NATIONAL TOXICOLOGY PROGRAM
Technical Report Series
No. 222

CARCINOGENESIS BIOASSAY OF C. I. DISPERSE YELLOW 3

(CAS NO. 2832-40-8)

IN F344/N RATS AND B6C3F$_1$ MICE (FEED STUDY)

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
National Institutes of Health

NATIONAL TOXICOLOGY PROGRAM

The National Toxicology Program (NTP), established in 1978, develops and evaluates scientific information about potentially toxic and hazardous chemicals. This knowledge can be used for protecting the health of the American people and for the primary prevention of chemically induced disease. By bringing together the relevant programs, staff, and resources from the U.S. Public Health Service, DHHS, the National Toxicology Program has centralized and strengthened activities relating to toxicology research, testing and test development/ validation efforts, and the dissemination of toxicological information to the public and scientific communities and to the research and regulatory agencies.

The NTP is comprised of four charter DHHS agencies: the National Cancer Institute, National Institutes of Health; the National Institute of Environmental Health Sciences, National Institutes of Health; the National Center for Toxicological Research, Food and Drug Administration; and the National Institute for Occupational Safety and Health, Centers for Disease Control. In July 1981, the Carcinogenesis Bioassay Testing Program, NCI, was transferred to the NIEHS.

NTP Technical Report

on the

CARCINOGENESIS BIOASSAY

of

C. I. DISPERSE YELLOW 3

(CAS No. 2832-40-8)

IN F344/N RATS AND B6C3F$_1$/N MICE
(FEED STUDY)

NATIONAL TOXICOLOGY PROGRAM
Research Triangle Park
Box 12233
North Carolina 27709
and
Bethesda, Maryland 20205

May 1982

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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NOTE TO THE READER

This is one in a series of experiments designed to determine whether selected chemicals produce cancer in animals. Chemicals selected for testing in the NTP carcinogenesis bioassay program are chosen primarily on the bases of human exposure, level of production, and chemical structure. Selection per se is not an indicator of a chemical's carcinogenic potential. Negative results, in which the test animals do not have a greater incidence of cancer than control animals, do not necessarily mean that a test chemical is not a carcinogen, inasmuch as the experiments are conducted under a limited set of conditions. Positive results demonstrate that a test chemical is carcinogenic for animals under the conditions of the test and indicate that exposure to the chemical is a potential hazard to humans. The determination of the risk to humans from chemicals found to be carcinogenic in animals requires a wider analysis which extends beyond the purview of this study.

This study was initiated by the National Cancer Institute's Carcinogenesis Testing Program, now part of the National Institute of Environmental Health Sciences, National Toxicology Program.

Comments and questions about the National Toxicology Program Technical Reports on Carcinogenesis Bioassays should be directed to the National Toxicology Program, located at Room A-306, Landow Building, Bethesda, MD 20205 (301-496-1152) or at Research Triangle Park, NC 27709 (919-541-3991).

Although every effort is made to prepare the Technical Reports as accurately as possible, mistakes may occur. Readers are requested to communicate any mistakes to the Deputy Director, NTP (P.O. Box 12233, Research Triangle Park, NC 27709), so that corrective action may be taken. Further, anyone who is aware of related ongoing or published studies not mentioned in this report is encouraged to make this information known to the NTP.

These NTP Technical Reports are available for sale from the National Technical Information Service, U.S. Department of Commerce, 5285 Port Royal Road, Springfield, VA 22161 (703-487-4650).

Single copies of this carcinogenesis bioassay technical report are available without charge (and while supplies last) from the NTP Public Information Office, National Toxicology Program, P.O. Box 12233, Research Triangle Park, NC 27709.

TABLE OF CONTENTS

TABLES

FIGURES

APPENDIXES

ABSTRACT

A carcinogenesis bioassay of C. I. Disperse Yellow 3 (87.6% dye), a textile dye, was conducted by feeding diets containing 5,000 or 10,000 ppm of the test substance to groups of 50 F344 rats of either sex for 103 weeks. Similar groups of 50 B6C3F1 mice received diets containing 2,500 or 5,000 ppm of the test substance for 103 weeks. Groups of 50 untreated rats and mice of each sex served as controls.

Throughout the bioassay, mean body weights of dosed rats and mice of either sex were lower than those of the controls. Survival of dosed rats of either sex was significantly greater than that of the corresponding controls. No other compound-related clinical signs or effects on survival were observed.

A significant increase in neoplastic nodules of the liver occurred in dosed male rats as compared to controls (controls 1/49, 2%; low-dose 15/50, 30%; $P < 0.001$; high-dose, 10/50, 20%; $P < 0.01$). No increase was observed for female rats.

Stomach tumors, rare in F344 rats (10/2960, 0.3%), were found in the dosed male rats: one adenocarcinoma and a sarcoma in a high-dose male and in the low-dose group a squamous cell papilloma, fibrosarcoma, adenoma, and mucinous adenocarcinoma. The incidence of these tumors was not significantly greater than that in controls; thus, the association between the administration of C. I. Disperse Yellow 3 and the stomach tumors in male rats is not clearly established.

Negative trends in the incidences of certain primary tumors in dosed rats included: decreased lymphocytic leukemia in both sexes; decreased malignant mesothelioma and C-cell carcinoma of the thyroid in males; and decreased pituitary chromophobe adenoma and endometrial stromal polyps in females.

Hepatocellular adenomas occurred in dosed female mice at incidences significantly higher than that in the controls (control 0/50, 0%; low-dose 6/50, 12%, $P < 0.05$; high-dose 12/50, 24%, $P < 0.001$). The incidences of hepatocellular carcinomas were also higher in the dosed female mice than in the controls, but the increased incidences were not statistically significant (2/50, 4/50, 5/50). A significantly ($P < 0.05$) lower incidence of hepatocellular adenomas was detected among low-dose (7/50, 1/49, 7/49) male mice.

Alveolar/bronchiolar adenomas occurred in high-dose male mice at an incidence significantly ($P < 0.05$) higher than that in the controls (control 2/50, 4%; low-dose 6/49, 12%; high-dose 9/49, 18%). However, the high-dose effect was not significant when adenomas and carcinomas were combined; the incidence among low-dose female mice was significantly reduced as compared with controls. Thus, the incidence of alveolar/bronchiolar adenomas among males is not considered to be related to treatment with C. I. Disperse Yellow 3.

Malignant lymphomas occurred in a dose-related ($P < 0.05$) trend in female mice and at incidences greater ($P < 0.05$) in the high-dose group than that in the controls (10/50, 16/50, 19/50). However, because of the range of variability in the historical incidence of this tumor and because of the lack of a similar effect in male mice or in male and female rats, this increase was not regarded as being unequivocally related to the administration of C. I. Disperse Yellow 3.

Under the conditions of this bioassay, C. I. Disperse Yellow 3 was considered carcinogenic for male F344 rats, causing an increased incidence of neoplastic nodules of the liver; this dye was not carcinogenic for female F344 rats. In addition, the stomach tumors found in the male rats may have been induced by the administration of the test chemical. C. I. Disperse Yellow 3 was carcinogenic for female B6C3F1 mice, as evidenced by the increased incidence of hepatocellular adenomas; C. I. Disperse Yellow 3 was not carcinogenic for male B6C3F1 mice. Also, the increased incidence of malignant lymphoma in female mice may have been associated with the administration of C. I. Disperse Yellow 3.

CONTRIBUTORS

This bioassay was conducted at Battelle Columbus Laboratories, Columbus, Ohio, under a subcontract to Tracor Jitco, Inc., Rockville, Maryland, prime contractor for the NCI/NTP Carcinogenesis Testing Program. The prechronic studies were initiated in June 1976 and finished in December 1976. The chronic studies were begun in March 1977 and finished in April 1979.

Dr. A. Peters (1) was the principal investigator for this study. Doses of the test chemical were selected by Drs. A. Peters and J. Robens (2,3). Drs. A. Peters, H. Harroff (1), and P. Stromberg (1) were in charge of animal care.

Necropsies were directed by Drs. G. S. Dill (1), R. Persing (1), R. Everett (1,4), and D. Thake (1). Histopathologic evaluations were performed by Drs. G. S. Dill (rats) and R. Persing (mice) (1). The pathology report and selected slides were evaluated by the NCI Pathology Working Group as described by Ward et al. (1978). The diagnoses represent a consensus of contracting pathologists and the NCI Pathology Working Group, with final approval by the NCI Pathology Working Group.

Animal pathology tables and survival tables were compiled at EG&G Mason Research Institute (5). Statistical analyses were performed by Dr. J. R. Joiner (2) and Mr. J. Warner (2) using methods selected for the bioassay program by Dr. J. J. Gart (6). Chemical analyses were conducted at Midwest Research Institute (7). Dosage analysis was supervised by Drs. R. Freudenthal (1) and P. Leber (1,8) and by Mr. D. Emmerling (1).

This report was prepared at Tracor Jitco (2) under the direction of Dr. C. Cueto (9), Director of the Bioassay Program; Dr. S. S. Olin, Associate Director; Dr. J. E. Tomaszewski, chemist; Dr. M. A. Stedham, pathologist; Dr. W. D. Theriault, reports manager; Dr. A. C. Jacobs, bioscience writer; and Ms. M. W. Glasser, technical editor.

The following scientists at NCI/NTP (10) were responsible for evaluating the bioassay experiment, interpreting the results, and reporting the findings: Dr. J. Fielding Douglas, Dr. Charles Grieshaber, Dr. Larry Hart, Dr. William V. Hartwell, Dr. Joseph Haseman, Dr. James Huff, Dr. Ernest E. McConnell, Dr. John H. Mennear (Chemical Manager), Dr. John A. Moore, Dr. Sherman F. Stinson, Dr. Raymond Tennant, and Dr. Jerrold M. Ward.

