

TRADE SECRET

Study Title

H-24648 and H-24020: Repeated-Dose Oral Toxicity Study
14-Day Feeding Study in Mice

Laboratory Project ID: DuPont-5206

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STUDY COMPLETED ON: June 13, 2001

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CERTIFICATION

We, the undersigned, declare that this report provides an accurate evaluation of data obtained from this study.

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STUDY INFORMATION

Test Substance No. 1

9th Collective Nomenclature: [REDACTED]

Synonyms/Codes:

- [REDACTED]

- [REDACTED]

- H-24648

- [REDACTED]

Haskell Number: 24648

CAS Registry Number: [REDACTED]

Composition: [REDACTED]

Known Impurities: [REDACTED]

Physical Characteristics: Colorless liquid

Stability: The test substance appeared to be stable under the conditions of the study; no evidence of instability was observed.

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STUDY INFORMATION (CONTINUED)

Test Substance No. 2

9th Collective Nomenclature: [REDACTED]

Synonyms/Codes: • [REDACTED]
• [REDACTED]
• [REDACTED]
• [REDACTED]
• [REDACTED]
• H-24020
• [REDACTED]

Haskell Number: 24020

CAS Registry Number: [REDACTED]

Composition: [REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]

Known Impurities: [REDACTED]

Physical Characteristics: White solid

Stability: The test substance appeared to be stable under the conditions of the study; no evidence of instability was observed.

Sponsor: Daikin Industries, Ltd.
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Osaka 566-8585 Japan

Study Initiated/Completed: 03-Nov-2000 / (see report cover page)

In-Life Initiated/Completed: 06-Nov-2000 / 20-Nov-2000

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SUMMARY

This study evaluated the relative potency of the two test substances, H-24020 and H-24648, to produce liver enlargement in mice. Groups of 5 male and 5 female mice were exposed for 14 days to control diet (0 ppm) or diet containing H-24020 or H-24648. Dietary concentrations for the two test substances were 1, 3, 10, 30, 100, or 300 ppm. Body weights, food consumption, and clinical observations were evaluated weekly. After the 14-day exposure period, all non-fasted mice were sacrificed and livers were removed and weighed.

Mean overall (test day 0-14) daily intake of H-24020 in male mice exposed to 1, 3, 10, 30, 100, or 300 ppm was 0.20, 0.57, 1.84, 5.76, 24.1, or 62.4 mg/kg/day, respectively; mean daily intake in female mice was 0.28, 0.68, 2.52, 7.28, 26.0, or 102 mg/kg/day, respectively. Mean daily intake of H-24648 in male mice exposed to 1, 3, 10, 30, 100, or 300 ppm was 0.19, 0.57, 1.83, 6.41, 23.8, or 83.0 mg/kg/day, respectively; mean daily intake in female mice was 0.21, 0.66, 2.37, 7.38, 25.6, or 98.8 mg/kg/day, respectively.

No compound-related deaths occurred and no clinical observations were considered to be a direct response to exposure to either test substance.

Overall (test day 0-14) body weight loss was observed in male mice fed 100 or 300 ppm of each test substance. Body weight losses were also observed in female mice fed 100 or 300 ppm of H-24648 or 300 ppm of H-24020. This severe toxicity prevents meaningful interpretation of liver weight effects in these groups. Compound-related reductions (compared to control) in body weight and body weight gain were also observed in male mice fed 30 ppm H-24648. No reductions in food consumption were observed in any group, therefore, effects on body weight gain reflected effects on food efficiency in male and female mice exposed to both test substances.

Both test substances produced compound-related increases in liver weights compared to controls. No consistent differences in absolute or relative liver weight were observed between the two test substances.

In male mice, statistically significant increases in both absolute and relative liver weights were observed in all groups fed diets containing either test substance. With both test substances, a monotonic dose-response was observed in mice exposed up to 100 ppm. No further increases in liver weight were observed in either male 300 ppm group. This lack of further increase was attributed to the body weight loss in these mice.

In female mice, statistically significant increases in both absolute and relative liver weights were observed in mice fed diets that contained 3 ppm and above, with both test substances. With both test substances, a monotonic dose-response was observed up to 300 ppm, except for the absolute liver weight in female mice exposed to H-24020, where a plateau was observed in mice exposed to the two highest doses.

Dietary exposure to H-24020 and H-24648 produced similar effects on liver weight in mice. Exposure to H-24648 produced a small, but consistently greater, effect on in-life parameters compared to H-24020. Under the conditions of this study, the no-observed-effect level (NOEL) for increased liver weight was less than 1 ppm in male mice (0.20 and 0.19 mg/kg/day for H-24020 and H-24648, respectively) and 1 ppm in female mice (0.28 and 0.21 mg/kg/day for H-24020 and H-24648, respectively). No notable differences in the magnitude of liver weight effect were observed between the two test substances. Males were more sensitive than females to the in-life and liver weight effects of both test substances; however, the magnitude of effect at the highest exposure level was similar for males and females exposed to both test substances.

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INTRODUCTION

The test substances, H-24648 and H-24020, are isomeric mixtures of [REDACTED] containing different amounts of straight and branched chain forms of the test substance. H-24648 contains only the straight chain form, while H-24020 contains both straight chain and branched chain forms. The sample of H-24020 tested in this study contained approximately 75% straight chain and 25% branched chain forms. In a previous study,⁽¹⁾ the isomeric mixture contained in H-24020 produced elevated liver weights in male and female mice following dietary exposures of 3 ppm or greater for either 14 or 21 days. No increase was observed with dietary exposures of 1 ppm or less.⁽¹⁾ No data are available to assess the potential for the isomeric mixture contained in H-24648.

The objective of this study was to compare the 2 isomers for their relative potential to produce liver enlargement in male and female mice. The oral route of administration was selected because it was the route of exposure previously used to demonstrate liver enlargement with H-24020.⁽¹⁾

MATERIALS AND METHODS

A. Test Guidelines

None were applicable.

B. Test Substance

The following substances were tested:

- H-24648 (10% solution in water of active ingredient)
- H-24020 (white solid)

H-24648 was supplied by Daikin Industries, Ltd. H-24020 was supplied by DuPont Chemical Solutions Enterprise. The test substance appeared to be stable under the conditions of the study. No evidence of instability, such as a change in color or physical state, was observed.

C. Test Species

On 26-Oct-2000, 71 male and 71 female Crl:CD-1[®](ICR)BR mice, with an assigned birth date of 18-Sep-2000, were received from Charles River Laboratories, Inc., Raleigh, North Carolina.

The Crl:CD-1[®](ICR)BR strain was chosen because the Crl:CD-1[®] mouse was the strain and species used previously to evaluate liver responses to H-24020.⁽¹⁾ Furthermore, extensive background information is available from the literature, the supplier and previous studies at

Haskell Laboratory. This species/strain also is considered suitable relative to longevity, hardiness, sensitivity to the test substance, and low incidence of spontaneous diseases.

D. Animal Husbandry

1. Housing and Environmental Conditions

All mice were housed in stainless steel, wire-mesh cages suspended above cage boards. Mice were housed 3 per cage, sexes separate, prior to assignment to groups and individually after assignment to groups. Cage racks were relocated within the animal room each week. Animal rooms were maintained on a 12-hour light/dark cycle (fluorescent light) and at a temperature of $22 \pm 3^{\circ}\text{C}$ and a relative humidity of $50 \pm 20\%$.

2. Feed and Water

Tap water was provided *ad libitum*. All mice were fed PMI Nutrition International, Inc. Certified Rodent LabDiet® 5002 *ad libitum*. During the test (exposure) period, test substance was incorporated into the food at concentrations specified by study design.

3. Identification

Prior to assignment to groups, each mouse was temporarily identified by either the presence or absence of a colored tail mark and cage identification. The information on the cage labels included the unique 6-digit Haskell animal number and the individual identification number assigned to each mouse. After assignment to groups, the last 3-4 digits of the individual identification number were marked on the tail of each mouse.

4. Health Monitoring Program

As specified in the Haskell Laboratory animal health and environmental monitoring program, the following procedures are performed periodically to ensure that contaminant levels are below those that would be expected to impact the scientific integrity of the study:

- Water samples are analyzed for total bacterial counts, and the presence of coliforms, lead, and other contaminants.
- Feed samples are analyzed for total bacterial, spore and fungal counts.
- Samples from freshly washed cages and cage racks are analyzed to ensure adequate sanitation by the cagewashers.

Certified animal feed is used, guaranteed by the manufacturer to meet specified nutritional requirements and not to exceed stated maximum concentrations of key contaminants, including specified heavy metals, aflatoxin, chlorinated hydrocarbons, and organophosphates. The presence of these contaminants below the maximum concentration stated by the manufacturer would not be expected to impact the integrity of the study.

The animal health and environmental monitoring program is administered by the attending laboratory animal veterinarian. Data are maintained separately from study records and are not included in the final report. Evaluation of these data did not indicate any conditions that affected the validity of the study.

E. Quarantine and Pretest Period

Upon arrival at Haskell Laboratory, the mice were quarantined for 6 days of the 11 day pretest period. The mice were observed daily for any clinically apparent signs of disease or injury and were weighed 3 times.

On the bases of acceptable body weight gains and clinical observations, all mice were released from quarantine on test day -5 by the laboratory animal veterinarian designee.

F. Study Design

Group		No./Group	Dietary Conc. (ppm) ^a	Test Substance
Male	Female			
I	II	5	0 ppm	Control
III	IV	5	1 ppm	H-24020
V	VI	5	3 ppm	H-24020
VII	VIII	5	10 ppm	H-24020
IX	X	5	30 ppm	H-24020
XI	XII	5	100 ppm	H-24020
XIII	XIV	5	300 ppm	H-24020
XV	XVI	5	1 ppm	H-24648
XVII	XVIII	5	3 ppm	H-24648
XIX	XX	5	10 ppm	H-24648
XXI	XXII	5	30 ppm	H-24648
XXIII	XXIV	5	100 ppm	H-24648
XXV	XXVI	5	300 ppm	H-24648

^a Weight/weight concentration of test substance (adjusted for purity).

G. Assignment to Groups and Study Start

Mice were selected for study use on the bases of adequate body weight gain, freedom from any clinical signs of disease or injury, and a body weight within $\pm 20\%$ of the mean within a sex. The selected mice were distributed by computerized, stratified randomization so that there were no statistically significant differences among group body weight means within a sex.

Dietary administration of H-24648 and H-24020 began on test day 0 when the mice were approximately 42 days of age.

