4-2-64	8.2	10.0	303	3.03	45	0.45
80048	M	1-7-64	7.2	9.6	380	3.96	44	0.46
80094	F	4-20-64	9.0	9.6	225	2.34	33	0.34
80059	M	2-20-64	8.4	12.4	355	2.86	50	0.40
Mean	-	-	8.2	10.0	303	3.03	43	0.43
0.104% Glyoxal in Diet								
80074	F	3-9-64	8.2	8.2	227	2.77	36	0.44
80035	M	11-27-63	8.0	10.8	342	3.17	51	0.47
80083	F	4-2-64	8.4	11.8	330	2.80	49	0.42
80044	M	1-7-64	9.4	10.4	246	2.36	53	0.51
80095	F	4-20-64	10.8	11.2	227	2.03	34	0.30
80054	M	2-6-64	9.2	10.8	301	2.79	40	0.37
Mean	-	-	9.0	10.5	279	2.65	44	0.42
0.000% Glyoxal in Diet								
80075	F	3-9-64	10.8	10.6	250	2.36	35	0.33
80031	M	11-6-63	9.6	11.4	304	2.67	55	0.48
80089	F	4-6-64	10.2	12.4	366	2.95	45	0.36
80043	M	1-7-64	9.2	10.2	282	2.76	44	0.43
80096	F	4-20-64	7.8	8.6	237	2.76	34	0.40
80053	M	2-6-64	7.2	10.0	288	2.88	39	0.39
Mean	-	-	9.1	10.5	288	2.73	42	0.40

Stock and Source: Beagles bred at the Chemical Hygiene Laboratory

0026

Table 29-3
 Synopsis of Micro and Gross Pathology; Rats

	Males					Females				
	Gm./Kg. in Diet					Gm./Kg. in Diet				
	0.25	0.125	0.0625	0.03125	0.015625	0.25	0.125	0.0625	0.03125	0.015625
Number Examined Grossly:	10	10	10	10	10	10	10	10	10	10
LIVER: Number Examined	2	1	1	1	1	2	0	0	1	0
Bile duct prominence	1	1	1	1	1	4	0	0	5	2
Bile duct proliferation	0	3	1	1	1	2	3	2	2	4
Round cell accumulations	0	0	1	1	0	0	0	0	0	0
Granulomas	10	10	10	10	10	10	10	10	10	10
KIDNEY: Number Examined	0	0	0	0	0	0	1	0	0	0
Dilated renal pelvis	1	0	0	0	0	0	1	1	1	1
Dilated renal pelvis	0	1	0	0	0	0	1	0	0	0
Tubular degeneration	0	1	0	0	1	0	2	0	0	0
Dilated tubules	0	1	0	0	0	0	2	0	0	0
Pink casts	0	0	0	0	0	0	0	0	0	0
Calcium casts	0	0	0	0	0	0	0	0	0	0
Fibrosis	0	1	0	0	0	0	1	0	0	0
Round cell accumulations	0	2	0	0	0	0	1	0	2	0
Section of parasites	1	0	0	0	0	0	0	0	0	0
*Degree of involvement +2	0	0	0	0	0	0	0	0	0	0
+1	0	1	0	4	0	0	2	1	1	0
LUNG: Number Examined	10	10	10	10	10	10	10	10	10	10
Inhaled blood	0	0	0	0	0	0	1	0	0	0
Inhaled blood	0	0	0	0	0	0	1	0	0	0
Lipid foci	0	0	0	0	0	0	0	0	0	0
Bronchiectasis	0	0	0	0	0	0	0	0	0	0
Bronchiectasis	0	1	0	0	0	0	0	0	0	0
Chronic pneumonia	1	0	0	0	0	0	0	0	0	0
Chronic bronchopneumonia	1	0	0	0	0	1	0	0	0	0
Acute pneumonia	1	0	0	0	0	0	0	0	0	0
Interstitial pneumonia	0	0	0	0	0	0	0	0	1	0
Chronic abscessed pneumonia	0	1	0	0	0	0	0	0	0	0
Chronic abscessed bronchopneumonia	0	1	0	0	0	0	0	0	0	0
Atelectasis	0	0	0	0	0	0	0	0	0	0
Atelectasis	1	0	0	0	0	0	0	0	0	0
Suppurative bronchitis	0	0	0	0	0	0	0	0	0	0
Emphysema	0	0	0	0	0	0	0	0	0	0
Foam cell foci	2	1	1	1	1	0	1	0	0	0

* Degree of degeneration and quantity of kidney involved in reference to dilated tubules, casts, tubular degeneration and regeneration.