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PEER REVIEW COMMENTS

On February 18, 1981 this report underwent peer review and was approved by the National Toxicology Program Board of Scientific Counselors' Technical Reports Review Subcommittee and associated Panel of Experts at an open meeting held in Building 31C, National Institutes of Health, Bethesda, Maryland.

Dr. Williams, as a principal reviewer for the report on the bioassay of C. I. Disperse Yellow 3, agreed with the conclusion that under the conditions of the bioassay Yellow 3 induced liver tumors in F344 male rats and B6C3F1 female mice. In addition, stomach tumors in male rats may have been induced by the chemical. An increased incidence of pulmonary adenomas occurred in male mice, but the higher incidence in historical controls and a negative effect in female mice may limit the significance of this finding. His major concern about the study was that the degree of depression of weight gain in the high-dose rats indicated the maximum tolerated dose was exceeded. In his opinion, the development of a variety of nonneoplastic changes substantiated the observation that the high dose was not a tolerated dose. In spite of these considerations, he proposed that the close structural similarity of C. I. Disperse Yellow 3 to the amino azo dyes indicated the carcinogenic effect could arise from a genotoxic action, and suggested that additional genetic toxicology be performed.

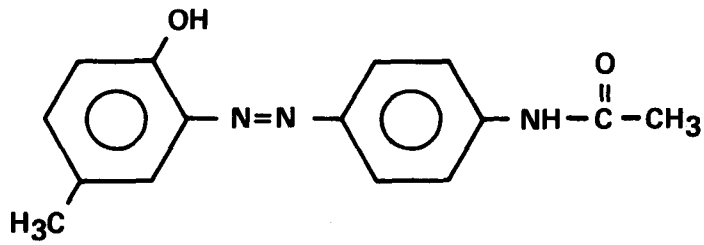
As the second principal reviewer, Dr. Swenberg opined that although there was an increased incidence of hepatic neoplastic nodules in male rats and hepatocellular adenomas in female mice, no apparent progression to hepatic carcinoma was demonstrated in either case. He reiterated the development of stomach tumors in male rats. He commented on striking dose-related decreases in the incidence of lymphocytic leukemia, C-cell carcinoma of the thyroid, and mesotheliamas of multiple organs in male rats, and similar decreases in pituitary adenomas and endometrial stromal polyps of the uterus in females. Based on the evidence, Dr. Swenberg considered C. I. Disperse Yellow 3 to have limited carcinogenic activity in male rats and female mice. He stated that the summary should qualify the significance of several of the tumor diagnoses, should mention the dose-related decrease in several tumor types, and should reflect the limited carcinogenic activity of the chemical.

Dr. Highland disagreed with Dr. Swenberg as to the "limited" nature of the evidence for carcinogenicity. Dr. Swenberg said he based his qualification on the facts that the results for the finding of pulmonary adenomas in male mice were equivocal and that the hepatic nodules in rats and adenomas in mice are lesions which sometimes occur spontaneously and are difficult to classify as malignant by histological criteria alone. Drs. Moore and Highland agreed that a possible compromise would be to state that "under the conditions of the bioassay, C. I. Disperse Yellow 3 was found to be a carcinogen as evidenced by an increased induction of hepatic neoplastic nodules in male rats and hepatocellular adenomas in female mice."

Dr. Williams requested that the portion of the discussion in the report dealing with the issue of whether or not hepatic nodules are precursors of carcinomas should be expanded to read along the lines of a similar discussion in the report on the bioassay of C. I. Solvent Yellow 14.

Dr. Williams moved that in the report on the bioassay of C. I. Disperse Yellow 3 adequate evidence exists for the carcinogenicity of the chemical and the report should be accepted with the revisions noted. Dr. Swenberg seconded the motion, and the report was approved unanimously by the Peer Review Panel.

I. INTRODUCTION



C. I. DISPERSE YELLOW 3

CAS NO. 2832-40-8 **COLOUR INDEX NO. 11855**

C. I. Disperse Yellow 3, also known as Disperse Fast Yellow 6 and Acetamine Yellow CG, is a monoazo dye, of low aqueous solubility, used to color nylon, polyvinyl chloride and acrylic fibers, wools and furs, cellulose acetate, polystyrene, and other thermoplastics. Finished products containing C. I. Disperse Yellow 3 include clothing, hosiery, and carpeting (Society of Dyers and Colourists, 1971; Kirk-Othmer, 1978; Gray and Hunter, 1977).

Current production figures are not available (USITC, 1979); however, 1,277,000 kilograms were produced in the United States in 1972 (IARC, 1975).

C. I. Disperse Yellow 3 has been reported to produce allergic eczema in persons wearing nylon hosiery dyed with this compound (Foussereau et al., 1972).

C. I. Disperse Yellow 3 was reported to be "mutagenic in some bacteria," but details of the study were not given (Gray and Hunter, 1977).

Boyland et al. (1964) observed one adenoma and six carcinomas in stock mice (7/25) 25 weeks after the mice received urinary bladder implants of cholesterol pellets containing C. I. Disperse Yellow 3 (concentration not

given). In 77 control animals implanted with cholesterol alone, a total of 4 papillomas and 5 carcinomas were diagnosed. The small number of animals, short duration, exposure method, and reporting render these borderline increases inadequate for evaluation.

C. I. Disperse Yellow 3 was tested by the Carcinogenesis Testing Program because of its widespread use and because the only previous test (Boyland et al., 1964) was considered to be inadequate.

II. MATERIALS AND METHODS

A. Chemical

C. I. Disperse Yellow 3 -- N-(4-((2-hydroxy-5-methylphenyl)azo)phenyl) acetamide -- was obtained from E. I. duPont de Nemours and Company, Wilmington, Delaware. Lot No. 19-007630 was used for the repeated-dose, subchronic, and chronic studies.

The results of analyses performed at Midwest Research Institute (Kansas City, MO) indicated that Lot No. 19-007630 was 87.6% dye based on titration of the azo group with titanous chloride (Appendix E). Results of carbon and nitrogen analyses were 89% and 86%, those of the theoretical values for 100% dye. The separate determinations of chloride and carbonate contents (3.47% and 0.65%, respectively) contribute 5.72% and 1.15% to the total, as sodium salts. The total of these values, the dye content (87.6%), and the water content (6.62%) as determined by Karl Fisher titration was 101% of the theoretical value. Two minor and two trace impurities were indicated by thin-layer chromatography and at least four impurities comprising 2.7% of the major peak were detected by high-pressure liquid chromatography; these impurities were not identified. The ultraviolet, visible, and infrared spectra were consistent with the structure and the literature spectra. This batch of C. I. Disperse Yellow 3 was considered to be representative of C. I. Disperse Yellow 3 commercially available for industrial purposes and was therefore considered suitable for use in the Bioassay Program.

The test chemical was stored in the dark at 23°C, and periodic bulk chemical analysis indicated that the chemical was stable throughout the study.

B. Dietary Preparation

Diets were formulated by mixing weighed amounts of Purina® Laboratory Chow animal meal (Table 1) and the test chemical in an intensifier-bar equipped Patterson-Kelly® twin-shell blender for 15 minutes. Formulated

Table 1. Specifications and Sources of Materials Used for Animal Maintenance

Item	Specifications	Source
Bedding	Absorb-dri® hardwood Chips	Lab Products, Inc. (Garfield, NJ)
Cages	Solid bottom, polycarbonate	Lab Products, Inc. (Garfield, NJ)
Feed	Purina® Laboratory Chow	Ralston Purina Co. (Richmond, IN)
Watering System	Edstrom Automatic	Edstrom Industries (Waterford, WI)

diets containing 100,000 ppm C. I. Disperse Yellow 3 were analyzed at Midwest Research Institute and were found to be stable for 2 weeks at temperatures up to 45°C (Appendix F). Formulated diets were stored at 23°C for no longer than 10 days.

The mean analytical concentrations of C. I. Disperse Yellow 3 in selected batches of formulated diets were within ±10% of the desired concentration (Appendix G). Homogeneity of the chemical-diet mix was verified analytically.

C. Animals

For both the subchronic and chronic studies, 4-week old F344 rats and B6C3F1 mice of either sex were obtained from NCI Frederick Cancer Research Center (Frederick, MD), isolated and maintained in separate quarters for 2 weeks, and assigned to cages according to a table of random numbers. The cages were then assigned to control or dosed groups according to another table of random numbers.

D. Animal Maintenance

Rats and mice were housed five per cage in solid-bottom polycarbonate cages (Table 1) supplied with hardwood chip bedding. Cages and bedding were changed twice per week. Control and test diets were available ad libitum in feed hoppers that were changed weekly. Water was available ad libitum from an automatic watering system.

The temperature in the animal rooms was 21° to 23°C and the relative humidity was 40%-60%. Room air was changed 15 times per hour. Fluorescent lighting was provided 12 hours per day.

Rats and mice fed C. I. Disperse Yellow 3 were housed by species in the same room as animals of the same species on feeding studies of D and C Red No. 9 (CAS No. 5160-02-1) and C. I. Solvent Yellow 14 (CAS No. 842-07-9). Each study had a separate set of controls.

E. Single-Day Dosing and Repeated-Dose Studies

Single-day dosing and 14-day repeated-dose studies were conducted using F344 rats and B6C3F1 mice to determine the concentrations of C. I. Disperse Yellow 3 to be used in the subchronic studies.

In the single-day dosing study, animals were randomized into groups of five males and five females of each species according to a table of random numbers. Groups of animals of each sex and species were offered diets containing 6,000, 12,500, 25,000, 50,000, or 100,000 ppm C. I. Disperse Yellow 3 for 24 hours and then laboratory chow for the remainder of the study. Feed consumption by rats was inversely proportional to dose during the 24-hour period when dosed feed was available (Table 2). Mice ate negligible amounts of feed. All animals were killed on day 15. No deaths occurred among the rats or mice and no overt signs of toxicity were observed.