H. Diet Preparation and Administration

H-24648 was received from the sponsor as a 10% solution in water. H-24020 was dissolved in deionized water, to the same concentration of active ingredient as H-24648, prior to mixing with diet. The same vehicle, deionized water, was added to control diets at the same volume as that used in the high concentration diets. H-24020 and H-24648 were added to PMI Nutrition International, Inc. Certified Rodent LabDiet® 5002 and thoroughly mixed for 3 minutes. Control diets were mixed for the same period of time. Diets were prepared once, prior to the first day of dietary exposure, and refrigerated until used.

I. Body Weights

All mice were weighed once per week.

J. Food Consumption, Food Efficiency, and Intake of H-24648 and H-24020

The amount of food consumed by each mouse over each weighing interval was determined throughout the study. From these determinations and body weight data, mean daily food consumption, mean food efficiency, and mean daily intake of H-24648 and H-24020 were calculated.

K. Clinical Observations and Mortality

Cage-site examinations to detect moribund or dead mice and abnormal behavior and appearance among mice were conducted at least once daily throughout the study. At every weighing, each mouse was individually handled and examined for abnormal behavior and appearance. Animal 124579 in Group IV was found dead on test day 1 and discarded without pathological evaluation.

L. Liver Weights

Surviving, non-fasted mice were sacrificed following the 14-day exposure period (test day 14). Mice were euthanatized by carbon dioxide anesthesia and exsanguination. The order of sacrifice was random among all treatment groups within a sex.

The liver from one mouse in group XXIII (male; 100 ppm H-24648) was inadvertently not weighed. The livers from all other mice sacrificed by design were removed and weighed. Relative liver weights (percent of final body weight) were calculated, using final body weights determined just prior to necropsy.

M. Statistical Analyses

Significance was judged at $p < 0.05$. The following statistical methods were used to compare data from the test groups to data from the control group.

Parameter	Preliminary Test	Method of Statistical Analysis	
		If preliminary test is not significant	If preliminary test is significant
Body Weight Body Weight Gain Food Consumption Food Efficiency Liver Weight	Test for lack of trend ⁽²⁾	Sequential application ⁽³⁾ of the Jonckheere-Terpstra trend test ⁽⁴⁾	Preliminary tests for pairwise comparison
	OR ^a		
	Levene's test for homogeneity ⁽⁵⁾ and Shapiro-Wilk test ⁽⁶⁾ for normality ^b	One-way analysis of variance ⁽⁷⁾ followed with Dunnett's test ⁽⁸⁾	Kruskal-Wallis test ⁽⁸⁾ followed with Dunn's test ⁽⁹⁾
Incidence of Clinical Observations	None	Cochran-Armitage test for trend ^{(7)c}	

- a Pairwise comparisons and associated preliminary tests were only conducted if the test for lack of trend was significant.
- b If the Shapiro-Wilk test was not significant but Levene's test was significant, a robust version of Dunnett's test was used.
- c If the incidence was not significant, but a significant lack of fit occurred, then Fisher's exact test⁽¹⁰⁾ with a Bonferroni correction was used.

Absolute and relative (to body weight) liver weights were also compared between mice exposed to the two test substances using 2-way analysis of variance, followed by linear contrasts.⁽²⁾

RECORDS AND SAMPLE STORAGE

All data and records for analytical characterizations conducted by the sponsor will be archived by the sponsor.

Raw data and the final report will be retained at Haskell Laboratory, Newark, Delaware, or at Iron Mountain Records Management, Wilmington, Delaware

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RESULTS AND DISCUSSION

A. Mean Body Weights and Body Weight Gain (Tables 1-4, Appendix B)

In mice exposed to H-24020, exposure to 100 ppm (males only) or 300 ppm (males and females) produced reductions (compared to control) in mean final body weight and overall body weight gain (variable statistical significance). In males, mean final body weight in the 100 and 300 ppm groups was 84% and 72% of control, respectively. Both groups lost weight over the 14-day exposure period. Males exposed to 100 and 300 ppm H-24020 lost 8% and 23%, respectively, of initial body weight. Mean body weight and body weight gain in male groups exposed to 30 ppm or below were comparable to control. In females, mean final body weight in the 300 ppm group was 78% of control and this group lost 13% of initial body weight over the 14-day exposure period. The female groups exposed to 30 and 100 ppm had mean body weight loss over the first week of exposure (3% and 1% of initial body weight, respectively), but body weight gain over the second week exceeded that of control, resulting in overall (test day 0-14) body weight gain that was comparable to control. Some of this increased weight gain over the second week of exposure represents increased liver weight (observed at necropsy).

In mice exposed to H-24648, exposure to 30 ppm and above (males) and to 100 or 300 ppm (females) produced reductions (compared to control) in mean final body weight and overall body weight gain (variable statistical significance). Exposure to 100 or 300 ppm produced mean overall (test day 0-14) body weight loss in both sexes. Mean final body weight in males exposed to 100 and 300 ppm were 81% and 70% of control, respectively. Males exposed to 100 and 300 ppm of H-24648 lost 12% and 22%, respectively, of initial body weight. Mean final body weight in females exposed to 100 and 300 ppm were 89% and 76% of control, respectively. Females exposed to 100 and 300 ppm of H-24648 lost 2% and 18%, respectively, of initial body weight. In males exposed to 30 ppm, mean overall body weight gain was 53% of control (not statistically significant), due to body weight loss over the second week of exposure. Mean final body weight in this group was 93% of control. These differences were all considered biologically significant due to the magnitude of effect, although not all were statistically significant.

Males were more sensitive than females to the body weight effects of exposure to both compounds. Exposure to H-24648 produced effects on body weight and body weight gain that were generally of greater magnitude than those produced by exposure to H-24020.

B. Mean Food Consumption, Food Efficiency, and Intake of H-24648 and H-24020 (Tables 5-10, Appendix C)

No compound-related effects on food consumption were produced by exposure to H-24020 in male or female mice or by exposure to H-24648 in male mice. Statistically significant increases in mean food consumption over test days 0-7 and 0-14 were observed in female mice exposed to

300 ppm H-24648. Food consumption in female mice exposed to 100 ppm and below of H-24648 was comparable to control.

In mice exposed to H-24020, exposure to 100 ppm (males only) or 300 ppm (males and females) produced reductions in overall food efficiency, compared to controls. In mice exposed to H-24648, exposure to 30 ppm and above in males and 100 ppm and 300 ppm in females produced reductions in overall food efficiency, compared to controls. Food efficiency reflected body weight gain effects in all groups. The gender- and compound-related patterns observed with body weight gain were also observed with food efficiency

Mean overall (test day 0-14) daily intake of H-24020 in male mice exposed to 1, 3, 10, 30, 100, or 300 ppm was 0.20, 0.57, 1.84, 5.76, 24.1, or 62.4 mg/kg/day, respectively. Mean daily intake of H-24020 in female mice exposed to 1, 3, 10, 30, 100, or 300 ppm was 0.28, 0.68, 2.52, 7.28, 26.0, or 102 mg/kg/day, respectively. Mean daily intake of H-24648 in male mice exposed to 1, 3, 10, 30, 100, or 300 ppm was 0.19, 0.57, 1.83, 6.41, 23.8, and 83.0 mg/kg/day, respectively. Mean daily intake of H-24648 in female mice exposed to 1, 3, 10, 30, 100, or 300 ppm was 0.21, 0.66, 2.37, 7.38, 25.6, or 98.8 mg/kg/day, respectively.

Overall (test day 0-14) intake of H-24648 by male mice in the 300 ppm group was 33% higher than intake by the 300 ppm males exposed to H-24020. However, in general, mean daily intake of the 2 test substances was similar between groups of the same gender exposed to the same dietary concentration. Therefore, responses were compared in mice exposed to the same approximate administered dose, as well as the same dietary concentration.

C. Clinical Observations and Mortality (Tables 11-12, Appendix D)

One female mouse exposed to 1 ppm of H-24020 was found dead on test day 1. The cause of death was not determined but it was not considered to be compound related as there were no deaths in mice exposed to higher concentrations of H-24020. No other early deaths and no compound-related clinical observations occurred in mice exposed to H-24020.

No early deaths occurred in mice exposed to H-24648. Enophthalmus was observed in 2 male and 1 female mouse exposed to 300 ppm H-24648 (not statistically significant). This effect is not considered to be a direct compound-related effect, but may have been secondary to the severe body weight effect observed in this group. No other clinical signs were observed that were attributed to exposure to H-24648.

D. Liver Weights (Tables 11-12, Appendix E)

Exposure to H-24020 and H-24648 produced statistically significant increases in absolute and relative (liver weight/final body weight) liver weights in all treated male groups. Exposure to H-24020 and H-24648 produced statistically significant increases in absolute and relative liver weights in female groups exposed to 3 ppm and above.

In male mice exposed to H-24020, the increase in absolute and relative liver weights demonstrated a dose-response up to the 100 ppm concentration. Absolute and relative liver weights were also increased in the 300 ppm group (compared to control) but the magnitude of the effect was less than that of the 100 ppm group. Mean absolute liver weights in the 1-100 ppm groups ranged from 117%-275% of control; mean absolute liver weight in the 300 ppm group was 229% of control. Mean relative liver weights in the 1-100 ppm groups ranged from 116%-329% of control; mean relative liver weight in the 300 ppm group was 319% of control.

In male mice exposed to H-24648, the increase in absolute and relative liver weights demonstrated a dose-response up to the 100 ppm concentration. Absolute and relative liver weights were also increased in the 300 ppm group (compared to control) but the magnitude of the effect was less than that of the 100 ppm group. Mean absolute liver weights in the 1-100 ppm groups ranged from 131%-279% of control; mean absolute liver weight in the 300 ppm group was 213% of control. Mean relative liver weights in the 1-100 ppm groups ranged from 124%-344% of control; mean relative liver weight in the 300 ppm group was 305% of control. Therefore, exposure to H-24020 and H-24648 produced the same effect on liver weight, relative to control, in male mice.

In female mice exposed to H-24020, the increase in absolute and relative liver weights demonstrated a dose-response in mice exposed to 3-300 ppm. Mean absolute liver weights in the 3-300 ppm groups ranged from 108%-254% of control. Mean relative liver weights in the 3-300 ppm groups ranged from 114%-314% of control. Mean absolute and relative liver weights in the 1 ppm group were comparable to control (101% and 104% of control, respectively).