Table 29-3
(Continued)

	Males					Females					
	0.25	0.125	0.03125	Gm./Kg. in Diet	0.0625	0.03125	0.125	0.0625	0.03125	0.0625	0.00
Inflammatory cell foci	1	0	0	0	0	0	0	0	0	0	0
Round cell accumulations	2	1	1	2	1	1	1	1	1	1	1
Interstitial thickening	0	0	0	1	0	0	0	0	0	0	0
TRACHEA: Number Examined	10	3	5	10	10	1	1	1	1	1	10
Dilated tracheal glands	1	0	0	1	2	0	0	0	0	0	0
Chronic tracheitis	2	0	0	6	2	0	0	0	0	0	3
ESOPHAGUS: Number Examined	10	3	5	10	10	1	1	1	1	1	10
Hyperkeratosis	0	0	0	0	0	0	0	0	0	0	0
Dilatation	0	0	0	1	0	0	0	0	0	0	2
THYROID: Number Examined	9	3	5	10	10	1	1	1	1	1	10
Embryological duct formation	0	0	0	0	0	0	0	0	0	0	0
Hyperthrophied epithelial lining	0	0	0	1	0	0	0	0	0	0	0
HEART: Number Examined	10	10	10	10	10	10	10	10	10	10	10
Mast cell accumulations	0	1	0	1	0	0	0	0	0	0	0
Round cell accumulations	0	1	0	1	0	0	0	0	0	0	0
Markedly dilated ventricles	0	0	1	0	0	0	0	0	0	0	0
SPLEEN: Number Examined	9	10	10	10	10	10	10	10	10	10	10
Lymphoid hyperplasia	0	1	0	1	0	0	1	1	1	1	0
Hemosiderosis	0	0	0	1	0	0	0	0	0	0	0
ADRENAL: Number Examined	10	10	9	10	10	10	10	10	10	10	10
Vacuolization, cortical cells	1	0	0	0	0	0	0	0	0	0	0
URINARY BLADDER: Number Examined	10	0	0	10	10	10	10	10	10	10	10
Protein concretion	4	-	-	2	0	0	0	0	0	0	0
Section, parasites	3	-	-	4	2	0	0	1	0	0	2
Encapsulated abscess	0	-	-	0	0	0	0	0	0	0	0
TESTICLE: Number Examined	10	0	0	10	0	0	0	0	0	0	0
Atrophy	1	0	0	0	0	0	0	0	0	0	0
Interstitial edema	1	-	-	0	0	0	0	0	0	0	0
UTERUS: Number Examined	-	-	-	-	-	-	10	1	1	1	10
Hydrometre	-	-	-	-	-	-	0	0	0	0	0
Dilated	-	-	-	-	-	-	0	0	0	0	0
COLOR: Number Examined	9	0	0	10	0	0	9	1	1	1	10
Parasites	4	-	-	0	-	-	0	0	0	0	0