In the repeated-dose study, groups of five males and five females of each species were fed diets containing 0, 6,000, 12,500, 25,000, 50,000, or 100,000 ppm for 2 weeks. All surviving animals were killed on day 15.

Weight gain was depressed by 15% or more in all groups of dosed rats as compared with controls (Table 3). Rats receiving 50,000 ppm or 100,000 ppm lost weight. Weight gain was depressed by 25% or more in all groups of dosed mice except for males receiving 6,000 ppm and females receiving 12,500 or 50,000 ppm (Table 4). Feed consumption was not measured, but it was estimated to be 25%-35% less for rats and mice receiving 50,000 or 100,000 ppm as compared with controls.

All rats receiving the 100,000-ppm diet and 1/5 male and 1/5 female rats receiving 50,000 ppm died. The rats receiving the 100,000-ppm diet were emaciated; the fat deposits, usually observed around the kidneys, adrenals, and heart, were depleted. Spleens, kidneys, and livers were uniformly dark red to black. Similar, but milder changes were present in rats fed the 50,000-ppm diet. Rats receiving 25,000 ppm had the normal amount of body fat and livers of normal color, although spleens and kidneys were dark red.

Table 2. Feed Consumption in the Single-Day Dosing Study of C. I. Disperse Yellow 3

Dose (ppm)	Average Feed Consumption per Animal (grams)			
	Rats		Mice	
	Male	Female	Male	Female
6,000	13.6	10.8	0	0
12,500	10.4	10.2	0	1
25,000	8.0	7.4	0	0
50,000	7.0	4.2	0	0.4
100,000	6.2	2.4	1	0

Table 3. Dosage, Survival, and Mean Body Weight Gain of Rats Fed Diets Containing C. I. Disperse Yellow 3 for 14 Days

Dose (ppm)	Survival (a) (day of death)	Mean Body Weights (b) Initial (g)	Final (g)	Change (g)	Weight Change Relative to Controls (Percent) (c)
Male					
0	5/5	107	127	+20	
6,000	5/5	112	118	+ 6	- 70
12,500	5/5	102	119	+17	- 15
25,000	5/5	101	106	+ 5	- 75
50,000	4/5(11)	93	75	-18	-190
100,000	0/5(6,7,10, 10,11)	92	-	-	-
Female					
0	5/5	101	121	+20	
6,000	5/5	101	113	+12	- 40
12,500	5/5	101	108	+ 7	- 65
25,000	5/5	87	97	+10	- 50
50,000	4/5(13)	96	85	-11	-155
100,000	0/5(9,14,14, 15,15)	96	67	-29	-245

(a) Number surviving/number per group.
(b) Animals were weighed by cage.
(c) Weight Change Relative to Controls =

$$\frac{\text{Weight Change (Dosed Group)} - \text{Weight Change (Control Group)}}{\text{Weight Change (Control Group)}} \times 100$$

Table 4. Dosage, Survival, and Mean Body Weight Gain of Mice Fed C. I. Disperse Yellow 3 for 14 Days

Dose (ppm)	Survival (a) (day of death)	Mean Body Weights (b) Initial (g)	Final (g)	Change (g)	Weight Change Relative to Controls (Percent) (c)
Male					
0	5/5	26	30	+ 4	
6,000	5/5	24	29	+ 5	+ 25
12,500	5/5	25	28	+ 3	- 25
25,000	5/5	23	26	+ 3	- 25
50,000	5/5	25	26	+ 1	- 75
100,000	1/5(10,10,11, 11)	26	22	- 4	-200
Female					
0	5/5	19	21	+ 2	
6,000	5/5	20	21	+ 1	- 50
12,500	5/5	20	22	+ 2	0
25,000	5/5	20	19	- 1	-150
50,000	5/5	19	22	+ 3	+ 50
100,000	3/5(11,14)	20	20	0	-100

(a) Number surviving/number per group.
(b) Animals were weighed by cage.
(c) Weight Change Relative to controls =

$$\frac{\text{Weight Change (Dosed Group)} - \text{Weight Change (Control Group)}}{\text{Weight Change (Control Group)}} \times 100$$

Among the mice receiving 100,000 ppm, 4/5 males and 2/5 females died. The spleens and kidneys were dark red to black and the livers were reddish tan; the changes were less severe than those found in rats at the same dose level. Enlarged spleens and dark red to black kidneys and spleens were observed in mice receiving 25,000 or 50,000 ppm.

F. Subchronic Studies

Subchronic studies were conducted to determine the dietary concentrations of C. I. Disperse Yellow 3 to be used in the chronic studies. Animals were randomized into groups of 10 males and 10 females of each species and were fed diets containing 0, 1,250, 2,500, 5,000, 10,000, or 20,000 ppm C. I. Disperse Yellow 3 for 91 days (Table 5 and Table 6). Animals were observed for mortality twice daily and individual animals were weighed weekly. At the end of the dosing period, the animals were killed, necropsies were performed, and tissues (as described in section H) were taken for histopathologic examination.

Rats: One male receiving 1,250 ppm and one female receiving 20,000 ppm died. Weight gain was depressed by 18% or more among rats fed diets containing 10,000 or 20,000 ppm. Feed consumption by male or female rats fed 20,000 ppm was 58% that of the controls. Feed consumption by male or female rats fed 10,000 ppm was 98% and 89%, respectively, that of the controls (Table 5).

The compound-related histopathologic findings are summarized in Table 7. Thyroid hyperplasia, splenic discoloration and mild hypertrophy, and kidney discoloration were observed at necropsy in rats fed 20,000 ppm. Rats fed 20,000 ppm had nonneoplastic lesions in the pituitary, thyroid, spleen, and kidney, including vacuolar degeneration of the pituitary pars distalis in 10/10 males and 6/6 females; thickened fibrous capsules in the thyroid in 10/10 males and 9/9 females; follicular hyperplasia in 10/10 males and in 9/9 females; follicular-cell adenomas in the thyroid in 3/10 males and 1/9 females; hemosiderosis in the spleen in 10/10 males and in 9/9

Table 5. Dosage, Survival, and Mean Body Weights of Rats Fed Diets Containing C. I. Disperse Yellow 3 for 91 Days

Dose (ppm)	Survival (a)	Mean Body Weights (grams) (b) Initial	Final	Change	Weight Change Relative to Controls (%)(c)	Mean Total Feed Consumption Per Animal (grams)
Male						
0	10/10	115.3(3.84)	286.1(6.65)	+170.8(6.10)		1270
1,250	9/10(d)	117.6(2.64)	287.9(3.33)	+170.3(3.97)	0	1370
2,500	10/10	113.4(2.75)	292.8(9.55)	+179.4(7.66)	+ 5	1380
5,000	10/10	124.7(6.10)	276.4(4.32)	+151.7(5.15)	-11	1350
10,000	10/10	111.0(3.07)	251.5(5.25)	+140.5(4.66)	-18	1240
20,000	10/10	110.3(3.40)	182.3(5.02)	+ 72.0(4.08)	-58	880
Female						
0	10/10	99.9(3.27)	185.1(3.25)	+85.2(3.48)		990
1,250	10/10	102.4(3.42)	182.3(3.32)	+79.9(3.71)	- 6	950
2,500	9/9	96.3(2.96)	182.1(4.22)	+85.8(2.62)	+ 1	970
5,000	10/10	92.8(2.95)	173.4(3.26)	+80.6(2.40)	- 5	940
10,000	10/10	94.1(2.81)	160.9(2.07)	+66.8(1.66)	-22	880
20,000	9/10(e)	96.7(3.56)	132.8(2.11)	+36.1(1.88)	-58	570

(a) Number surviving/number initially in the group.
(b) Mean weight change of the survivors of the group and standard error of the mean (in parentheses).
(c) Mean weight change of dosed survivors relative to the survivors of the controls =

$$\frac{\text{Weight Change (Dosed Group)} - \text{Weight Change (Control Group)}}{\text{Weight Change (Control Group)}} \times 100$$

(d) One animal died at week 7.
(e) One animal died at week 3.

Table 6. Dosage, Survival, and Mean Body Weights of Mice Fed Diets Containing C. I. Disperse Yellow 3 for 91 Days

Dose (ppm)	Survival (a)	Mean Body Weights (grams) Initial	Final	Change (b)	Weight Change Relative to Controls (%)(c)
Male					
0	10/10	23.7(0.63)	32.2(0.92)	+8.5(0.48)	
1,250	10/10	23.2(0.61)	32.3(0.78)	+9.1(0.59)	+ 7
2,500	10/10	24.3(0.54)	32.1(0.69)	+7.8(0.55)	- 8
5,000	10/10	24.0(0.39)	30.9(0.28)	+6.9(0.23)	-19
10,000	10/10	24.6(0.31)	31.8(0.66)	+7.2(0.44)	-15
20,000	10/10	23.4(0.50)	29.2(0.36)	+5.8(0.29)	-32
Female					
0	10/10	18.5(0.31)	23.4(0.43)	+4.9(0.31)	
1,250	10/10	19.1(0.41)	23.9(0.50)	+4.8(0.33)	- 2
2,500	10/10	18.5(0.22)	24.0(0.42)	+5.5(0.34)	+12
5,000	10/10	19.0(0.30)	23.5(0.43)	+4.5(0.37)	- 8
10,000	10/10	19.0(0.42)	23.4(0.34)	+4.4(0.27)	-10
20,000	10/10	18.2(0.36)	21.9(0.31)	+3.7(0.30)	-25

(a) Number surviving/number initially in the group.
(b) Mean weight change of the group and standard error of the mean (in parentheses).
(c) Mean weight change of dosed mice relative to that of controls =

$$\frac{\text{Weight Change (Dosed Group)} - \text{Weight Change (Control Group)}}{\text{Weight Change (Control Group)}} \times 100$$