In female mice exposed to H-24648, the increase in absolute and relative liver weights demonstrated a dose-response in mice exposed to 3-300 ppm. Mean absolute liver weights in the 3-300 ppm groups ranged from 123%-275% of control. Mean relative liver weights in the 3-300 ppm groups ranged from 125%-358% of control. Mean absolute and relative liver weights in the 1 ppm group were higher than in control (106% and 111% of control, respectively). These differences were not statistically significant from control nor from each other and there was overlap between the ranges of the 2 groups. Therefore, the small increase in liver weight in the 1 ppm groups was not considered biologically significant, but was probably close to the threshold for liver weight effects. Thus, exposure to H-24020 and H-24648 produced the same effect on liver weight, relative to control, in female mice.

Similar general trends in liver weight responses were observed with both test substances, although males demonstrated greater sensitivity than females to the liver effects of both test substances. Males demonstrated enlarged livers in all exposed groups. Liver enlargement was not observed in females exposed to 1 ppm of H-24020. Small increases in liver weight were observed in females exposed to 1 ppm of H-24648 but the differences were not considered biologically significant. The magnitude of the liver weight effect reached a plateau and/or decreased at the highest concentration in males, while the effect increased or demonstrated a plateau up to the highest concentration tested in females. This was attributed to the body weight loss observed in these mice. The magnitude of the peak effect was similar in males and females.

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In a previous study,⁽¹⁾ increased liver weights were not observed in male mice fed 1 ppm of the isomeric mixture contained in H-24020. The mean daily intake of the test substance was not reported for that study; therefore, the reason for the difference in the no-observed-effect level cannot be determined.

There was no biologically significant difference observed in the liver response to the two test substances. Both demonstrated the same approximate NOEL, the same sex difference in sensitivity, and the same plateau and/or decrease in response at the highest concentration in males. At a given dietary concentration and for a given gender, the magnitude of response to H-24648 was almost always higher than that of the response to H-24020, when compared to control. When the absolute and relative liver weights were compared statistically between mice exposed to the 2 test substances, a few statistically significant differences were observed. However, they occurred sporadically (only at one or two doses per sex). There was no consistent pattern to the differences, and the magnitude of differences was small. Therefore, they were not considered to be biologically significant.

CONCLUSIONS

Under the conditions of this study, there was no biologically significant difference in the liver response of mice fed the two test substances.

There was no NOEL for liver weight gain in male mice exposed to H-24020 or H-24648, as increases in absolute and relative (liver weight/final body weight) liver weights were observed in all treated male groups. The NOEL for liver weight effects in female mice exposed to H-24020 and H-24648 was 1 ppm, as statistically significant increases in absolute and relative liver weights were observed in female groups exposed to 3 ppm and above. Exposure to H-24648 produced a small but consistently greater effect on in-life parameters than H-24020.

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REFERENCES

1. Kennedy G.L. (1987). Increase in mouse liver weight following feeding of [REDACTED] and related fluorochemicals. [REDACTED]
2. Draper, N.R. and Smith, H. (1981). *Applied Regression Analysis*, 2nd edition, pp 266-273. Wiley, New York.
3. Selwyn, M.R. (1995). The use of trend tests to determine a no-observable-effect level in animal safety studies. *Journal of the American College of Toxicology* 14(2), 158-168.
4. Jonckheere, A.R. (1954). A distribution-free K-sample test against ordered alternatives. *Biometrika* 41, 133-145.
5. Levene, H. (1960). Robust test for equality of variances. *Contributions to Probability and Statistics* (J. Olkin, ed.), pp 278-292. Stanford University Press, Palo Alto.
6. Shapiro, S.S. and Wilk, M.B. (1965). An analysis of variance test for normality (complete samples). *Biometrika* 52, 591-611.
7. Snedecor, G.W. and Cochran, W.G. (1967). *Statistical Methods*, 6th edition, pp 246-248 and 349-352. The Iowa State University Press, Iowa.
8. Dunnett, C.W. (1955). A multiple comparison procedure for comparing several treatments with a control. *J. Amer. Statist. Assoc.* 50, 1096-1121.
9. Kruskal, W.H. and Wallis, W.A. (1952). Use of ranks in one-criterion analysis of variance. *J. Amer. Statist. Assoc.* 47, 583-621.
10. Fisher, R.A. (1985). *Statistical Methods for Research Workers*, 13th edition. Haffner, New York.

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TABLES

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TABLE I
MEAN BODY WEIGHTS OF MALE MICE

Mean Body Weights (g) of Mice Fed Diet Containing H-24020									
	Group I 0 ppm	Group III 1 ppm	Group V 3 ppm	Group VII 10 ppm	Group IX 30 ppm	Group XI 100 ppm	Group XIII 300 ppm		
Day 0	29.3 1.8(5)	29.2 1.9(5)	29.4 2.6(5)	29.5 2.2(5)	29.5 1.7(5)	29.3 1.2(5)	30.1 1.8(5)		
Day 7	30.6 2.1(5)	31.3 1.7(5)	31.0 2.9(5)	31.2 2.2(5)	31.8 1.6(5)	29.3 1.2(5)	25.2# 0.9(5)		
Day 14	32.3 2.4(5)	32.8 2.0(5)	32.5 3.3(5)	32.8 2.4(5)	33.0 1.2(5)	27.0 1.3(5)	23.3# 1.1(5)		
Mean Body Weights (g) of Mice Fed Diet Containing H-24648									
	Group I 0 ppm	Group XV 1 ppm	Group XVII 3 ppm	Group XIX 10 ppm	Group XXI 30 ppm	Group XXIII 100 ppm	Group XXV 300 ppm		
Day 0	29.3 1.8(5)	30.0 1.4(5)	29.7 1.5(5)	28.0 1.8(5)	28.4 1.7(5)	29.7 3.0(5)	29.1 1.3(5)		
Day 7	30.6 2.1(5)	32.7 1.6(5)	31.6 2.0(5)	30.0 1.4(5)	30.3 2.0(5)	27.5# 2.3(5)	24.0# 2.2(5)		
Day 14	32.3 2.4(5)	34.1 1.8(5)	33.8 1.8(5)	32.2 2.0(5)	30.0 2.7(5)	26.2# 1.2(5)	22.7# 1.2(5)		

Data summarized as: Mean

Standard Deviation (n)

Statistical Methods: Trend test (Jonckheere-Terpstra).

Statistically significant difference at $p < 0.05$.

TABLE 2
MEAN BODY WEIGHTS OF FEMALE MICE

Mean Body Weights (g) of Mice Fed Diet Containing H-24020									
	Group II 0 ppm	Group IV 1 ppm	Group VI 3 ppm	Group VIII 10 ppm	Group X 30 ppm	Group XII 100 ppm	Group XIV 300 ppm		
Day 0	24.2 1.0(5)	23.7 0.6(5)	23.5 0.7(5)	23.5 1.4(5)	24.0 1.3(5)	23.9 1.2(5)	24.0 1.3(5)		
Day 7	25.0 1.7(5)	24.6 0.4(4)	24.8 0.7(5)	25.4 2.0(5)	23.4 0.9(5)	23.6 1.4(5)	21.3# 0.6(5)		
Day 14	26.8 0.8(5)	25.7 0.2(4)	25.3 1.0(5)	26.5 2.0(5)	26.5 0.9(5)	26.1 2.6(5)	21.0# 0.8(5)		

Mean Body Weights (g) of Mice Fed Diet Containing H-24648									
	Group II 0 ppm	Group XVI 1 ppm	Group XVIII 3 ppm	Group XX 10 ppm	Group XXII 30 ppm	Group XXIV 100 ppm	Group XXVI 300 ppm		
Day 0	24.2 1.0(5)	23.7 1.4(5)	24.0 1.2(5)	23.6 1.7(5)	23.1 1.3(5)	24.4 1.8(5)	25.0 1.3(5)		
Day 7	25.0 1.7(5)	24.6 1.5(5)	25.3 1.4(5)	24.2 1.9(5)	24.5 0.9(5)	24.4 1.4(5)	21.3# 1.6(5)		
Day 14	26.8 0.8(5)	25.6 1.7(5)	26.4 1.3(5)	26.0 2.6(5)	26.5 1.1(5)	23.8 1.9(5)	20.5# 1.2(5)		

Data summarized as: Mean

Standard Deviation (n)

Statistical Methods: Trend test (Jonckheere-Terpstra).

Statistically significant difference at $p < 0.05$.

TABLE 3
MEAN BODY WEIGHT GAINS OF MALE MICE

Mean Body Weight Gains (g) of Mice Fed Diet Containing H-24020									
	Group I 0 ppm	Group III 1 ppm	Group V 3 ppm	Group VII 10 ppm	Group IX 30 ppm	Group XI 100 ppm	Group XIII 300 ppm		
Day 0 - Day 7	1.4 0.5(5)	2.1 0.6(5)	1.6 0.4(5)	1.6 0.5(5)	2.3 0.5(5)	-0.0 1.0(5)	-4.9# 1.7(5)		
Day 7 - Day 14	1.7 0.4(5)	1.4 0.4(5)	1.5 0.5(5)	1.6 0.5(5)	1.2 0.5(5)	-2.3# 1.1(5)	-1.9# 1.1(5)		
Day 0 - Day 14	3.0 0.8(5)	3.5 0.8(5)	3.1 0.9(5)	3.3 0.6(5)	3.5 0.9(5)	-2.4 1.3(5)	-6.8# 2.1(5)		

Mean Body Weight Gains (g) of Mice Fed Diet Containing H-24648									
	Group I 0 ppm	Group XV 1 ppm	Group XVII 3 ppm	Group XIX 10 ppm	Group XXI 30 ppm	Group XXIII 100 ppm	Group XXV 300 ppm		
Day 0 - Day 7	1.4 0.5(5)	2.7 0.3(5)	1.8 0.9(5)	2.1 0.6(5)	1.9 1.0(5)	-2.2 2.9(5)	-5.1# 2.5(5)		
Day 7 - Day 14	1.7 0.4(5)	1.5 0.3(5)	2.3 0.4(5)	2.1 0.8(5)	-0.3 2.0(5)	-1.3# 1.4(5)	-1.3# 1.4(5)		
Day 0 - Day 14	3.0 0.8(5)	4.1 0.6(5)	4.1 0.6(5)	4.2 1.0(5)	1.6 1.7(5)	-3.5# 3.0(5)	-6.4# 1.5(5)		

Data summarized as: Mean

Standard Deviation (n)

Statistical Methods: Trend test (Jonckheere-Terpstra).

Statistically significant difference at $p < 0.05$.