0 = Gross M = Microscopic

Table 29-5
Mean Body Weight - Dogs

Weeks of Doses	0.417		0.2083		0.104		0.000		Homo-ogeneity of Variance, Chi Sq.	Analysis of Variance, F
	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation		
0	9.37	1.38	8.23	0.61	9.00	1.04	9.13	1.39	5.3	1.09
				Weight on Day of First Dose, Kg.						
				Body Weight Change, Kg.						
1	0.27	0.43	0.47	0.58	0.43	0.37	0.43	0.29	2.4	0.26
2	0.60	0.73	0.90	0.82	0.67	0.71	0.53	0.59	0.5	0.30
3	0.67	0.74	0.97	0.95	0.77	0.89	0.73	0.66	0.8	0.18
4	0.67	0.79	1.03	0.92	0.97	0.92	0.77	0.82	0.2	0.25
5	0.77	0.96	1.07	0.94	0.87	0.98	0.77	0.86	0.1	0.14
6	0.83	0.99	1.33	1.07	1.20	0.91	1.10	0.92	0.1	0.28
7	0.83	1.13	1.13	1.19	1.10	1.11	0.83	0.96	0.2	0.13
8	0.87	1.38	1.33	1.26	0.90	1.13	1.03	0.94	1.7	0.19
9	0.70	1.03	1.37	1.35	0.87	1.22	0.90	1.02	0.6	0.36
10	0.67	1.21	1.57	1.29	1.07	1.28	1.17	1.17	0.1	0.53
11	0.67	1.09	1.43	1.49	1.13	1.31	1.07	1.09	0.8	0.38
12	0.83	1.10	1.37	1.46	1.13	1.24	1.07	1.11	0.5	0.19
13	1.20	1.28	1.70	1.52	1.43	1.46	1.37	1.08	0.6	0.14

Table 29-6

Mean Diet Consumption and Dosage for Dogs

Dates, 1965	Percentage of Glyoxal in the Diet of Dogs		Diet Consumption		Dosage; gm. Glyoxal/kg. body weight/dog/day (gross diet/kg. for controls)	
	0.417	0.2083	gm./dog/day		0.417	0.2083
7-27 to 8-23	301	292	302	277	0.129	0.069
8-24 to 9-16	290	314	312	299	0.120	0.070
9-17 to 10-27	253	277	275	243	0.102	0.060
					0.104	0.000

Table 29-7

Individual and Mean Biochemical and Hematological Results

Dog Number	No. of Doses	Blood Urea Nitrogen	Alkaline Phosphatase	Bromsul-falein Retention	Hemato-crit	Hemo-globin	Red Blood Cells ^x	White Blood Cells ^x
0.417% Glyoxal in the Diet								
80045	Prelim.	19.0	2.61	-	46.9	-	-	-
	11 weeks	21.8	0.85	2.20	50.5	16.8	6.95	11.6
80037	Prelim.	14.0	1.05	-	43.5	-	-	-
	11 weeks	16.0	1.05	1.85	51.0	17.0	7.42	6.9
80077	Prelim.	18.0	0.90	-	48.5	-	-	-
	11 weeks	20.0	1.00	3.40	54.0	18.8	7.23	4.3
80049	Prelim.	20.5	0.95	-	40.0	-	-	-
	11 weeks	24.5	1.20	2.20	42.0	13.0	5.61	10.3
80091	Prelim.	17.5	0.71	-	49.2	-	-	-
	11 weeks	19.5	0.70	4.20	52.1	18.0	6.67	14.1
80060	Prelim.	15.0	0.58	-	49.5	-	-	-
	11 weeks	15.5	0.55	2.45	52.0	17.0	7.40	7.4
Mean	Prelim.	17.3	1.13	-	47.1	-	-	-
	11 weeks	19.6	0.89	2.72	50.3	16.8	6.88	9.1
0.2083% Glyoxal in the Diet								
80047	Prelim.	20.0	0.85	-	59.5	-	-	-
	11 weeks	22.0	0.90	4.30	55.9	19.0	8.12	9.8
80036	Prelim.	15.0	0.95	-	48.0	-	-	-
	11 weeks	20.0	1.95	1.70	52.0	17.0	6.95	7.3
80082	Prelim.	15.0	1.75	-	48.5	-	-	-
	11 weeks	20.5	1.20	2.95	51.8	17.2	7.39	10.1
80048	Prelim.	21.5	1.05	-	37.0	-	-	-
	11 weeks	22.0	1.35	1.70	38.5	12.0	5.32	10.6
80094	Prelim.	15.0	0.85	-	42.3	-	-	-
	11 weeks	19.0	0.55	2.35	47.9	15.0	6.84	8.9
80059	Prelim.	15.0	0.55	-	40.2	-	-	-
	11 weeks	15.0	0.85	1.75	49.8	16.0	7.19	9.1
Mean	Prelim.	16.9	1.00	-	45.9	-	-	-
	11 weeks	19.8	1.13	2.46	49.3	16.0	6.97	9.3
0.104% Glyoxal in the Diet								
80074	Prelim.	14.5	0.52	-	49.0	-	-	-
	11 weeks	19.0	0.69	1.40	50.0	16.5	6.76	7.0
80035	Prelim.	22.5	3.35	-	40.1	-	-	-
	11 weeks	14.5	0.90	1.40	44.1	14.0	6.23	10.0
80083	Prelim.	15.0	0.85	-	43.1	-	-	-
	11 weeks	14.0	1.45	2.05	45.4	14.0	6.31	14.2