Table 7. Compound-Related Histopathologic Findings in Rats Fed Diets Containing C. I. Disperse Yellow 3 for 91 Days

	Dose (ppm)											
	Control		1,250		2,500		5,000		10,000		20,000	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female(b)
Pituitary, pars distalis vacuolar degeneration	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	10/10	6/6[a]
Thyroid, capsule, fibrous thickening	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	10/10	0/10	10/10	9/9
Thyroid, follicular hyperplasia, mild	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	10/10	10/10	0/10	0/9
Thyroid, follicular hyperplasia, moderate	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	10/10	9/9
Thyroid, adenomatous hyperplasia	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	1/9
Thyroid, adenoma	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	3/10	1/9
Thyroid, capsule, inflammatory infiltrate, nonsuppurative, mild	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	1/10	0/9

Table 7. Compound-Related Histopathologic Findings in Rats Fed Diets Containing C. I. Disperse Yellow 3 for 91 Days

(Continued)

	Dose (ppm)											
	Control		1,250		2,500		5,000		10,000		20,000	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female(b)
Spleen, hemosiderosis, mild	0/10	0/10	0/10	0/10	0/10	0/10	4/10	8/10	10/10	10/10	0/10	0/9
Spleen, hemosiderosis, moderate	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	10/10	9/9
Spleen, lymphocytic depletion, mild	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	10/10	8/9
Kidney, cortical tubules, pigment deposition, mild	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	10/10	10/10	0/10	0/9
Kidney, cortical tubules, pigment deposition, moderate	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	10/10	9/9

(a) Three pituitaries missing.
(b) One female died early.

females; and pigment deposition in the cortical tubules of the kidney in 10/10 males and 9/9 females. These lesions were present to a lesser extent in rats fed 5,000 or 10,000 ppm but were not seen in the controls or animals fed the 1,250 and 2,500 ppm diets.

Doses selected for the chronic study with rats were 5,000 and 10,000 ppm C. I. Disperse Yellow 3 in feed. Because of weight gain depression and the severity of histopathologic effects, 5,000 ppm could have been selected as the high dose. However, 10,000 ppm was selected as the high dose to maximize the possibility of reproducing the thyroid pathology detected during the subchronic study.

Mice: None of the mice died. Mean weight gain was depressed 10% or more in male mice receiving 5,000-20,000 ppm and in female mice receiving 10,000 or 20,000 ppm. Feed consumption data could not be interpreted because of fecal matter and urine in the feed containers. Hemosiderosis of the renal tubular epithelium was observed in all mice receiving 10,000 or 20,000 ppm; hemosiderosis of the spleen was observed in all mice receiving 5,000 ppm or more; and cytoplasmic swelling of the centrilobular hepatocytes was observed in 6/10 males and 6/10 females receiving 10,000 ppm and in 10/10 males and 8/10 females receiving 20,000 ppm (Table 8).

In the subchronic study, mild hemosiderosis of the spleen was the only histopathologic effect seen at 5,000 ppm. Although weight gain depression for male mice receiving 5,000 ppm was greater than 10% as compared with controls, the 15% weight gain depression for male mice receiving 10,000 ppm was less than that seen in mice receiving 5,000 ppm. Weight gain depression for female mice receiving 5,000 ppm was less than 10% as compared with controls.

Doses selected for mice for the chronic study were 2,500 and 5,000 ppm C. I. Disperse Yellow 3 in the feed.

G. Chronic Studies

The test groups, doses administered, and durations of the chronic studies are shown in Table 9.

Table 8. Compound-Related Histopathologic Findings in Mice Fed Diets Containing C. I. Disperse Yellow 3 for 91 Days

Dose (ppm)	Kidney, Cortex, Proximal Tubules, Hemosiderosis	Spleen, Hemosiderosis	Liver, Centrilobular Hepatocyte, Swelling
MALES			
Control	0/10	0/10	0/10
1,250	0/10	0/10	0/10
2,500	0/10	0/10	0/10
5,000	0/10	10/10	0/10
10,000	10/10	10/10	6/10
20,000	10/10	10/10	10/10
FEMALES			
Control	0/10	0/10	0/10
1,250	0/10	0/10	0/10
2,500	0/10	0/10	0/10
5,000	0/10	10/10	0/10
10,000	10/10	10/10	6/10
20,000	10/10	10/10	8/10

Table 9. Experimental Design of Chronic Feeding Studies with C. I. Disperse Yellow 3 in Rats and Mice

Test Group (a)	Initial No. of Animals	C. I. Disperse Yellow 3 (ppm)	Weeks on Study (b) Dosed	Observed
Male Rats				
Control	50	0	0	104
Low-Dose	50	5,000	103	1
High-Dose	50	10,000	103	1
Female Rats				
Control	50	0	0	104
Low-Dose	50	5,000	103	1
High-Dose	50	10,000	103	1
Male Mice				
Control	50	0	0	104
Low-Dose	50	2,500	103	2
High-Dose	50	5,000	103	2
Female Mice				
Control	50	0	0	105
Low-Dose	50	2,500	103	2
High-Dose	50	5,000	103	2

(a) The control and dosed animals were of the same strain, sex, and age range and from the same source and shipment. All animals of the same strain shared the same room, and all aspects of animal care and maintenance were similar. Animals were randomized to dosed and control groups as described in Section IIc.

(b) The start dates were March 10, 1977, for male rats, March 23, 1977, for female rats, April 8, 1977, for male mice, and April 14, 1977, for female mice.

H. Clinical Examinations and Pathology

All animals were observed twice daily to discern sick or moribund animals. Clinical examinations and palpation for masses were performed each month, and the animals were weighed (by cage) every 4 weeks. Moribund animals and animals that survived to the end of the bioassay were killed using carbon dioxide and necropsied.

Gross and microscopic examinations were performed on major tissues, major organs, and all gross lesions from killed animals and from animals found dead. The tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. The following tissues were examined microscopically: skin (abdominal), lungs and bronchi, trachea, bone, bone marrow (femur), thigh muscle, spleen, lymph nodes, thymus, heart, salivary glands, liver, pancreas, esophagus, stomach, duodenum, jejunum, ileum, cecum, colon, kidney, urinary bladder, pituitary, adrenal, thyroid, parathyroid, testis, prostate, mammary gland, uterus, ovary, brain, epididymus, eye, and all tissue masses.

Necropsies were performed on all animals found dead, unless precluded in whole or in part by autolysis or cannibalization. Thus, the number of animals from which particular organs or tissues were examined microscopically varies and does not necessarily represent the number of animals that were placed on study in each group.

I. Data Recording and Statistical Analyses

Data on this experiment were recorded in the Carcinogenesis Bioassay Data System (Linhart et al., 1974). The data elements include descriptive information on the chemicals, animals, experimental design, clinical observations, survival, body weight, and individual pathologic results, as recommended by the International Union Against Cancer (Berenblum, 1969). Probabilities of survival were estimated by the product-limit procedure of Kaplan and Meier (1958) and are presented in this report in the form of graphs. Animals were statistically censored as of the time that they died

of other than natural causes or were found to be missing; animals dying from natural causes were not statistically censored. Statistical analyses for a possible dose-related effect on survival used the method of Cox (1972) for testing two groups for equality and Tarone's (1975) extensions of Cox's methods for testing for a dose-related trend. One-tailed P values have been reported for all tests except the departure from linearity test, which is reported only when its two-tailed P value is less than 0.05.

The incidence of neoplastic or nonneoplastic lesions has been given as the ratio of the number of animals bearing such lesions at a specific anatomic site (numerator) to the number of animals in which that site is examined (denominator). In most instances, the denominators included only those animals for which that site was examined histologically. However, when macroscopic examination was required to detect lesions (e.g., skin or mammary tumors) before histologic sampling or when lesions could have appeared at multiple sites (e.g., lymphomas), the denominators consist of the numbers of animals necropsied.

The purpose of the statistical analyses of tumor incidence is to determine whether animals receiving the test chemical developed a significantly higher proportion of tumors than did the control animals. As a part of these analyses, the one-tailed Fisher exact test (Cox, 1970) was used to compare the tumor incidence of a control group with that of a group of dosed animals at each dose level. When the results from two dosed groups are compared simultaneously with that for a control group, a correction to ensure an overall significance level of 0.05 may be made. The Bonferroni inequality criterion (Miller, 1966) requires that the P values for any comparison be less than or equal to 0.025. When this correction was used, it is discussed in the narrative section. It is not presented in the tables, where the Fisher exact P values are shown.

The Cochran-Armitage test for linear trend in proportions, with continuity correction (Armitage, 1971), was also used. Under the assumption of a linear trend, this test determines if the slope of the dose-response curve is different from zero at the one-tailed 0.05 level of significance.

Unless otherwise noted, the direction of the significant trend is a positive dose relationship. This method also provides a two-tailed test of departure from linear trend.

A time-adjusted analysis was applied when numerous early deaths resulted from causes that were not associated with the formation of tumors. In this analysis, deaths that occurred before the first tumor was observed were excluded by basing the statistical tests on animals that survived at least 52 weeks, unless a tumor was found at the anatomic site of interest before week 52. When such an early tumor was found, comparisons were based exclusively on animals that survived at least as long as the animal in which the first tumor was found. Once this reduced set of data was obtained, the standard procedures for analyses of the incidence of tumors (Fisher exact tests, Cochran-Armitage tests, etc.) were followed.

Life table methods were used to analyze the incidence of tumors. Curves of the proportions surviving without an observed tumor were computed as in Saffiotti et al. (1972). The week during which an animal died naturally or was killed was entered as the time point of tumor observation. The methods of Cox and of Tarone were used for the statistical tests of the groups. The statistical tests were one-tailed.