TABLE 4
MEAN BODY WEIGHT GAINS OF FEMALE MICE

Mean Body Weight Gains (g) of Mice Fed Diet Containing H-24020									
	Group II 0 ppm	Group IV 1 ppm	Group VI 3 ppm	Group VIII 10 ppm	Group X 30 ppm	Group XII 100 ppm	Group XIV 300 ppm		
Day 0 - Day 7	0.8 1.1(5)	0.7 0.6(4)	1.3 0.8(5)	1.9 1.3(5)	-0.6 1.1(5)	-0.3# 0.5(5)	-2.6# 1.7(5)		
Day 7 - Day 14	1.8 1.1(5)	1.1 0.5(4)	0.5 0.5(5)	1.1 0.6(5)	3.1 0.7(5)	2.5 1.8(5)	-0.3@ 0.8(5)		
Day 0 - Day 14	2.6 0.7(5)	1.9 0.4(4)	1.8 1.2(5)	3.0 1.2(5)	2.5 0.7(5)	2.2 1.7(5)	-2.9 1.6(5)		

Mean Body Weights Gains (g) of Mice Fed Diet Containing H-24648									
	Group II 0 ppm	Group XVI 1 ppm	Group XVIII 3 ppm	Group XX 10 ppm	Group XXII 30 ppm	Group XXIV 100 ppm	Group XXVI 300 ppm		
Day 0 - Day 7	0.8 1.1(5)	0.8 0.5(5)	1.2 0.5(5)	0.6 0.4(5)	1.4 0.7(5)	0.1 1.9(5)	-3.7# 1.1(5)		
Day 7 - Day 14	1.8 1.1(5)	1.0 0.3(5)	1.1 0.6(5)	1.8 1.3(5)	1.9 0.3(5)	-0.6 1.1(5)	-0.8# 1.0(5)		
Day 0 - Day 14	2.6 0.7(5)	1.8 0.7(5)	2.3 0.9(5)	2.4 1.2(5)	3.3 0.4(5)	-0.6 2.6(5)	-4.5# 0.7(5)		

Data summarized as: Mean

Standard Deviation (n)

Statistical Methods: Trend test (Jonckheere-Terpstra) and/or non-parametric test (Dunn's).

Statistically significant difference at $p < 0.05$ using Jonckheere-Terpstra.

@ Statistically significant difference at $p < 0.05$ using Dunn's test.

TABLE 5
MEAN DAILY FOOD CONSUMPTION BY MALE MICE

Mean Daily Food Consumption (g) by Mice Fed Diet Containing H-24020									
	Group I 0 ppm	Group III 1 ppm	Group V 3 ppm	Group VII 10 ppm	Group IX 30 ppm	Group XI 100 ppm	Group XIII 300 ppm		
Day 0 - Day 7	5.9 0.7(5)	6.2 0.8(5)	5.6 0.3(5)	5.9 0.3(5)	5.7 0.5(5)	5.6 0.7(5)	5.0 0.9(5)		
Day 7 - Day 14	6.1 0.9(5)	6.3 0.5(5)	6.3 0.6(5)	5.9 0.3(5)	6.7 1.4(5)	7.8 1.1(5)	5.1 1.6(5)		
Day 0 - Day 14	6.0 0.7(5)	6.3 0.6(5)	6.0 0.3(5)	5.9 0.2(5)	6.2 0.9(5)	6.7 0.8(5)	5.0 1.2(5)		
Mean Daily Food Consumption (g) by Mice Fed Diet Containing H-24648									
	Group I 0 ppm	Group XV 1 ppm	Group XVII 3 ppm	Group XIX 10 ppm	Group XXI 30 ppm	Group XXIII 100 ppm	Group XXV 300 ppm		
Day 0 - Day 7	5.9 0.7(5)	6.2 0.3(5)	6.3 0.4(5)	5.9 0.2(5)	5.9 0.8(5)	6.6 1.6(5)	6.8 0.9(5)		
Day 7 - Day 14	6.1 0.9(5)	6.5 0.5(5)	6.1 0.5(5)	5.5 0.5(5)	6.8 0.8(5)	6.0 1.1(5)	6.1 0.9(5)		
Day 0 - Day 14	6.0 0.7(5)	6.4 0.4(5)	6.2 0.4(5)	5.7 0.3(5)	6.4 0.6(5)	6.3 1.2(5)	6.4 0.7(5)		

Data summarized as: Mean

Standard Deviation (n)

Statistical Methods: Trend test (Jonckheere-Terpstra).

Statistically significant difference at $p < 0.05$.

TABLE 6
MEAN DAILY FOOD CONSUMPTION BY FEMALE MICE

Mean Daily Food Consumption (g) by Mice Fed Diet Containing H-24020									
	Group II 0 ppm	Group IV 1 ppm	Group VI 3 ppm	Group VIII 10 ppm	Group X 30 ppm	Group XII 100 ppm	Group XIV 300 ppm		
Day 0 - Day 7	5.9 1.1(5)	7.2 2.6(4)	5.1 0.5(5)	6.0 0.8(5)	5.8 0.5(5)	6.0 1.0(5)	7.0 1.6(5)		
Day 7 - Day 14	6.2 1.3(5)	7.0 0.9(4)	6.3 0.9(5)	6.9 1.4(5)	6.3 0.9(5)	7.0 1.6(5)	7.4 1.6(5)		
Day 0 - Day 14	6.1 1.2(5)	7.1 1.6(4)	5.7 0.6(5)	6.5 1.0(5)	6.1 0.5(5)	6.5 1.0(5)	7.2 1.5(5)		

Mean Daily Food Consumption (g) by Mice Fed Diet Containing H-24648									
	Group II 0 ppm	Group XVI 1 ppm	Group XVIII 3 ppm	Group XX 10 ppm	Group XXII 30 ppm	Group XXIV 100 ppm	Group XXVI 300 ppm		
Day 0 - Day 7	5.9 1.1(5)	5.5 0.5(5)	5.5 0.5(5)	6.1 1.5(5)	5.7 0.8(5)	6.4 0.4(5)	8.0# 1.5(5)		
Day 7 - Day 14	6.2 1.3(5)	5.1 0.2(5)	5.8 1.0(5)	5.8 0.8(5)	6.8 1.9(5)	5.9 0.7(5)	5.7 0.6(5)		
Day 0 - Day 14	6.1 1.2(5)	5.3 0.4(5)	5.7 0.6(5)	5.9 1.1(5)	6.3 1.3(5)	6.1 0.4(5)	6.8# 1.0(5)		

Data summarized as: Mean

Standard Deviation (n)

Statistical Methods: Trend test (Jonckheere-Terpstra).

Statistically significant difference at $p < 0.05$.

TABLE 7
MEAN DAILY FOOD EFFICIENCY OF MALE MICE

Mean Daily Food Efficiency of Mice Fed Diet Containing H-24020
(g body weight gain/g food consumption)

	Group I 0 ppm	Group III 1 ppm	Group V 3 ppm	Group VII 10 ppm	Group IX 30 ppm	Group XI 100 ppm	Group XIII 300 ppm
Day 0 - Day 7	0.032 0.009 (5)	0.049 0.017 (5)	0.040 0.010 (5)	0.040 0.011 (5)	0.059 0.011 (5)	-0.002 0.029 (5)	-0.149# 0.070 (5)
Day 7 - Day 14	0.039 0.009 (5)	0.033 0.009 (5)	0.034 0.009 (5)	0.040 0.012 (5)	0.024 0.008 (5)	-0.043# 0.021 (5)	-0.059# 0.038 (5)
Day 0 - Day 14	0.036 0.007 (5)	0.041 0.009 (5)	0.037 0.008 (5)	0.040 0.007 (5)	0.040 0.006 (5)	-0.025 0.014 (5)	-0.105# 0.049 (5)

Mean Daily Food Efficiency of Mice Fed Diet Containing H-24648
(g body weight gain/g food consumption)

	Group I 0 ppm	Group XV 1 ppm	Group XVII 3 ppm	Group XIX 10 ppm	Group XXI 30 ppm	Group XXIII 100 ppm	Group XXV 300 ppm
Day 0 - Day 7	0.032 0.009 (5)	0.061 0.007 (5)	0.042 0.019 (5)	0.051 0.017 (5)	0.046 0.022 (5)	-0.058 0.076 (5)	-0.111# 0.065 (5)
Day 7 - Day 14	0.039 0.009 (5)	0.032 0.006 (5)	0.054 0.012 (5)	0.056 0.020 (5)	-0.005 0.044 (5)	-0.036# 0.036 (5)	-0.033# 0.038 (5)
Day 0 - Day 14	0.036 0.007 (5)	0.046 0.005 (5)	0.048 0.008 (5)	0.053 0.013 (5)	0.019 0.022 (5)	-0.046 0.046 (5)	-0.072# 0.019 (5)

Data summarized as: Mean

Standard Deviation (n)

Statistical Methods: Trend test (Jonckheere-Terpstra).

Statistically significant difference at $p < 0.05$.

TABLE 8
MEAN DAILY FOOD EFFICIENCY OF FEMALE MICE

Mean Daily Food Efficiency of Mice Fed Diet Containing H-24020
(g body weight gain/g food consumption)

	Group II 0 ppm	Group XVI 1 ppm	Group XVIII 3 ppm	Group XX 10 ppm	Group XXII 30 ppm	Group XXIV 100 ppm	Group XXVI 300 ppm
Day 0 - Day 7	0.017 0.026(5)	0.018 0.020(4)	0.038 0.024(5)	0.049 0.038(5)	-0.014 0.026(5)	-0.007 0.011(5)	-0.055# 0.030(5)
Day 7 - Day 14	0.044 0.029(5)	0.023 0.010(4)	0.010 0.008(5)	0.024 0.013(5)	0.070 0.009(5)	0.051 0.037(5)	-0.007 0.015(5)
Day 0 - Day 14	0.031 0.010(5)	0.020 0.008(4)	0.022 0.013(5)	0.036 0.018(5)	0.030 0.011(5)	0.025 0.020(5)	-0.030 0.015(5)

Mean Daily Food Efficiency of Mice Fed Diet Containing H-24648
(g body weight gain/g food consumption)

	Group II 0 ppm	Group XVI 1 ppm	Group XVIII 3 ppm	Group XX 10 ppm	Group XXII 30 ppm	Group XXIV 100 ppm	Group XXVI 300 ppm
Day 0 - Day 7	0.017 0.026(5)	0.022 0.011(5)	0.032 0.014(5)	0.015 0.011(5)	0.036 0.020(5)	0.002 0.043(5)	-0.066# 0.016(5)
Day 7 - Day 14	0.044 0.029(5)	0.028 0.010(5)	0.029 0.021(5)	0.044 0.028(5)	0.042 0.009(5)	-0.014 0.023(5)	-0.021# 0.026(5)
Day 0 - Day 14	0.031 0.010(5)	0.025 0.009(5)	0.031 0.016(5)	0.029 0.011(5)	0.039 0.010(5)	-0.006 0.031(5)	-0.048# 0.010(5)

Data summarized as: Mean

Standard Deviation (n)

Statistical Methods: Trend test (Jonckheere-Terpstra).