x Coulter Count

(Continued)

0028

Table 29-7
(Continued)

Dog Number	No. of Doses	Blood Urea Nitrogen	Alkaline Phosphatase	Bromsul-falein Retention	Hemato-crit	Hemo-globin	Red Blood Cells ^x	White Blood Cells ^x
80044	Prelim.	15.0	0.68	-	47.7	-	-	-
	11 weeks	20.5	0.75	3.45	51.9	17.5	7.30	7.4
80095	Prelim.	20.0	0.78	-	54.6	-	-	-
	11 weeks	20.5	0.80	3.35	50.0	16.0	7.05	10.9
80054	Prelim.	15.5	1.03	-	43.0	-	-	-
	11 weeks	20.5	1.15	1.95	50.5	17.0	6.81	11.4
Mean	Prelim.	17.1	1.20	-	46.2	-	-	-
	11 weeks	18.2	0.96	2.26	48.6	15.8	6.75	10.2
0.000% Glyoxal in the Diet								
80075	Prelim.	18.0	0.70	-	46.6	-	-	-
	11 weeks	15.0	0.67	3.30	50.9	17.0	7.18	12.0
80031	Prelim.	20.0	0.75	-	54.0	-	-	-
	11 weeks	15.0	0.85	2.20	45.8	14.2	6.78	7.3
80089	Prelim.	15.0	0.85	-	50.8	-	-	-
	11 weeks	16.8	0.90	4.05	50.5	15.5	6.76	13.2
80043	Prelim.	15.0	1.33	-	51.0	-	-	-
	11 weeks	19.3	0.85	1.90	49.4	16.0	6.64	12.0
80096	Prelim.	14.5	0.80	-	50.1	-	-	-
	11 weeks	20.0	0.93	2.75	40.6	14.5	6.15	10.9
80053	Prelim.	16.5	1.35	-	40.0	-	-	-
	11 weeks	19.0	1.55	2.30	43.0	14.1	6.22	6.5
Mean	Prelim.	16.5	0.96	-	48.8	-	-	-
	11 weeks	17.5	0.96	2.75	46.7	15.2	6.62	10.3
x Coulter Count								

Table 29-8

Individual and Mean Results of Differential Count

Dog Number	Differential Count - 200 Cells					
	<u>Baso-phil</u>	<u>Eosino-phil</u>	<u>Stabs</u>	<u>Polymorpho-nuclear</u>	<u>Lympho-cytes</u>	<u>Mono-cytes</u>
0.417% Glyoxal in the Diet						
80045	0	4	12	100	78	6
80037	1	2	9	109	71	8
80077	0	4	8	112	66	10
80049	0	2	8	112	72	6
80091	2	4	10	102	78	4
80060	3	1	9	103	75	9
Mean	1.0	2.8	9.3	106.3	73.3	7.2
0.2083% Glyoxal in the Diet						
80047	0	4	14	92	80	10
80036	1	1	8	106	76	8
80082	1	1	8	119	64	7
80048	0	0	4	104	84	8
80094	0	4	6	103	84	3
80059	2	0	8	118	66	6
Mean	0.7	1.7	8.0	107.0	75.7	7.0
0.104% Glyoxal in the Diet						
80074	0	4	13	109	63	11
80035	0	4	8	76	104	8
80083	1	2	11	121	58	7
80044	0	4	8	110	72	6
80095	2	1	7	101	78	11
80054	3	3	10	120	56	8
Mean	1.0	3.0	9.5	106.2	71.8	8.5
0.00% Glyoxal in the Diet						
80075	2	2	10	104	72	10
80031	3	3	8	114	68	4
80089	2	2	12	98	80	6
80043	0	2	6	116	66	10
80096	1	0	5	116	68	10
80053	0	0	9	113	71	7
Mean	1.3	1.5	8.3	110.2	70.8	7.8