The approximate 95 percent confidence interval for the relative risk of each dosed group compared with its control was calculated from the exact interval on the odds ratio (Gart, 1971). The lower and upper limits of the confidence interval of the relative risk have been included in the tables of statistical analyses. The interpretation of the limits is that, in approximately 95% of a large number of identical experiments, the true ratio of the risk in a dosed group of animals to that in a control group would be within the interval calculated from the experiment. When the lower limit of the confidence interval is greater than one, it can be inferred that a statistically significant result has occurred (P less than 0.025 one-tailed test when the control incidence is not zero, P less than 0.050 when the control incidence is zero). When the lower limit is less than unity but the upper limit is greater than unity, the lower limit indicates the absence of

a significant result while the upper limit indicates that there is a theoretical possibility of the induction of tumors by the test chemical, which could not be detected under the conditions of this test.

III. RESULTS - RATS

A. Body Weights and Clinical Signs (Rats)

Throughout the bioassay, mean body weights of dosed rats of either sex were lower than those of the corresponding controls, and the decrements in mean body weight gain were dose related (Figure 1 and Table 10). No other compound-related clinical signs were observed. Feed consumption by dosed and control groups was comparable (Appendix H).

B. Survival (Rats)

Estimates of the probabilities of survival of male and female rats administered C. I. Disperse Yellow 3 at the concentrations of this bioassay, together with those of the control group, are shown by the Kaplan and Meier curves in Figure 2. Both sexes of rats had a wide range of survival between the different groups. In males, the low-dose group had significantly ($P < 0.05$) greater survival than did the controls, with the high-dose intermediate between the two. In females, the high-dose group had significantly ($P < 0.05$) greater survival than did the controls, with the low-dose intermediate between them.

In male rats, 31/50 (62%) of the control group, 45/50 (90%) of the low-dose group, and 39/50 (78%) of the high-dose group lived to the end of the study at 104 weeks. In female rats, 33/50 (66%) of the control group, 40/50 (80%) of the low-dose group, and 46/50 (92%) of the high-dose group lived to the end of the study at 104 weeks.

C. Pathology (Rats)

Histopathologic findings on neoplasms in rats are summarized in Appendix A, Tables A1 and A2; Tables A3 and A4 give the survival and tumor status for each individual animal in the male and female rat studies. Findings on nonneoplastic lesions are summarized in Appendix C, Tables C1 and C2.

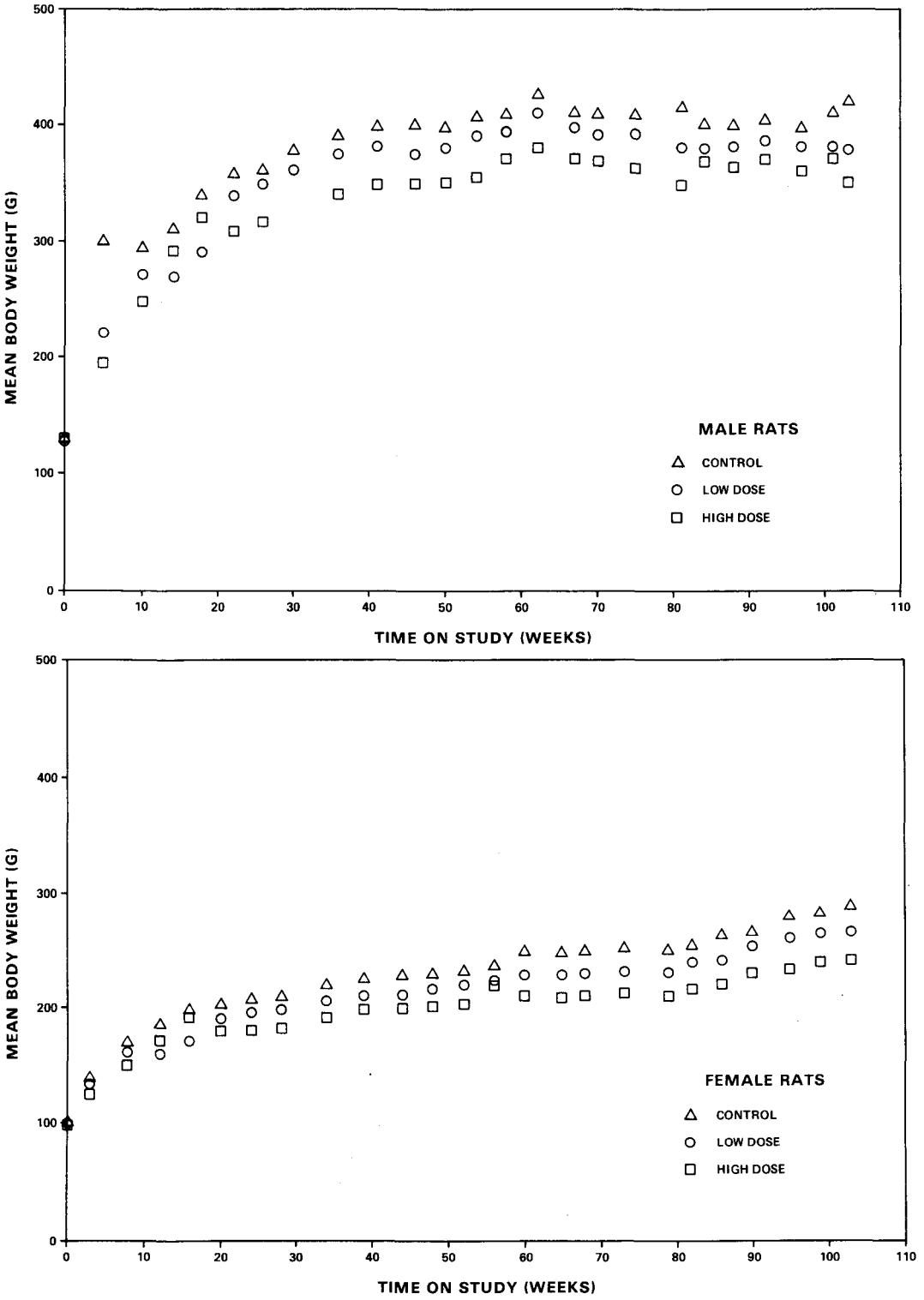


Figure 1. Growth Curves for Rats Fed Diets Containing C. I. Disperse Yellow 3

Table 10. Mean Body Weight Change (Relative to Controls) of Rats Fed Diets Containing C. I. Disperse Yellow 3

	Week No.	Mean Body Weight Change From Week 1 (grams) Control	Low Dose	High Dose	Weight Change Relative to Control (Percent) (a) Low Dose	High Dose
Male Rats	1	129 (b)	127 (b)	128 (b)		
	5	171	92	66	-46	-61
	26	233	221	189	- 5	-19
	46	271	248	221	- 8	-18
	67	284	270	243	- 5	-14
	88	271	254	236	- 6	-13
	103	291	251	225	-14	-23
Female Rats	1	102 (b)	100 (b)	98 (b)		
	3	37	34	27	- 8	-27
	24	105	96	82	- 9	-22
	44	126	112	100	-11	-21
	65	145	128	111	-12	-23
	86	162	141	123	-13	-24
	103	187	166	142	-11	-24

(a) Weight Change Relative to Controls =

$$\frac{\text{Weight Change (Dosed Group)} - \text{Weight Change (Control Group)}}{\text{Weight Change (Control Group)}} \times 100$$

(b) Weight at end of week 1.