Statistically significant difference at $p < 0.05$.

TABLE 9

MEAN DAILY INTAKE OF THE TEST SUBSTANCE BY MALE MICE

Mean Daily Intake of H-24020 (mg/kg/day)										
	Group I 0 ppm	Group III 1 ppm	Group V 3 ppm	Group VII 10 ppm	Group IX 30 ppm	Group XI 100 ppm	Group XIII 300 ppm			
Day 0 - Day 7	0.00 0.00(5)	0.20 0.02(5)	0.55 0.06(5)	1.89 0.11(5)	5.38 0.67(5)	19.09 1.87(5)	59.87 11.72(5)			
Day 7 - Day 14	0.00 0.00(5)	0.19 0.02(5)	0.58 0.03(5)	1.80 0.08(5)	6.14 1.35(5)	29.07 4.72(5)	64.98 19.17(5)			
Day 0 - Day 14	0.00 0.00(5)	0.20 0.01(5)	0.57 0.03(5)	1.84 0.08(5)	5.76 0.97(5)	24.08 2.83(5)	62.43 14.81(5)			

Mean Daily Intake of H-24648 (mg/kg/day)										
	Group I 0 ppm	Group XV 1 ppm	Group XVII 3 ppm	Group XIX 10 ppm	Group XXI 30 ppm	Group XXIII 100 ppm	Group XXV 300 ppm			
Day 0 - Day 7	0.00 0.00(5)	0.19 0.01(5)	0.60 0.07(5)	1.97 0.11(5)	5.88 0.68(5)	24.44 6.76(5)	85.72 16.42(5)			
Day 7 - Day 14	0.00 0.00(5)	0.19 0.01(5)	0.54 0.07(5)	1.70 0.10(5)	6.94 1.38(5)	23.08 4.88(5)	80.35 12.02(5)			
Day 0 - Day 14	0.00 0.00(5)	0.19 0.01(5)	0.57 0.07(5)	1.83 0.07(5)	6.41 0.94(5)	23.76 5.52(5)	83.04 12.39(5)			

Data summarized as: Mean
Standard Deviation (n)

TABLE 10

MEAN DAILY INTAKE OF THE TEST SUBSTANCE BY FEMALE MICE

Mean Daily Intake of H-24020 (mg/kg/day)							
	Group II 0 ppm	Group XVI 1 ppm	Group XVIII 3 ppm	Group XX 10 ppm	Group XXII 30 ppm	Group XXIV 100 ppm	Group XXVI 300 ppm
Day 0 - Day 7	0.00 0.00(5)	0.29 0.11(4)	0.62 0.06(5)	2.38 0.44(5)	7.41 0.64(5)	25.33 4.13(5)	98.49 24.27(5)
Day 7 - Day 14	0.00 0.00(5)	0.27 0.03(4)	0.75 0.08(5)	2.66 0.76(5)	7.16 0.86(5)	26.70 5.43(5)	105.79 21.31(5)
Day 0 - Day 14	0.00 0.00(5)	0.28 0.07(4)	0.68 0.05(5)	2.52 0.58(5)	7.28 0.53(5)	26.01 3.82(5)	102.14 21.72(5)

Mean Daily Intake of H-24648 (mg/kg/day)							
	Group II 0 ppm	Group XVI 1 ppm	Group XVIII 3 ppm	Group XX 10 ppm	Group XXII 30 ppm	Group XXIV 100 ppm	Group XXVI 300 ppm
Day 0 - Day 7	0.00 0.00(5)	0.29 0.11(4)	0.62 0.06(5)	2.38 0.44(5)	7.41 0.64(5)	25.33 4.13(5)	98.49 24.27(5)
Day 7 - Day 14	0.00 0.00(5)	0.27 0.03(4)	0.75 0.08(5)	2.66 0.76(5)	7.16 0.86(5)	26.70 5.43(5)	105.79 21.31(5)
Day 0 - Day 14	0.00 0.00(5)	0.21 0.02(5)	0.66 0.08(5)	2.37 0.35(5)	7.38 1.49(5)	25.55 2.48(5)	98.84 18.75(5)

TABLE 11
SUMMARY OF CLINICAL OBSERVATIONS OF MALE MICE

Clinical Observations of Mice Fed Diet Containing H-24020

Group	I	III	V	VII	IX	XI	XIII
Concentration (ppm)	0	1	3	10	30	100	300
Animals in Group	5	5	5	5	5	5	5

There were no abnormalities detected.

Clinical Observations of Mice Fed Diet Containing H-24648

Group	I	XV	XVII	XIX	XXI	XXIII	XXV
Concentration (ppm)	0	1	3	10	30	100	300
Animals in Group	5	5	5	5	5	5	5
Eye Observations							
Enophthalmus							
Incidence	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (40%)
Mean onset (Days)							7

Incidence - The number of animals (percent of group) for which an observation was recorded.
Mean onset (Days) - The mean of the first test day an observation was recorded for that group.

Statistical Methods: Trend test (Cochran-Armitage).

There were no statistically significant differences at $p < 0.05$.

TABLE 12
SUMMARY OF CLINICAL OBSERVATIONS OF FEMALE MICE

Clinical Observations of Mice Fed Diet Containing H-24020

Group	II	IV	VI	VIII	X	XII	XIV
Concentration (ppm)	0	1	3	10	30	100	300
Animals in Group	5	5	5	5	5	5	5
Wound							
Superficial							
Incidence	0 (0%)	0 (0%)	1 (20%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Mean onset (Days)			7				
Misshapen Tail							
Incidence	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (20%)
Mean onset (Days)							7

Clinical Observations of Mice Fed Diet Containing H-24648

Group	II	XVI	XVIII	XX	XXII	XXIV	XXVI
Concentration (ppm)	0	1	3	10	30	100	300
Animals in Group	5	5	5	5	5	5	5
Eye Observations							
Enophthalmus							
Incidence	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (20%)
Mean onset (Days)							7

Incidence - The number of animals (percent of group) for which an observation was recorded.
Mean onset (Days) - The mean of the first test day an observation was recorded for that group.
Statistical Methods: Trend test (Cochran-Armitage).
There were no statistically significant differences at $p < 0.05$.

TABLE 13
MEAN FINAL BODY AND LIVER WEIGHTS OF MALE MICEMean Final Body Weights, Absolute Liver Weights, and Relative Liver Weights (g)
of Mice Fed Diet Containing H-24020

WEIGHT	Group I 0 ppm	Group III 1 ppm	Group V 3 ppm	Group VII 10 ppm	Group IX 30 ppm	Group XI 100 ppm	Group XIII 300 ppm
LIVER	1.72 0.20 (5)	2.02# 0.11 (5)	2.22# 0.16 (5)	2.79# 0.27 (5)	4.01# 0.22 (5)	4.72# 0.46 (5)	3.95# 0.19 (5)
FINAL BODY	32.30 2.39 (5)	32.78 2.02 (5)	32.50 3.34 (5)	32.80 2.40 (5)	32.98 1.20 (5)	26.98 1.29 (5)	23.28# 1.07 (5)
LIVER/ FINAL BODY * 100	5.32 0.44 (5)	6.17# 0.32 (5)	6.85# 0.21 (5)	8.50# 0.38 (5)	12.18# 0.88 (5)	17.48#* 0.91 (5)	16.98# 1.09 (5)

Mean Final Body Weights, Absolute Liver Weights, and Relative Liver Weights (g)
of Mice Fed Diet Containing H-24648

WEIGHT	Group I 0 ppm	Group XV 1 ppm	Group XVII 3 ppm	Group XIX 10 ppm	Group XXI 30 ppm	Group XXIII 100 ppm	Group XXV 300 ppm
LIVER	1.72 0.20 (5)	2.26# 0.11 (5)	2.56# 0.31 (5)	2.96# 0.30 (5)	4.10# 0.44 (5)	4.79# 0.41 (4)	3.67# 0.35 (5)
FINAL BODY	32.30 2.39 (5)	34.12 1.81 (5)	33.84 1.84 (5)	32.18 2.03 (5)	29.98 2.69 (5)	26.20# 1.16 (5)	22.68# 1.25 (5)
LIVER/ FINAL BODY * 100	5.32 0.44 (5)	6.62# 0.18 (5)	7.56# 0.67 (5)	9.20# 0.53 (5)	13.69# 0.88 (5)	18.30#* 1.79 (4)	16.22# 1.87 (5)

Data summarized as: Mean

Standard Deviation (n)

Statistically significant difference from control at $p < 0.05$ by Jonckheere-Terpstra trend test.* Statistically significant difference between test substances at $p < 0.05$ by linear contrasts test.

TABLE 14

MEAN FINAL BODY AND LIVER WEIGHTS OF FEMALE MICE

Mean Final Body Weights, Absolute Liver Weights, and Relative Liver Weights (g)
of Mice Fed Diet Containing H-24020

WEIGHT	Group II 0 ppm	Group IV 1 ppm	Group VI 3 ppm	Group VIII 10 ppm	Group X 30 ppm	Group XII 100 ppm	Group XIV 300 ppm
LIVER	1.44 0.15(5)	1.45 0.04(4)	1.56# 0.07(5)	2.12# 0.18(5)	2.95# 0.16(5)	3.67# 0.48(5)	3.56#* 0.36(5)
FINAL BODY	26.78 0.81(5)	25.73 0.22(4)	25.32 1.01(5)	26.54 2.02(5)	26.50 0.91(5)	26.12 2.65(5)	21.02# 0.79(5)
LIVER/ FINAL BODY * 100	5.40 0.61(5)	5.64 0.19(4)	6.16# 0.26(5)	8.01#* 0.80(5)	11.14# 0.35(5)	14.08# 1.56(5)	16.96# 1.63(5)

Mean Final Body Weights, Absolute Liver Weights, and Relative Liver Weights (g)
of Mice Fed Diet Containing H-24648

WEIGHT	Group I 0 ppm	Group XV 1 ppm	Group XVII 3 ppm	Group XIX 10 ppm	Group XXI 30 ppm	Group XXIII 100 ppm	Group XXV 300 ppm
LIVER	1.44 0.15(5)	1.53 0.07(5)	1.78# 0.19(5)	2.38# 0.34(5)	3.15# 0.19(5)	3.71# 0.52(5)	3.97#* 0.58(5)
FINAL BODY	26.78 0.81(5)	25.56 1.73(5)	26.36 1.25(5)	25.98 2.59(5)	26.48 1.07(5)	23.78 1.85(5)	20.48# 1.22(5)
LIVER/ FINAL BODY * 100	5.40 0.61(5)	5.99 0.27(5)	6.75# 0.53(5)	9.14#* 0.38(5)	11.89# 0.42(5)	15.59# 1.42(5)	19.33# 2.03(5)

Data summarized as: Mean

Standard Deviation (n)

Statistically significant difference from control at $p < 0.05$ by Jonckheere-Terpstra trend test.