Table 29-9
Synopsis of Micro and Gross Pathology; Dogs

	Males			Females			
	0.417	0.2083	0.104	Glyoxal; % in Diet	0.417	0.2083	0.104
Number Examined Grossly	3	3	3	3	3	3	3
<u>LIVER: Number Examined</u>	(M)	(M)	(M)	(M)	(M)	(M)	(M)
Round cell accumulations	0	0	0	3	3	3	3
Bile duct proliferation	3	2	1	3	2	1	2
Bile duct prominence	0	0	0	3	2	0	0
Cloudy swelling, hepatic cord cells	2	2	3	0	1	2	1
Vacuolated cord cells	0	0	0	2	0	0	0
Granulomas	0	0	0	0	0	0	0
<u>KIDNEY: Number Examined</u>	(M)	(M)	(M)	(M)	(M)	(M)	(M)
Chronic inflammatory cells	3	3	3	3	3	3	3
Round cell accumulations	0	1	0	0	0	0	0
Lymphoid accumulations	3	2	1	1	1	0	1
Calcium spicules	0	1	0	0	0	0	0
Calcium spicules	3	1	1	0	0	0	0
Protein casts	1	1	1	0	0	0	0
Pink casts	0	0	0	0	0	0	0
<u>LUNG: Number Examined</u>	(M)	(M)	(M)	(M)	(M)	(M)	(M)
Puncture wound (anesthetic injection)	3	3	3	3	3	3	3
Inhaled blood	1	0	0	0	0	0	0
Focal fibrosis	1	1	0	0	0	0	0
Foam cell foci	0	1	1	1	1	0	1
Round cell foci	0	1	0	0	0	0	0
Hemorrhage	0	0	1	0	0	0	0
Interstitial thickening	0	0	0	0	0	0	0
<u>HEART: Number Examined</u>	(M)	(M)	(M)	(M)	(M)	(M)	(M)
Nonpatent subaortic defect	3	1	0	3	3	0	3
Dilated lymphatic duct	0	0	0	0	0	0	0
<u>SPLEEN: Number Examined</u>	(G)	(G)	(G)	(G)	(G)	(G)	(G)
Mesodermoid	0	0	0	0	0	0	0
<u>MAMMARY GLAND: Number Examined</u>	(M)	(M)	(M)	(M)	(M)	(M)	(M)
Active	0	1	0	0	1	0	0
Secretion in alveoli	0	0	0	0	0	0	0
<u>ADRENAL: Number Examined</u>	(M)	(M)	(M)	(M)	(M)	(M)	(M)
Round cell accumulations	3	0	0	3	0	0	0
<u>THYROID: Number Examined</u>	(M)	(M)	(M)	(M)	(M)	(M)	(M)
Colloid cyst	3	0	0	3	0	0	0
Mucoid cyst	1	0	0	1	0	0	0
Follicular rests	0	0	0	0	0	0	0

(Continued)

Table 29-9
(Continued)