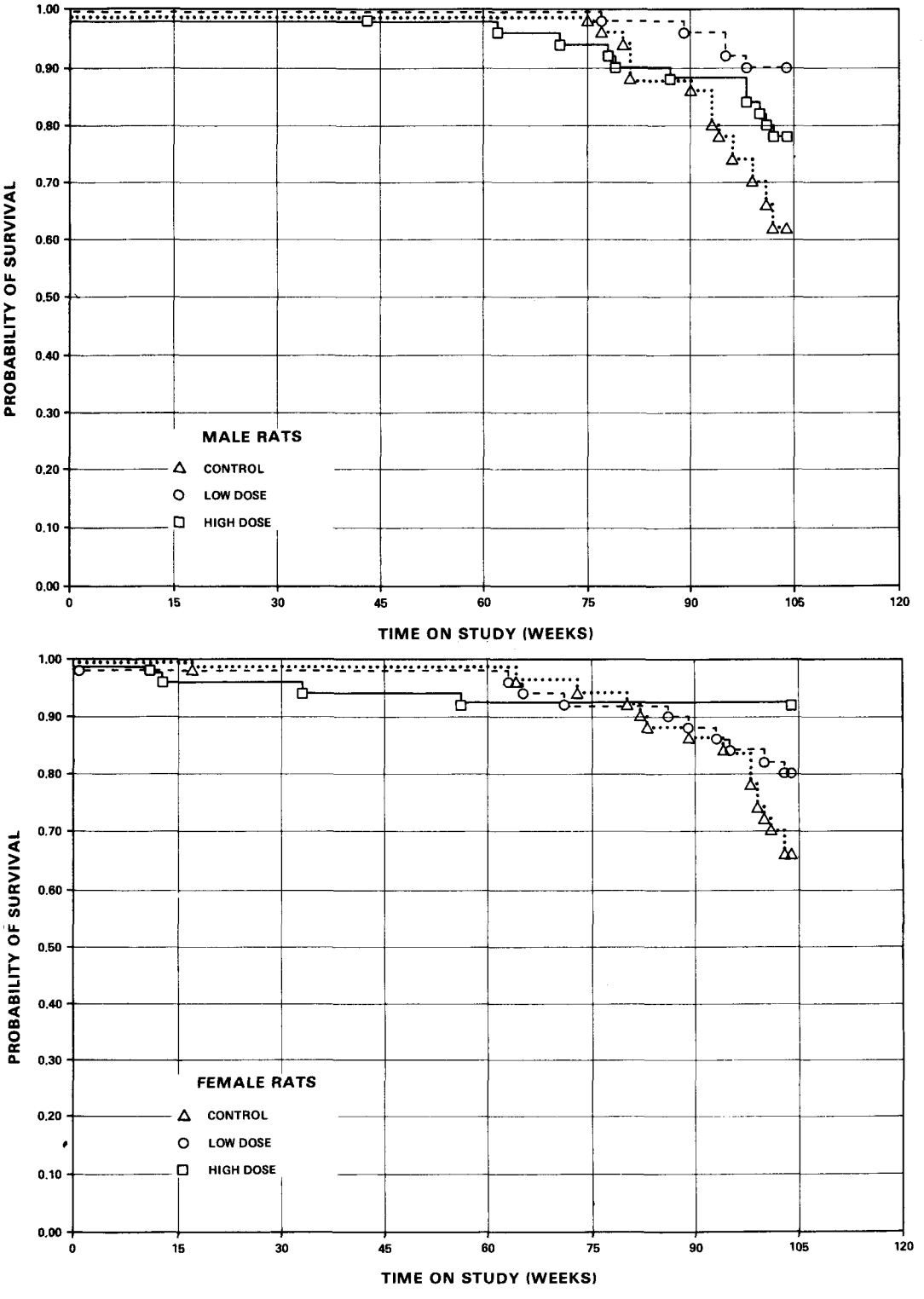


Figure 2. Survival Curves for Rats Fed Diets Containing C. I. Disperse Yellow 3

Various neoplasms were detected among both dosed and control animals. These lesions have been encountered previously in aging control F344 rats (Goodman et al., 1979).

Focal hepatic cellular change in males was dose related (controls 1/49; low-dose 4/50; and high-dose 17/50). These foci were different than the usual basophilic type found in controls and were usually composed of vacuolated, clear, or eosinophilic hepatocytes. The neoplastic nodules in dosed males were frequently multiple, of moderate to small size, and composed of basophilic hepatocytes. A few nodules were composed of eosinophilic cells. Carcinomas were trabecular in type.

The incidence of neoplastic nodules in the livers of the male rats fed the chemical was markedly increased over that in the controls (controls 1/49, 2%; low-dose 15/50, 30%; high-dose 10/50, 20%). Hepatocellular carcinomas were also seen in one control and two high-dose male rats.

Stomach tumors were seen in five male rats (controls 0/49; low-dose 4/50; high-dose 1/50). The lesions in the high-dose rat were an adenocarcinoma and a sarcoma of the glandular portion of the stomach, while those in the low-dose group included two tumors (squamous papilloma and fibrosarcoma) in the nonglandular portion and two tumors (adenoma and mucinous adenocarcinoma) in the glandular portion. One low-dose and two high-dose male rats had gastric epithelial hyperplasia.

Various nonneoplastic lesions were observed among both control and dosed animals. These lesions have been encountered previously as spontaneous lesions in F344 rats (Goodman et al., 1979).

Renal pigmentation appeared to be related to dosing in female rats (0/50 controls; 8/50 low-dose; and 34/50 high-dose). In male rats, the incidences of renal pigmentation were 0/50 for controls, 1/50 for the low-dose group, and 3/50 in the high-dose group. The pigment was not identified.

The results of histopathologic examination provided evidence that C. I. Disperse Yellow 3 may have induced liver and stomach tumors in F344 male rats under the conditions of this bioassay.

D. Statistical Analyses of Results (Rats)

Tables 11 and 12 contain the statistical analyses of those primary tumors that occurred in at least two animals of one group and with an incidence of at least 5% in one or more groups.

Neoplastic nodules of the liver in male rats were observed in a statistically significant positive association in the dosed groups compared with the control group (1/49, 2% in the controls; 15/50, 30% in the low-dose; 10/50, 20% in the high-dose). The Cochran-Armitage test for linear trend was statistically significant in the positive direction (P=0.014), but there was a departure from linear trend (P=0.004) due to the higher incidence in the low-dose group compared with the other two groups. The Fisher exact test between the control group and either dosed group was significant (P=0.004 in the high-dose and P less than 0.001 in the low-dose). This tumor has been observed in 40/2,960 (1.4%) male F344 control rats in the Bioassay Program and in 5/140 (3.6%) F344 male rats at this laboratory. This tumor was not observed in statistically significant proportions in female rats.

Lymphocytic leukemia of the hematopoeitic system in male rats was observed in a statistically significant negative relation in the dosed groups compared with the controls (13/50, 26% in the controls; 2/50, 4% in the low-dose; and 1/50, 2% in the high-dose). The Cochran-Armitage test for linear trend was statistically significant in the negative direction (P less than 0.001). The Fisher exact test between the control group and either of the dosed groups was significant (P less than 0.001 in the high-dose and P=0.002 in the low-dose). This tumor was also found in female rats in a statistically significant negative relation (8/50, 16% in the controls; 2/50, 4% in the low-dose; 1/50, 2% in the high-dose). The Cochran-Armitage test for linear trend was statistically significant in the negative

direction (P=0.007). The Fisher exact tests between the dosed groups and the controls were significant (P=0.015 in the high-dose and P=0.046 in the low-dose), but the value of P=0.046 is above the value of P=0.025 required by the Bonferroni inequality criterion for an overall significance of P=0.05 when two dosed groups are compared with a common control group. The historical incidence of rats with leukemia at this laboratory is 73/240 (30%) for males and 50/238 (21%) for females.

C-Cell carcinomas of the thyroid in male rats were observed in decreasing incidence (4/49, 8% in the controls; 1/50, 2% in the low-dose; 0/48, 0% in the high-dose). The Cochran-Armitage test for linear trend was statistically significant in the negative direction (P=0.026). The Fisher exact tests were not significant. In female rats, this tumor was not observed in statistically significant proportions.

Mesotheliomas, malignant in multiple organs, were observed in male rats in decreasing incidence (4/50, 8% in the controls; 2/50, 4% in the low-dose; 0/50, 0% in the high-dose). The Cochran-Armitage test for linear trend was statistically significant in the negative direction (P=0.037). The Fisher exact tests were not significant. In female rats, this tumor was not observed in a statistically significant proportion.

Chromophobe adenomas of the pituitary in female rats were observed in decreased incidence in the dosed groups, compared with the control group (15/44, 34% in the controls; 15/48, 31% in the low-dose; 8/49, 16% in the high-dose). The Cochran-Armitage test for linear trend was statistically significant in the negative direction (P=0.033). The Fisher exact test between the high-dose group and the matched control group was significant (P=0.041), but this is above the value of P=0.025 required by the Bonferroni inequality criterion for an overall significance of P=0.05 when two dosed groups are compared with a common control group. In male rats, this tumor was not observed in statistically significant proportions.

Endometrial stromal polyps of the uterus in female rats were observed in a statistically significant negative relation (14/50, 28% in the controls;

7/48, 15% in the low-dose; 3/50, 6% in the high-dose). The Cochran-Armitage test for linear trend was statistically significant in the negative direction (P=0.002). The Fisher exact test between the high-dose group and the control group was significant (P=0.003). No significant incidence was observed in the low-dose group; however, this tumor occurred in decreased incidence in the low-dose group compared with the control group.

Fibroadenomas of the mammary gland in female rats and tumors of the stomach in male rats were observed in increased incidences in the low-dose groups compared with the other two groups. The Cochran-Armitage tests for linear trend were not significant. Departures from linear trend occurred due to increased incidences in the low-dose groups. The Fisher exact tests were not significant.

One high-dose male rat and five female rats (one control, one low dose, and three high dose) died before 52 weeks, and time-adjusted tests were not significantly different from those reported above.

Life table analysis based on the time to observation of tumors did not materially alter the above results.

Table 11. Analyses of the Incidence of Primary Tumors in Male Rats Fed Diets Containing C. I. Disperse Yellow 3 (a)

	Control	Low Dose	High Dose
Subcutaneous Tissue: Fibroma (b)	3/50(6)	1/50(2)	1/50(2)
P Values (c), (d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.333	0.333
Lower Limit		0.006	0.006
Upper Limit		3.983	3.983
Weeks to First Observed Tumor	93	104	104
Hematopoietic System: Lymphocytic Leukemia (b)	13/50(26)	2/50(4)	1/50(2)
P Values (c), (d)	P less than 0.001(N)	P=0.002(N)	P less than 0.001(N)
Relative Risk (Control) (e)		0.154	0.077
Lower Limit		0.018	0.002
Upper Limit		0.632	0.480
Weeks to First Observed Tumor	81	98	98
Hematopoietic System: Lymphoma or Leukemia (b)	13/50(26)	3/50(6)	1/50(2)
P Values (c), (d)	P less than 0.001(N)	P=0.006(N)	P less than 0.001(N)
Relative Risk (Control (e)		0.231	0.077
Lower Limit		0.045	0.002
Upper Limit		0.777	0.480
Weeks to First Observed Tumor	81	98	98

Table 11. Analyses of the Incidence of Primary Tumors in Male Rats Fed Diets Containing C. I. Disperse Yellow 3 (a)

(Continued)

	Control	Low Dose	High Dose
Liver: Neoplastic Nodule (b)	1/49(2)	15/50(30)	10/50(20)
P Values (c), (d)	P=0.014	P less than 0.001	P=0.004
Departure from Linear Trend (f)	P=0.004		
Relative Risk (Control) (e)		14.700	9.800
Lower Limit		2.419	1.482
Upper Limit		601.480	414.931
Weeks to First Observed Tumor	104	104	104
Liver: Neoplastic Nodule or Hepatocellular Carcinoma (b)	2/49(4)	15/50(30)	11/50(22)
P Values (c), (d)	P=0.016	P=0.001	P=0.008
Departure from Linear Trend (f)	P=0.012		
Relative Risk (Control) (e)		7.350	5.390
Lower Limit		1.844	1.262
Upper Limit		63.184	47.937
Weeks to First Observed Tumor	104	104	104
Stomach, Cardiac Stomach, or Pylorus: All Tumors (b)	0/49(0)	4/50(8)	1/50(2)
P Values (c), (d)	N.S.	N.S.	N.S.
Departure from Linear Trend (f)	P=0.025		
Relative Risk (Control) (e)		Infinite	Infinite
Lower Limit		0.909	0.053
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	104	104