* Statistically significant difference between test substances at $p < 0.05$ by linear contrasts test.

APPENDICES

Company Sanitized. Does not contain TSCA CRJ

APPENDIX A
INDIVIDUAL BODY WEIGHTS

Company Sanitized. Does not contain TSCA CBI

Individual Body Weights (g) of Control Mice

	Day 0	Day 7	Day 14
Male, I Control			
124503	31.9	33.2	35.3
124504	28.0	29.0	30.7
124505	27.8	28.8	30.4
124506	30.3	32.6	34.5
124507	28.4	29.6	30.6

Female, II Control

124574	24.1	24.7	26.1
124575	24.1	23.3	26.1
124576	24.8	26.7	27.8
124577	22.7	23.3	26.4
124578	25.2	26.8	27.5

Company Sanitized. Does not contain TSCA CBI

Individual Body Weights (g) of Mice Fed Diet Containing H-24020

	Day 0	Day 7	Day 14
Male, III 1 ppm H-24020			
124508	30.4	32.7	34.7
124509	27.1	30.2	31.4
124510	27.6	29.2	30.2
124511	31.8	33.4	34.8
124512	29.3	31.2	32.8

Male, V 3 ppm H-24020			
124513	29.9	31.4	32.7
124514	29.5	30.6	32.0
124515	25.7	26.9	28.0
124516	29.0	30.9	32.4
124517	32.9	35.0	37.4

Male, VII 10 ppm H-24020			
124518	29.4	31.8	33.1
124519	26.8	28.1	29.5
124520	28.2	30.0	31.9
124521	30.9	32.2	33.4
124522	32.3	33.7	36.1

Male, IX 30 ppm H-24020			
124523	32.1	34.0	34.4
124524	30.3	32.6	33.5
124525	28.5	31.1	32.3
124526	27.8	29.7	31.3
124527	28.7	31.7	33.4

Male, XI 100 ppm H-24020			
124528	30.5	30.9	27.2
124529	27.7	28.6	26.9
124530	30.2	30.2	29.0
124531	28.6	28.9	25.6
124532	29.7	28.0	26.2

Male, XIII 300 ppm H-24020			
124533	30.3	24.4	23.8
124534	29.2	24.4	21.5
124535	32.4	25.4	23.1
124536	27.7	25.0	24.2
124537	30.7	26.6	23.8

Company Sanitized. Does not contain TSCA CBI

Individual Body Weights (g) of Mice Fed Diet Containing H-24020

	Day 0	Day 7	Day 14
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Female, IV 1 ppm H-24020

124579	23.0		
124580	24.2	24.4	25.8
124582	23.1	24.7	25.4
124583	24.3	25.1	25.8
124640	23.8	24.1	25.9

Female, VI 3 ppm H-24020

124584	22.9	25.6	26.8
124585	23.3	24.1	24.7
124586	23.3	24.2	24.2
124587	23.3	24.9	25.1
124588	24.7	25.4	25.8

Female, VIII 10 ppm H-24020

124589	22.4	23.1	23.7
124590	23.8	26.2	27.0
124591	21.9	23.6	25.3
124592	23.9	27.7	28.4
124593	25.5	26.4	28.3

Female, X 30 ppm H-24020

124594	23.8	23.3	26.0
124596	22.1	22.0	25.4
124597	23.7	24.5	26.9
124598	24.8	23.4	26.4
124641	25.7	23.7	27.8

Female, XII 100 ppm H-24020

124599	23.2	23.0	22.4
124600	24.9	25.1	28.2
124601	22.2	21.5	24.4
124602	24.1	24.2	27.0
124603	25.2	24.4	28.6

Female, XIV 300 ppm H-24020

124604	23.5	21.3	20.2
124605	23.9	21.9	21.2
124606	22.8	21.8	22.2
124607	23.5	21.1	20.4
124608	26.1	20.5	21.1

Company Sanitized. Does not contain TSCA CBI

Individual Body Weights (g) of Mice Fed Diet Containing H-24648

Day 0 Day 7 Day 14

Male, XV 1 ppm H-24648

124538	30.6	33.4	34.9
124539	30.9	33.6	35.2
124540	28.0	30.5	32.0
124541	31.3	34.3	36.1
124542	29.2	31.5	32.4

Male, XVII 3 ppm H-24648

124543	28.5	30.0	32.8
124544	28.1	29.2	31.4
124545	31.8	33.0	35.6
124546	30.7	33.9	35.7
124547	29.6	31.8	33.7

Male, XIX 10 ppm H-24648

124548	30.5	31.8	34.7
124549	26.5	29.1	31.5
124550	26.8	29.6	31.8
124552	29.2	31.1	33.5
124569	26.8	28.6	29.4

Male, XXI 30 ppm H-24648

124553	29.9	30.4	32.5
124554	27.7	30.4	29.2
124555	25.9	27.2	25.9
124556	28.3	30.9	32.3
124557	30.1	32.6	30.0

Male, XXIII 100 ppm H-2468

124558	29.4	27.7	26.6
124559	27.6	23.4	24.3
124560	26.8	28.8	27.3
124561	34.6	29.0	26.8
124562	30.2	28.6	26.0

Male, XXV 300 ppm H-24648

124563	30.6	22.7	22.9
124564	28.2	27.0	23.9
124566	28.7	23.9	23.3
124567	30.2	25.1	22.7
124570	27.6	21.2	20.6

Company Sanitized. Does not contain TSCA CBI

Individual Body Weights (g) of Mice Fed Diet Containing H-24648

Day 0 Day 7 Day 14

Female, XVI 1 ppm H-24648

124609	23.4	23.6	24.3
124610	24.6	25.9	27.4
124611	22.4	23.1	24.1
124612	22.5	23.8	24.5
124613	25.7	26.4	27.5

Female, XVIII 3 ppm H-24648

124614	25.5	27.1	27.7
124615	23.8	24.2	24.9
124616	22.5	24.0	26.1
124617	23.6	24.8	25.5
124618	24.8	26.3	27.6

Female, XX 10 ppm H-24648

124619	22.5	22.6	24.1
124620	24.4	25.5	26.2
124621	21.7	22.2	24.6
124622	23.1	23.9	24.6
124623	26.1	26.6	30.4

Female, XXII 30 ppm H-24648

124624	21.6	23.1	24.9
124625	23.3	24.8	26.6
124626	22.3	24.7	26.3
124627	23.5	24.7	26.7
124628	25.0	25.4	27.9

Female, XXIV 100 ppm H-24648

124629	23.0	22.1	21.8
124630	24.7	24.7	24.4
124632	24.4	24.4	22.1
124633	27.2	25.2	24.3
124639	22.5	25.7	26.3

Female, XXVI 300 ppm H-24648

124634	25.0	23.1	21.2
124635	23.8	19.5	20.2
124636	24.1	20.6	19.2
124637	24.8	20.3	19.6
124638	27.2	22.8	22.2

Company Sanitized. Does not contain TSCA CBI

APPENDIX B
INDIVIDUAL FOOD CONSUMPTION

Company Sanitized. Does not contain TSCA CBI

Company Sanitized. Does not contain TSCA CBI

Individual Food Consumption (g/day) by Control Mice

	Day 7	Day 14
Male, I Control		
124503	6.3	7.3
124504	5.1	5.0
124505	5.7	5.9
124506	6.9	6.4
124507	5.6	5.9

Female, II Control		
124574	6.3	6.6
124575	4.9	5.2
124576	7.7	8.3
124577	5.3	5.9
124578	5.2	5.3

Company Sanitized. Does not contain TSCA CBI

Individual Food Consumption (g/day) by Mice Fed Diet Containing H-24020

	Day 7	Day 14
Male, III 1 ppm H-24020		
124508	7.4	6.8
124509	5.8	6.3
124510	5.7	6.3
124511	6.6	6.7
124512	5.5	5.5

Male, V 3 ppm H-24020		
124513	5.1	6.6
124514	5.8	5.8
124515	5.7	5.6
124516	5.7	6.8
124517	5.9	6.9

Male, VII 10 ppm H-24020		
124518	5.9	6.0
124519	5.4	5.5
124520	6.2	5.8
124521	5.8	6.2
124522	6.1	6.0

Male, IX 30 ppm H-24020		
124523	5.3	5.4
124524	5.2	5.8
124525	5.6	6.3
124526	6.2	7.2
124527	6.2	9.0

Male, XI 100 ppm H-24020		
124528	5.7	6.9
124529	5.3	6.5
124530	6.4	8.4
124531	6.0	9.2
124532	4.7	8.1

Male, XIII 300 ppm H-24020		
124533	5.3	4.2
124534	4.8	5.0
124535	3.9	3.7
124536	6.4	7.8
124537	4.7	4.6

Company Sanitized. Does not contain TSCA CBI

Individual Food Consumption (g/day) by Mice Fed Diet Containing H-24020

	Day 7	Day 14
Female, IV 1 ppm H-24020		
124580	5.3	7.3
124582	4.8	5.7
124583	8.0	7.6
124640	10.5	7.5

Female, VI 3 ppm H-24020		
124584	5.1	7.8
124585	5.7	6.1
124586	4.7	5.5
124587	4.6	5.9
124588	5.4	6.2

Female, VIII 10 ppm H-24020		
124589	6.9	9.1
124590	6.3	6.4
124591	5.4	7.4
124592	4.9	5.3
124593	6.4	6.6

Female, X 30 ppm H-24020		
124594	5.7	6.0
124596	5.2	6.0
124597	5.4	6.0
124598	6.5	5.6
124641	6.0	8.0

Female, XII 100 ppm H-24020		
124599	6.4	6.4
124600	7.4	6.7
124601	5.9	7.1
124602	4.8	5.1
124603	5.4	9.4

Female, XIV 300 ppm H-24020		
124604	8.9	8.4
124605	4.9	6.5
124606	7.4	8.9
124607	5.8	5.1
124608	8.0	8.2