	Males			Females			
	0.417	0.2083	0.104	Glycocal; % in Diet	0.417	0.2083	0.104
<u>LYMPH NODE: Number Examined</u>	(M) 3	0	0	2	0	0	0
<u>Granuloma</u>	(M) 0	-	-	0	-	-	-
<u>ESOPHAGUS: Number Examined</u>	(M) 3	0	0	3	0	0	0
<u>Dilated esophageal gland ducts</u>	(M) 1	-	-	3	-	-	-
<u>TESTICLE: Number Examined</u>	(M) 3	0	0	1	-	-	-
<u>Immature</u>	(M) 2	-	-	-	-	-	-
<u>Calcium spicule</u>	(M) 0	-	-	3	-	-	-
<u>UTERUS: Number Examined</u>	(M) 0	-	-	1	-	-	-
<u>Inactive</u>	(M) -	-	-	-	-	-	-
<u>Highly cellular myometrium</u>	(M) -	-	-	2	-	-	-
<u>OVARY: Number Examined</u>	(M) -	-	-	3	-	-	-
<u>Cyst</u>	(M) -	-	-	1	-	-	-
<u>DIAPHRAGM: Number Examined</u>	(M) 3	0	0	3	0	0	0
<u>Round cell focus</u>	(M) 1	-	-	0	-	-	-
<u>COLON: Number Examined</u>	(M) 3	0	0	3	0	0	0
<u>Round cell focus</u>	(M) 1	-	-	0	-	-	-
<u>PANCREAS: Number Examined</u>	(M) 3	0	0	2	0	0	0
<u>Foamy-type cells</u>	(M) 0	-	-	1	-	-	-
<u>BRAIN: Number Examined</u>	(M) 3	0	0	3	0	0	0
<u>Hydrocephalus</u>	(G) 0	-	-	2	-	-	-
<u>Non-suppurative cuff</u>	(M) 0	-	-	3	-	-	-
<u>PITUITARY: Number Examined</u>	(M) 3	0	0	0	0	0	0
<u>Colloid cyst</u>	(M) 0	-	-	3	-	-	-

G = Gross M = Microscopic

Confidential
 Special Report 35-52
 4 Pages

R: 7-19-74

Chemical Hygiene Fellowship
 MELLON INSTITUTE
 Carnegie-Mellon University

Department of Transportation Corrosive Test

Results of 4-Hour Skin Exposure

(Samples Represent Current Production)

Author: C. S. Weil
 For: UNION CARBIDE CORPORATION, Chemicals and Plastics Operations Division

Contributor: N. I. Condra

Title 49 - Transportation
 Chapter 1 - Hazardous Materials Regulations Board
 Department of Transportation

*To amend §173.240 to provide a quantitative definition
 for corrosive materials by utilization of a 4-hr
 exposure time, using the rabbit test as described in
 21 CFR §191.11*

PRODUCT	CHF SAMPLE NO.	RESULTS AND CONCLUSION
Glyoxal, 40%	-320	0 of 6 rabbits with necrosis; NOT a corrosive material

0 0 3 3

Table 29-3
 Synopsis of Micro and Gross Pathology; Rats

	Males					Females				
	0.25	0.125	0.0625	Gm./Kg. in Diet	0.03125	0.125	0.0625	0.03125	0.015625	0.0078125
Number Examined Grossly:	10	10	10	10	10	10	10	10	10	10
LIVER: Number Examined	2	1	1	1	1	2	4	2	1	2
Bile duct prominence	1	1	1	1	1	0	0	0	1	2
Bile duct proliferation	0	3	1	1	1	2	2	3	2	1
Round cell accumulations	0	0	1	1	1	0	0	0	0	3
Granulomas	10	10	10	10	10	10	10	10	10	0
KIDNEY: Number Examined	0	0	0	0	0	0	0	0	0	10
Dilated renal pelvis	1	0	0	0	0	0	0	0	1	0
Dilated renal pelvis	0	1	0	0	0	0	0	1	1	0
Tubular degeneration	0	1	0	0	0	0	0	0	0	1
Dilated tubules	0	1	0	0	0	0	0	0	0	0
Pink casts	0	0	0	0	0	0	0	0	0	0
Calcium casts	0	0	0	0	0	0	0	0	0	0
Fibrosis	0	1	0	0	0	0	0	0	0	0
Round cell accumulations	0	2	0	0	0	0	0	0	2	0
Section of parasites	1	0	0	0	0	0	0	0	0	0
*Degree of involvement +2	0	0	0	0	0	0	0	0	0	0
+1	0	1	0	0	0	0	0	0	1	0
LUNG: Number Examined	10	10	10	10	10	10	10	10	10	10
Inhaled blood	0	0	0	0	0	0	0	0	0	0
Inhaled blood	0	0	0	0	0	0	0	0	0	0
Lipid foci	0	0	0	0	0	0	0	0	0	0
Bronchiectasis	0	0	0	0	0	0	0	0	0	0
Bronchiectasis	0	1	0	0	0	0	0	0	0	1
Chronic pneumonia	1	0	0	0	0	0	0	0	0	0
Chronic bronchopneumonia	1	0	0	0	0	0	0	0	0	0
Acute pneumonia	1	0	0	0	0	0	0	0	0	0
Interstitial pneumonia	0	0	0	0	0	0	0	0	0	0
Chronic abscessed pneumonia	0	1	0	0	0	0	0	0	0	0
Chronic abscessed bronchopneumonia	0	1	0	0	0	0	0	0	0	0
Atelectasis	0	0	0	0	0	0	0	0	0	0
Atelectasis	1	0	0	0	0	0	0	0	0	0
Suppurative bronchitis	0	0	0	0	0	0	0	0	0	0
Emphysema	0	0	0	0	0	0	0	0	0	0
Foam cell foci	2	1	1	1	1	0	0	0	0	0