Table 11. Analyses of the Incidence of Primary Tumors in Male Rats Fed Diets Containing C. I. Disperse Yellow 3 (a)

(Continued)

	Control	Low Dose	High Dose
Pituitary: Chromophobe Adenoma (b)	5/47(11)	7/49(14)	4/46(9)
P Values (c), (d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.343	0.817
Lower Limit		0.396	0.172
Upper Limit		5.010	3.557
Weeks to First Observed Tumor	81	104	104
Adrenal: Pheochromocytoma (b)	6/50(12)	8/50(16)	3/49(6)
P Values (c), (d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.333	0.510
Lower Limit		0.438	0.087
Upper Limit		4.331	2.243
Weeks to First Observed Tumor	94	104	104
Adrenal: Pheochromocytoma, Malignant (b)	1/50(2)	3/50(6)	2/49(4)
P Values (c), (d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		3.000	2.041
Lower Limit		0.251	0.110
Upper Limit		154.270	117.931
Weeks to First Observed Tumor	104	77	104

Table 11. Analyses of the Incidence of Primary Tumors in Male Rats Fed Diets Containing C. I. Disperse Yellow 3 (a)

(Continued)

	Control	Low Dose	High Dose
Thyroid: C-Cell Carcinoma (b)	4/49(8)	1/50(2)	0/48(0)
P Values (c), (d)	P=0.026(N)	N.S.	N.S.
Relative Risk (Control) (e)		0.245	0.000
Lower Limit		0.005	0.000
Upper Limit		2.362	1.100
Weeks to First Observed Tumor	96	104	--
Thyroid: C-Cell Adenoma or Carcinoma (b)	4/49(8)	2/50(4)	0/48(0)
P Values (c), (d)	P=0.038(N)	N.S.	N.S.
Relative Risk (Control) (e)		0.490	0.000
Lower Limit		0.046	0.000
Upper Limit		3.251	1.100
Weeks to First Observed Tumor	96	104	--
Testis: Interstitial-Cell Tumor (b)	46/49(94)	48/49(98)	43/50(86)
P Values (c), (d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.043	0.916
Lower Limit		0.950	0.826
Upper Limit		1.088	1.066
Weeks to First Observed Tumor	75	89	71

Table 11. Analyses of the Incidence of Primary Tumors in Male Rats Fed Diets Containing C. I. Disperse Yellow 3 (a)

(Continued)

	Control	Low Dose	High Dose
Tunica Vaginalis:			
Mesothelioma, NOS (b)	1/50(2)	3/50(6)	1/50(2)
P Values (c), (d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		3.000	1.000
Lower Limit		0.251	0.013
Upper Limit		154.270	76.790
Weeks to First Observed Tumor	104	104	104
Multiple Organs:			
Mesothelioma, Malignant (b)	4/50(8)	2/50(4)	0/50(0)
P Values (c), (d)	P=0.037(N)	N.S.	N.S.
Relative Risk (Control) (e)		0.500	0.000
Lower Limit		0.047	0.000
Upper Limit		3.318	1.079
Weeks to First Observed Tumor	80	104	--

(a) Dosed groups received doses of 5,000 or 10,000 ppm in the diet.
(b) Number of tumor-bearing animals/number of animals examined at site (percent).
(c) Beneath the incidence of tumors in the control group is the probability level for the Cochran-Armitage test when P is less than 0.05; otherwise, not significant (N.S.) is indicated. Beneath the incidence of tumors in a dosed group is the probability level for the Fisher exact test for the comparison of that dosed group with the control group when P is less than 0.05; otherwise, not significant (N.S.) is indicated.
(d) A negative trend (N) indicates a lower incidence in a dosed group than in a control group.
(e) The 95 percent confidence interval of the relative risk between each dosed group and the control group.
(f) The probability level for departure from linear trend is given when P is less than 0.05 for any comparison.

Table 12. Analyses of the Incidence of Primary Tumors in Female Rats Fed Diets Containing C. I. Disperse Yellow 3 (a)

	Control	Low Dose	High Dose
Hematopoietic System:			
Lymphocytic Leukemia (b)	8/50(16)	2/50(4)	1/50(2)
P Values (c), (d)	P=0.007(N)	P=0.046(N)	P=0.015(N)
Relative Risk (Control) (e)		0.250	0.125
Lower Limit		0.027	0.003
Upper Limit		1.176	0.880
Weeks to First Observed Tumor	82	1	104
Hematopoietic System:			
Lymphoma or Leukemia (b)	10/50(20)	4/50(8)	3/50(6)
P Values (c), (d)	P=0.020(N)	N.S.	P=0.036(N)
Relative Risk (Control) (e)		0.400	0.300
Lower Limit		0.098	0.056
Upper Limit		1.284	1.083
Weeks to First Observed Tumor	17	1	13
Liver: Neoplastic Nodule (b)	2/50(4)	1/49(2)	2/50(4)
P Values (c), (d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.510	1.000
Lower Limit		0.009	0.075
Upper Limit		9.474	13.326
Weeks to First Observed Tumor	104	104	104

Table 12. Analyses of the Incidence of Primary Tumors in Female Rats Fed Diets Containing C. I. Disperse Yellow 3 (a)

(Continued)

	Control	Low Dose	High Dose
Liver: Neoplastic Nodule or Hepatocellular Carcinoma (b)	2/50(4)	1/49(2)	3/50(6)
P Values (c), (d)	N.S.	N.S.	N.S.
Relative Risk (Control) (c)		0.510	1.500
Lower Limit		0.009	0.180
Upper Limit		9.474	17.329
Weeks to First Observed Tumor	104	104	104
Pituitary: Chromophobe Adenoma (b)	15/44(34)	15/48(31)	8/49(16)
P Values (c), (d)	P=0.033(N)	N.S.	P=0.041(N)
Relative Risk (Control) (e)		0.917	0.479
Lower Limit		0.478	0.197
Upper Limit		1.768	1.080
Weeks to First Observed Tumor	89	93	56
Adrenal: Pheochromocytoma (b)	2/50(4)	3/50(6)	0/50(0)
P Values (c), (d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.500	0.000
Lower Limit		0.180	0.000
Upper Limit		17.329	3.381
Weeks to First Observed Tumor	98	103	--

Table 12. Analyses of the Incidence of Primary Tumors in Female Rats Fed Diets Containing C. I. Disperse Yellow 3 (a)

(Continued)

	Control	Low Dose	High Dose
Thyroid: C-Cell Carcinoma (b)	1/49(2)	2/49(4)	3/50(6)
P Values (c), (d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		2.000	2.940
Lower Limit		0.108	0.246
Upper Limit		115.581	151.180
Weeks to First Observed Tumor	104	104	104
Mammary Gland: Fibroadenoma (b)	7/50(14)	11/50(22)	3/50(6)
P Values (c), (d)	N.S.	N.S.	N.S.
Departure from Linear Trend (f)	P=0.045		
Relative Risk (Control) (e)		1.571	0.429
Lower Limit		0.608	0.075
Upper Limit		4.394	1.759
Weeks to First Observed Tumor	104	104	104
Uterus: Endometrial Stromal Polyp (b)	14/50(28)	7/48(15)	3/50(6)
P Values (c), (d)	P=0.002(N)	N.S.	P=0.003(N)
Relative Risk (Control) (e)		0.521	0.214
Lower Limit		0.195	0.042
Upper Limit		1.250	0.709
Weeks to First Observed Tumor	94	100	104

Table 12. Analyses of the Incidence of Primary Tumors in Female Rats Fed Diets Containing C. I. Disperse Yellow 3 (a)

(Continued)

(a) Dosed groups received doses of 5,000 or 10,000 ppm in the diet.
(b) Number of tumor-bearing animals/number of animals examined at site (percent).
(c) Beneath the incidence of tumors in the control group is the probability level for the Cochran-Armitage test when P is less than 0.05; otherwise, not significant (N.S.) is indicated. Beneath the incidence of tumors in a dosed group is the probability level for the Fisher exact test for the comparison of that dosed group with the control group when P is less than 0.05; otherwise, not significant (N.S.) is indicated.
(d) A negative trend (N) indicates a lower incidence in a dosed group than in a control group.
(e) The 95 percent confidence interval of the relative risk between each dosed group and the control group.
(f) The probability level for departure from linear trend is given when P is less than 0.05 for any comparison.

IV. RESULTS - MICE

A. Body Weights and Clinical Signs (Mice)

Throughout the bioassay, mean body weights of dosed mice of either sex tended to be lower than those of the controls (Figure 3 and Table 13). Clinical signs and feed consumption by dosed and control animals were comparable (Appendix H).

B. Survival (Mice)

Estimates of the probabilities of survival of male and female mice administered C. I. Disperse Yellow 3 at the concentrations of this bioassay, together with those of the control group, are shown by the Kaplan and Meier curves in Figure 4. All the groups of mice had similar survival, and there were no significant differences between any of the groups of either sex.

In male mice, 43/50 (86%) of the control group, 39/50 (78%) of the low-dose group, and 42/50 (84%) of the high-dose group lived to the end of the study at 104-105 weeks. In female mice, 44/50 (88%) of the control group, 39/50 (78%) of the low-dose group, and 42/50 (84%) of the high-dose group lived to the end of the study at 105 weeks.