Company Sanitized. Does not contain TSCA CBI

Individual Food Consumption (g/day) by Mice Fed Diet Containing H-24648

	Day 7	Day 14
Male, XV 1 ppm H-24648		
124538	6.1	6.5
124539	6.8	7.1
124540	6.3	6.3
124541	6.1	6.8
124542	6.0	5.8

Male, XVII 3 ppm H-24648		
124543	6.6	6.0
124544	6.7	6.8
124545	5.7	5.6
124546	6.5	5.7
124547	6.0	6.2

Male, XIX 10 ppm H-24648		
124548	5.9	5.7
124549	5.8	4.9
124550	5.6	5.6
124552	6.0	6.0
124569	6.2	5.0

Male, XXI 30 ppm H-24648		
124553	5.6	6.7
124554	7.2	7.7
124555	5.3	7.6
124556	5.5	6.0
124557	6.1	6.2

Male, XXIII 100 ppm H-2468		
124558	5.2	6.2
124559	7.6	7.4
124560	8.0	6.4
124561	4.7	4.5
124562	7.8	5.6

Male, XXV 300 ppm H-24648		
124563	5.5	5.8
124564	6.6	5.0
124566	7.6	7.3
124567	6.5	6.6
124570	7.8	5.6

Company Sanitized. Does not contain TSCA CBI

Individual Food Consumption (g/day) by Mice Fed Diet Containing H-24648

Day 7 Day 14

Female, XVI 1 ppm H-24648

124609	5.6	5.3
124610	5.8	5.1
124611	5.4	4.9
124612	6.0	5.4
124613	4.6	4.8

Female, XVIII 3 ppm H-24648

124614	5.8	5.4
124615	5.6	7.4
124616	4.7	4.7
124617	5.6	5.7
124618	5.9	5.8

Female, XX 10 ppm H-24648

124619	6.5	6.1
124620	5.2	4.8
124621	4.8	5.2
124622	5.5	5.9
124623	8.6	6.8

Female, XXII 30 ppm H-24648

124624	5.5	6.7
124625	5.0	4.8
124626	5.5	5.6
124627	7.1	9.6
124628	5.6	7.4

Female, XXIV 100 ppm H-24648

124629	6.4	5.2
124630	5.8	5.7
124632	6.4	6.9
124633	6.9	6.1
124639	6.4	5.4

Female, XXVI 300 ppm H-24648

124634	5.9	5.1
124635	10.1	6.4
124636	8.5	5.4
124637	7.8	5.4
124638	7.5	6.2

Company Sanitized. Does not contain TSCA CBI

APPENDIX C
INDIVIDUAL CLINICAL OBSERVATIONS AND MORTALITY

Company Sanitized. Does not contain TSCA CB!

Individual Clinical Observations and Mortality of Control Mice

Male, I Control

<u>Animal</u>	<u>Observation</u>	<u>Days</u>
124503	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124504	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124505	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124506	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124507	General observation, No Abnormality Detected Sacrificed by design	0-14 14

Female, II Control

<u>Animal</u>	<u>Observation</u>	<u>Days</u>
124574	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124575	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124576	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124577	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124578	General observation, No Abnormality Detected Sacrificed by design	0-14 14

Individual Clinical Observations and Mortality of Mice Fed Diet Containing H-24020

Male, III 1 ppm H-24020

<u>Animal</u>	<u>Observation</u>	<u>Days</u>
124508	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124509	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124510	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124511	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124512	General observation, No Abnormality Detected Sacrificed by design	0-14 14

Male, V 3 ppm H-24020

<u>Animal</u>	<u>Observation</u>	<u>Days</u>
124513	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124514	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124515	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124516	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124517	General observation, No Abnormality Detected Sacrificed by design	0-14 14

H-24648 and H-24020: Repeated-Dose Oral Toxicity
14-Day Feeding Study in Mice

DuPont-5206

Individual Clinical Observations and Mortality of Mice Fed Diet Containing H-24020

Male, VII 10 ppm H-24020

<u>Animal</u>	<u>Observation</u>	<u>Days</u>
124518	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124519	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124520	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124521	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124522	General observation, No Abnormality Detected Sacrificed by design	0-14 14

Male, IX 30 ppm H-24020

<u>Animal</u>	<u>Observation</u>	<u>Days</u>
124523	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124524	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124525	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124526	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124527	General observation, No Abnormality Detected Sacrificed by design	0-14 14

Individual Clinical Observations and Mortality of Mice Fed Diet Containing H-24020

Male, XI 100 ppm H-24020

<u>Animal</u>	<u>Observation</u>	<u>Days</u>
124528	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124529	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124530	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124531	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124532	General observation, No Abnormality Detected Sacrificed by design	0-14 14

Male, XIII 300 ppm H-24020

<u>Animal</u>	<u>Observation</u>	<u>Days</u>
124533	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124534	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124535	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124536	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124537	General observation, No Abnormality Detected Sacrificed by design	0-14 14

H-24648 and H-24020: Repeated-Dose Oral Toxicity
14-Day Feeding Study in Mice

DuPont-5206

Individual Clinical Observations and Mortality of Mice Fed Diet Containing H-24020

Female, IV 1 ppm H-24020

<u>Animal</u>	<u>Observation</u>	<u>Days</u>
124579	General observation, No Abnormality Detected Found dead in cage.	0-1 1
124580	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124582	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124583	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124640	General observation, No Abnormality Detected Sacrificed by design	0-14 14

Female, VI 3 ppm H-24020

<u>Animal</u>	<u>Observation</u>	<u>Days</u>
124584	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124585	General observation, No Abnormality Detected Wound, Superficial, Neck Sacrificed by design	0, 14 7 14
124586	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124587	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124588	General observation, No Abnormality Detected Sacrificed by design	0-14 14

H-24648 and H-24020: Repeated-Dose Oral Toxicity
14-Day Feeding Study in Mice

DuPont-5206

Individual Clinical Observations and Mortality of Mice Fed Diet Containing H-24020

Female, VIII 10 ppm H-24020

<u>Animal</u>	<u>Observation</u>	<u>Days</u>
124589	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124590	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124591	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124592	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124593	General observation, No Abnormality Detected Sacrificed by design	0-14 14

Female, X 30 ppm H-24020

<u>Animal</u>	<u>Observation</u>	<u>Days</u>
124594	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124596	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124597	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124598	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124641	General observation, No Abnormality Detected Sacrificed by design	0-14 14

H-24648 and H-24020: Repeated-Dose Oral Toxicity
14-Day Feeding Study in Mice

DuPont-5206

Individual Clinical Observations and Mortality of Mice Fed Diet Containing H-24020

Female, XII 100 ppm H-24020

<u>Animal</u>	<u>Observation</u>	<u>Days</u>
124599	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124600	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124601	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124602	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124603	General observation, No Abnormality Detected Sacrificed by design	0-14 14

Female, XIV 300 ppm H-24020

<u>Animal</u>	<u>Observation</u>	<u>Days</u>
124604	General observation, No Abnormality Detected Misshapen Observations, Tail Sacrificed by design	0-7 14 14
124605	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124606	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124607	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124608	General observation, No Abnormality Detected Sacrificed by design	0-14 14

Individual Clinical Observations and Mortality of Mice Fed Diet Containing H-24648

Male, XV 1 ppm H-24648

<u>Animal</u>	<u>Observation</u>	<u>Days</u>
124538	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124539	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124540	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124541	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124542	General observation, No Abnormality Detected Sacrificed by design	0-14 14

Male, XVII 3 ppm H-24648

<u>Animal</u>	<u>Observation</u>	<u>Days</u>
124543	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124544	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124545	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124546	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124547	General observation, No Abnormality Detected Sacrificed by design	0-14 14

H-24648 and H-24020: Repeated-Dose Oral Toxicity
14-Day Feeding Study in Mice

DuPont-5206

Individual Clinical Observations and Mortality of Mice Fed Diet Containing H-24648

Male, XIX 10 ppm H-24648

<u>Animal</u>	<u>Observation</u>	<u>Days</u>
124548	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124549	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124550	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124552	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124569	General observation, No Abnormality Detected Sacrificed by design	0-14 14

Male, XXI 30 ppm H-24648

<u>Animal</u>	<u>Observation</u>	<u>Days</u>
124553	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124554	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124555	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124556	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124557	General observation, No Abnormality Detected Sacrificed by design	0-14 14

H-24648 and H-24020: Repeated-Dose Oral Toxicity
14-Day Feeding Study in Mice

DuPont-5206

Individual Clinical Observations and Mortality of Mice Fed Diet Containing H-24648

Male, XXIII 100 ppm H-2468

<u>Animal</u>	<u>Observation</u>	<u>Days</u>
124558	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124559	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124560	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124561	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124562	General observation, No Abnormality Detected Sacrificed by design	0-14 14

Male, XXV 300 ppm H-24648

<u>Animal</u>	<u>Observation</u>	<u>Days</u>
124563	General observation, No Abnormality Detected Eye Observations, Enophthalmus, Left Sacrificed by design	0 7-14 14
124564	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124566	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124567	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124570	General observation, No Abnormality Detected Eye Observations, Enophthalmus, Right Sacrificed by design	0 7-14 14

H-24648 and H-24020: Repeated-Dose Oral Toxicity
14-Day Feeding Study in Mice

DuPont-5206

Individual Clinical Observations and Mortality of Mice Fed Diet Containing H-24648

Female, XVI 1 ppm H-24648

<u>Animal</u>	<u>Observation</u>	<u>Days</u>
124609	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124610	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124611	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124612	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124613	General observation, No Abnormality Detected Sacrificed by design	0-14 14

Female, XVIII 3 ppm H-24648

<u>Animal</u>	<u>Observation</u>	<u>Days</u>
124614	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124615	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124616	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124617	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124618	General observation, No Abnormality Detected Sacrificed by design	0-14 14

H-24648 and H-24020: Repeated-Dose Oral Toxicity
14-Day Feeding Study in Mice

DuPont-5206

Individual Clinical Observations and Mortality of Mice Fed Diet Containing H-24648

Female, XX 10 ppm H-24648

Animal	Observation	Days
124619	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124620	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124621	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124622	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124623	General observation, No Abnormality Detected Sacrificed by design	0-14 14

Female, XXII 30 ppm H-24648

Animal	Observation	Days
124624	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124625	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124626	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124627	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124628	General observation, No Abnormality Detected Sacrificed by design	0-14 14

H-24648 and H-24020: Repeated-Dose Oral Toxicity
14-Day Feeding Study in Mice

DuPont-5206

Individual Clinical Observations and Mortality of Mice Fed Diet Containing H-24648

Female, XXIV 100 ppm H-24648

<u>Animal</u>	<u>Observation</u>	<u>Days</u>
124609	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124610	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124611	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124612	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124613	General observation, No Abnormality Detected Sacrificed by design	0-14 14