* Degree of degeneration and quantity of kidney involved in reference to dilated tubules, casts, tubular degeneration and regeneration.

Table 29-3
(Continued)

	Males					Females					
	0.25	0.125	0.03125	Gm./Kg. in Diet	0.0625	0.03125	0.125	0.0625	0.03125	0.0625	0.00
Inflammatory cell foci	1	0	0	0	0	0	0	0	0	0	0
Round cell accumulations	2	1	1	2	1	1	1	1	1	1	1
Interstitial thickening	0	0	0	1	0	0	0	0	0	0	0
TRACHEA: Number Examined	10	3	5	10	10	1	1	1	1	1	10
Dilated tracheal glands	1	0	0	1	2	0	0	0	0	0	0
Chronic tracheitis	2	0	0	6	2	0	0	0	0	0	3
ESOPHAGUS: Number Examined	10	3	5	10	10	1	1	1	1	1	10
Hyperkeratosis	0	0	0	0	0	0	0	0	0	0	0
Dilatation	0	0	0	1	0	0	0	0	0	0	2
THYROID: Number Examined	9	3	5	10	10	1	1	1	1	1	10
Embryological duct formation	0	0	0	0	0	0	0	0	0	0	0
Hyperthrophied epithelial lining	0	0	0	1	0	0	0	0	0	0	0
HEART: Number Examined	10	10	10	10	10	10	10	10	10	10	10
Mast cell accumulations	0	1	0	1	0	0	0	0	0	0	0
Round cell accumulations	0	1	0	1	0	0	0	0	0	0	0
Markedly dilated ventricles	0	0	1	0	0	0	0	0	0	0	0
SPLEEN: Number Examined	9	10	10	10	10	10	10	10	10	10	10
Lymphoid hyperplasia	0	1	0	1	0	0	1	1	1	1	0
Hemosiderosis	0	0	0	1	0	0	0	0	0	0	0
ADRENAL: Number Examined	10	10	9	10	10	10	10	10	10	10	10
Vacuolization, cortical cells	1	0	0	0	0	0	0	0	0	0	0
URINARY BLADDER: Number Examined	10	0	0	10	10	10	10	10	10	10	10
Protein concretion	4	-	-	-	2	0	0	0	0	0	0
Section, parasites	3	-	-	-	4	0	0	0	0	0	2
Encapsulated abscess	0	-	-	-	0	0	1	0	0	0	0
TESTICLE: Number Examined	10	0	0	10	0	0	0	0	0	0	0
Atrophy	1	0	0	0	0	0	-	-	-	-	-
Interstitial edema	1	-	-	-	0	0	-	-	-	-	-
UTERUS: Number Examined	-	-	-	-	-	-	10	1	1	1	10
Hydrometre	-	-	-	-	-	-	0	0	0	0	0
Dilated	-	-	-	-	-	-	0	0	0	0	0
COLOR: Number Examined	9	0	0	10	0	0	9	1	1	1	10
Parasites	4	-	-	-	0	0	0	0	0	0	0

0 = Gross M = Microscopic