Female, XXVI 300 ppm H-24648

124634	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124635	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124636	General observation, No Abnormality Detected Eye Observations, Enophthalmus, Right Sacrificed by design	0 7-14 14
124637	General observation, No Abnormality Detected Sacrificed by design	0-14 14
124638	General observation, No Abnormality Detected Sacrificed by design	0-14 14

APPENDIX D

INDIVIDUAL FINAL BODY AND LIVER WEIGHTS

Company Sanitized. Does not contain TSCA CBI

INDIVIDUAL FINAL BODY (FBW) AND LIVER WEIGHTS OF CONTROL MICE

Group : I 0 ppm Control Sex : MALES

ANIMAL	FBW (Gms)	LIVER (Gms)	%FBW
124503	35.30	2.044	5.7904
124504	30.70	1.501	4.8893
124505	30.40	1.753	5.7664
124506	34.50	1.695	4.9130
124507	30.60	1.608	5.2549

Group : II 0 ppm Control Sex : FEMALES

ANIMAL	FBW (Gms)	LIVER (Gms)	%FBW
124574	26.10	1.294	4.9579
124575	26.10	1.487	5.6973
124576	27.80	1.375	4.9460
124577	26.40	1.674	6.3409
124578	27.50	1.385	5.0364

Company Sanitized. Does not contain TSCA CBI

Individual Final Body (FBW) and Liver Weights of Mice
Fed Diet Containing H-24020

Group : III 1 ppm H-24020 Sex : MALES

ANIMAL	FBW (Gms)	LIVER	
		(Gms)	%FBW
124508	34.70	2.097	6.0432
124509	31.40	2.076	6.6115
124510	30.20	1.827	6.0497
124511	34.80	2.018	5.7989
124512	32.80	2.088	6.3659

Group : V 3 ppm H-24020 Sex : MALES

ANIMAL	FBW (Gms)	LIVER	
		(Gms)	%FBW
124513	32.70	2.244	6.8624
124514	32.00	2.206	6.8938
124515	28.00	1.975	7.0536
124516	32.40	2.248	6.9383
124517	37.40	2.432	6.5027

Group : VII 10 ppm H-24020 Sex : MALES

ANIMAL	FBW (Gms)	LIVER	
		(Gms)	%FBW
124518	33.10	2.947	8.9033
124519	29.50	2.344	7.9458
124520	31.90	2.722	8.5329
124521	33.40	2.934	8.7844
124522	36.10	3.009	8.3352

Group : IX 30 ppm H-24020 Sex : MALES

ANIMAL	FBW (Gms)	LIVER	
		(Gms)	%FBW
124523	34.40	4.175	12.137
124524	33.50	3.676	10.973
124525	32.30	4.195	12.988
124526	31.30	4.095	13.083
124527	33.40	3.922	11.743

Company Sanitized. Does not contain TSCA CBI

Individual Final Body (FBW) and Liver Weights of Mice
Fed Diet Containing H-24020

Group : XI 100 ppm H-24020 Sex : MALES

ANIMAL	FBW (Gms)	LIVER	
		(Gms)	%FBW
124528	27.20	4.866	17.890
124529	26.90	4.672	17.368
124530	29.00	5.392	18.593
124531	25.60	4.121	16.098
124532	26.20	4.572	17.450

Group : XIII 300 ppm H-24020 Sex : MALES

ANIMAL	FBW (Gms)	LIVER	
		(Gms)	%FBW
124533	23.80	3.887	16.332
124534	21.50	3.839	17.856
124535	23.10	4.239	18.351
124536	24.20	4.028	16.645
124537	23.80	3.741	15.718

Individual Final Body (FBW) and Liver Weights of Mice
Fed Diet Containing H-24020

Group : IV 1 ppm H-24020 Sex : FEMALES

ANIMAL	FBW (Gms)	LIVER	
		(Gms)	%FBW
124579	- ^a	-	-
124580	25.80	1.449	5.6163
124582	25.40	1.487	5.8543
124583	25.80	1.391	5.3915
124640	25.90	1.473	5.6873

Group : VI 3 ppm H-24020 Sex : FEMALES

ANIMAL	FBW (Gms)	LIVER	
		(Gms)	%FBW
124584	26.80	1.654	6.1716
124585	24.70	1.611	6.5223
124586	24.20	1.519	6.2769
124587	25.10	1.496	5.9602
124588	25.80	1.512	5.8605

Group : VIII 10 ppm H-24020 Sex : FEMALES

ANIMAL	FBW (Gms)	LIVER	
		(Gms)	%FBW
124589	23.70	2.013	8.4937
124590	27.00	2.314	8.5704
124591	25.30	2.102	8.3083
124592	28.40	1.881	6.6232
124593	28.30	2.285	8.0742

Group : X 30 ppm H-24020 Sex : FEMALES

ANIMAL	FBW (Gms)	LIVER	
		(Gms)	%FBW
124594	26.00	2.906	11.177
124596	25.40	2.789	10.980
124597	26.90	3.141	11.677
124598	26.40	2.834	10.735
124641	27.80	3.094	11.129

^a Mouse was found dead on test day 1.

Individual Final Body (FBW) and Liver Weights of Mice
Fed Diet Containing H-24020

Group : XII 100 ppm H-24020 Sex : FEMALES

ANIMAL	FBW (Gms)	LIVER	
		(Gms)	%FBW
124599	22.40	3.610	16.116
124600	28.20	3.872	13.730
124601	24.40	3.123	12.799
124602	27.00	3.374	12.496
124603	28.60	4.358	15.238

Group : XIV 300 ppm H-24020 Sex : FEMALES

ANIMAL	FBW (Gms)	LIVER	
		(Gms)	%FBW
124604	20.20	3.753	18.579
124605	21.20	3.604	17.000
124606	22.20	3.998	18.009
124607	20.40	3.443	16.877
124608	21.10	3.025	14.336

Company Sanitized. Does not contain TSCA CBI

Individual Final Body (FBW) and Liver Weights of Mice
Fed Diet Containing H-24648

Group : XV 1 ppm H-24648 Sex : MALES

ANIMAL	FBW (Gms)	LIVER (Gms)	%FBW
124538	34.90	2.312	6.6246
124539	35.20	2.396	6.8068
124540	32.00	2.123	6.6344
124541	36.10	2.285	6.3296
124542	32.40	2.165	6.6821

Group : XVII 3 ppm H-24648 Sex : MALES

ANIMAL	FBW (Gms)	LIVER (Gms)	%FBW
124543	32.80	2.299	7.0091
124544	31.40	2.453	7.8121
124545	35.60	2.669	7.4972
124546	35.70	3.055	8.5574
124547	33.70	2.329	6.9110

Group : XIX 10 ppm H-24648 Sex : MALES

ANIMAL	FBW (Gms)	LIVER (Gms)	%FBW
124548	34.70	3.387	9.7608
124549	31.50	2.629	8.3460
124550	31.80	3.014	9.4780
124552	33.50	3.077	9.1851
124569	29.40	2.714	9.2313

Group : XXI 30 ppm H-24648 Sex : MALES

ANIMAL	FBW (Gms)	LIVER (Gms)	%FBW
124553	32.50	3.988	12.271
124554	29.20	4.117	14.099
124555	25.90	3.481	13.440
124556	32.30	4.696	14.539
124557	30.00	4.222	14.073

Company Sanitized. Does not contain TSCA CBI

Individual Final Body (FBW) and Liver Weights of Mice
Fed Diet Containing H-24648

Group : XXIII 100 ppm H-24648 Sex : MALES

ANIMAL	FBW (Gms)	LIVER	
		(Gms)	%FBW
124558	26.60	5.084	19.113
124559	24.30	4.806	19.778
124560	27.30	5.075	18.590
124561	26.80	4.214	15.724
124562	26.00	- ^a	-

Group : XXV 300 ppm H-24648 Sex : MALES

ANIMAL	FBW (Gms)	LIVER	
		(Gms)	%FBW
124563	22.90	3.736	16.314
124564	23.90	3.313	13.862
124566	23.30	3.538	15.185
124567	22.70	4.225	18.612
124570	20.60	3.530	17.136

^a Due to error, the liver was not weighed.

Individual Final Body (FBW) and Liver Weights of Mice
Fed. Diet Containing H-24648

Group : XVI 1 ppm H-24648 Sex : FEMALES

ANIMAL	FBW (Gms)	LIVER	
		(Gms)	%FBW
124609	24.30	1.480	6.0905
124610	27.40	1.611	5.8796
124611	24.10	1.547	6.4191
124612	24.50	1.429	5.8327
124613	27.50	1.580	5.7455

Group : XVIII 3 ppm H-24648 Sex : FEMALES

ANIMAL	FBW (Gms)	LIVER	
		(Gms)	%FBW
124614	27.70	1.742	6.2888
124615	24.90	1.605	6.4458
124616	26.10	1.828	7.0038
124617	25.50	1.644	6.4471
124618	27.60	2.091	7.5761

Group : XX 10 ppm H-24648 Sex : FEMALES

ANIMAL	FBW (Gms)	LIVER	
		(Gms)	%FBW
124619	24.10	2.095	8.6929
124620	26.20	2.449	9.3473
124621	24.60	2.196	8.9268
124622	24.60	2.232	9.0732
124623	30.40	2.942	9.6776
Mean	25.98	2.383	9.1436
S.D.	2.59	0.338	0.3814

Group : XXII 30 ppm H-24648 Sex : FEMALES

ANIMAL	FBW (Gms)	LIVER	
		(Gms)	%FBW
124624	24.90	2.857	11.474
124625	26.60	3.248	12.211
124626	26.30	3.050	11.597
124627	26.70	3.325	12.453
124628	27.90	3.264	11.699

Individual Final Body (FBW) and Liver Weights of Mice
Fed Diet Containing H-24648

Group : XXIV 100 ppm H-24648 Sex : FEMALES

ANIMAL	FBW (Gms)	LIVER	
		(Gms)	%FBW
124629	21.80	3.307	15.170
124630	24.40	3.299	13.520
124632	22.10	3.421	15.480
124633	24.30	4.185	17.222
124639	26.30	4.360	16.578

Group : XXVI 300 ppm H-24648 Sex : FEMALES

ANIMAL	FBW (Gms)	LIVER	
		(Gms)	%FBW
124634	21.20	4.741	22.363
124635	20.20	4.019	19.896
124636	19.20	3.246	16.906
124637	19.60	3.588	18.306
124638	22.20	4.258	19.180

Company Sanitized. Does not contain TSCA CBI