C. Pathology (Mice)

Histopathologic findings on neoplasms in mice are summarized in Appendix B, Tables B1 and B2; Tables B3 and B4 give the survival and tumor status for individual animals in the male and female mouse studies. Findings on nonneoplastic lesions are summarized in Appendix D, Tables D1 and D2.

Tumors were uniformly distributed among dosed and control groups of mice except for tumors of the lung, liver, and hematopoietic system. Compared with controls, dosed male mice had a higher incidence of alveolar/bronchiolar adenomas (controls, 2/50; low-dose, 6/49; high-dose, 9/49) and

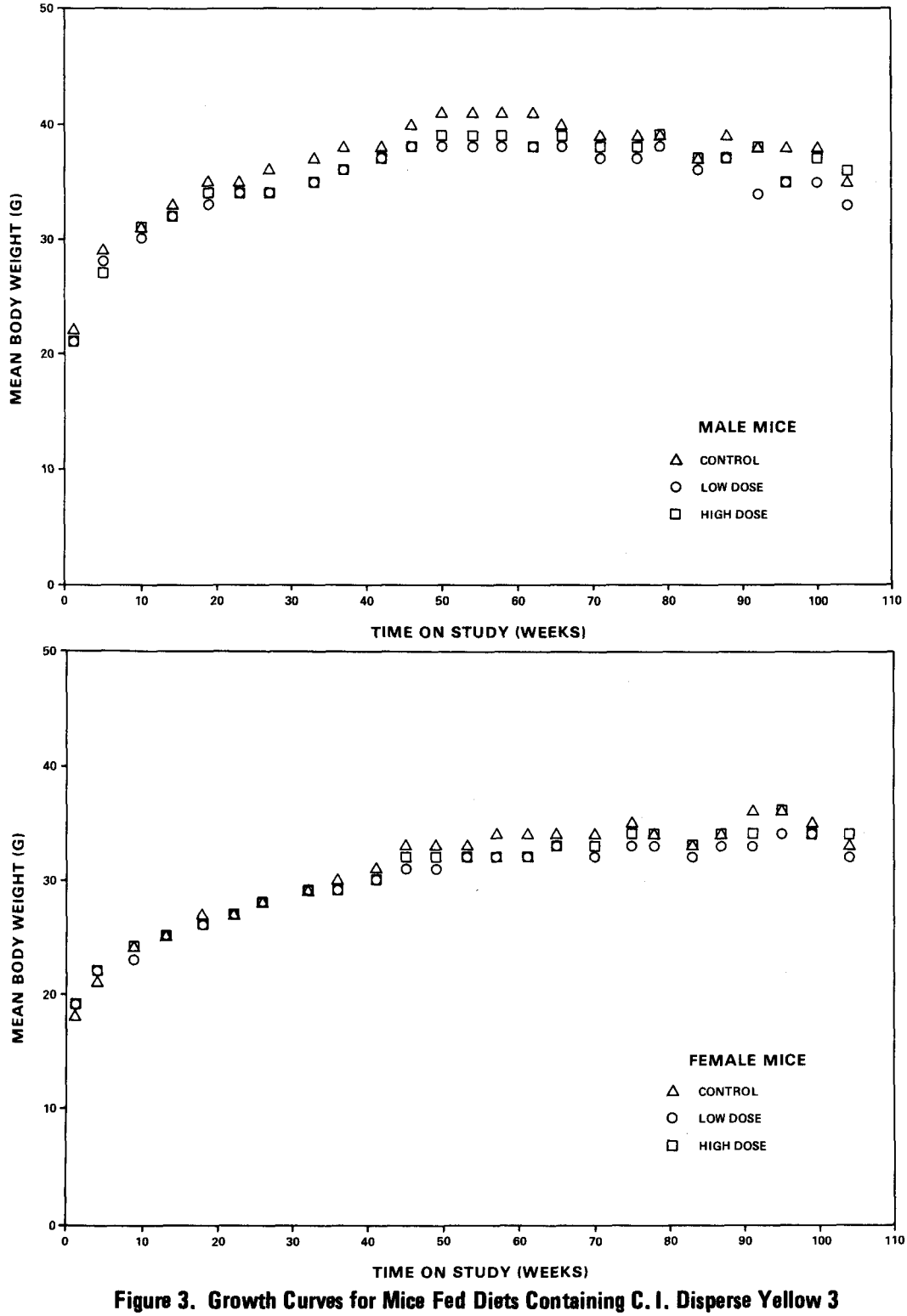


Figure 3. Growth Curves for Mice Fed Diets Containing C. I. Disperse Yellow 3

Table 13. Mean Body Weight Change (Relative to Controls) of Mice Fed Diets Containing C. I. Disperse Yellow 3

	Mean Body Weight Change From Week 1 (grams)			Weight Change Relative to Controls (%) (b)	
	Week No.	Control	Low Dose	High Dose	Low Dose	High Dose
Male Mice	1	22(b)	21(b)	21(b)		
	5	7	7	6	0	-14
	23	13	13	13	0	0
	42	16	16	16	0	0
	62	19	17	17	-11	-11
	84	15	15	16	0	+7
	104	13	12	15	-8	+15
Female Mice	1	18 (b)	19 (b)	19 (b)		
	4	3	3	3	0	0
	22	9	8	8	-11	-11
	41	13	11	11	-15	-15
	61	16	13	13	-19	-19
	83	15	13	14	-13	-7
	104	15	13	15	-13	0

(a) Weight Change Relative to Controls =

$$\frac{\text{Weight Change (Dosed Group)} - \text{Weight Change (Control Group)}}{\text{Weight Change (Control Group)}} \times 100$$

(b) Weight at the end of week 1.

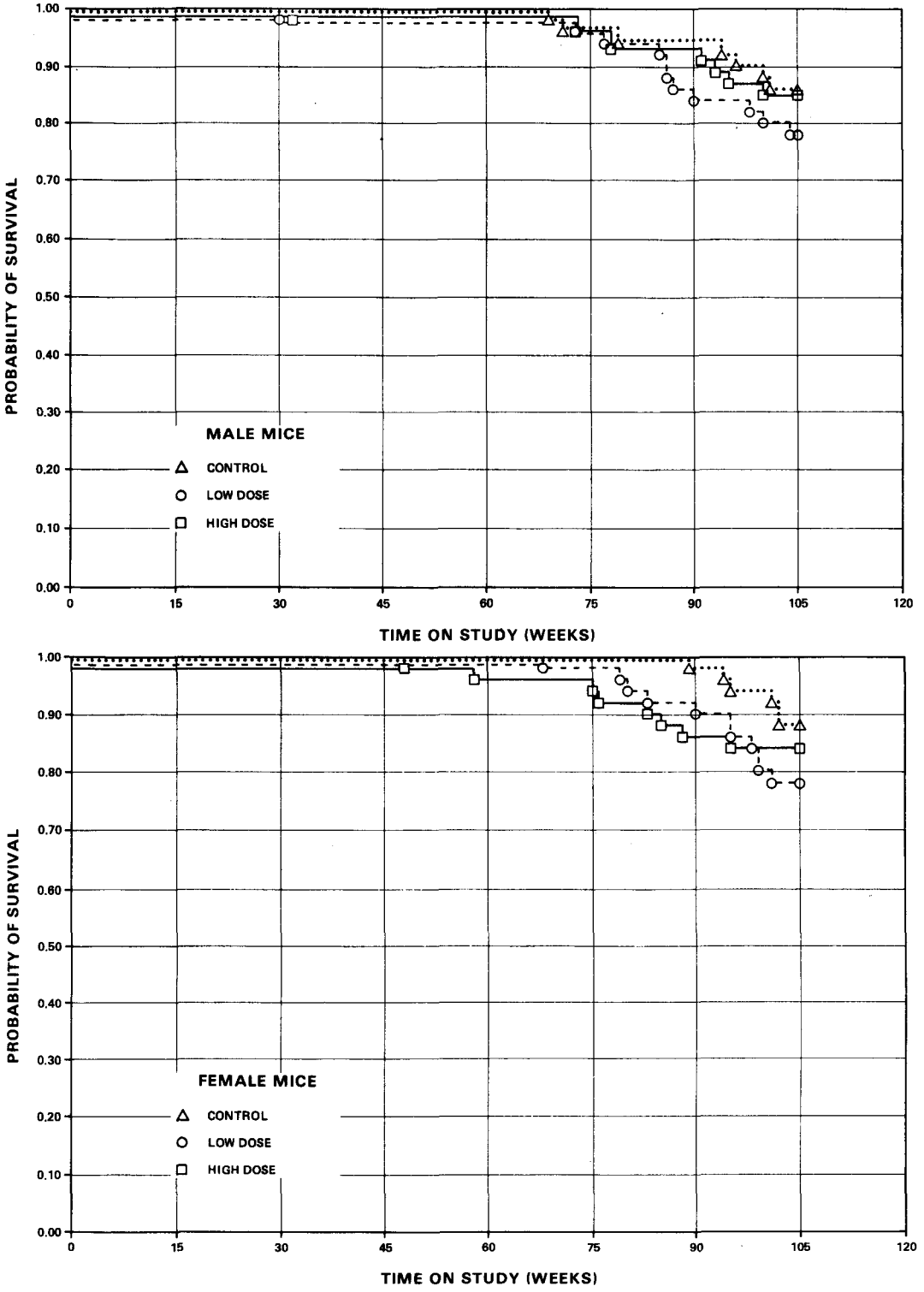


Figure 4. Survival Curves for Mice Fed Diets Containing C. I. Disperse Yellow 3

dosed females had higher incidences of hepatocellular adenomas (controls, 0/50; low-dose, 6/50; high-dose, 12/50) and lymphomas (controls, 10/50; low-dose, 16/50; high-dose, 19/50). The hepatocellular adenomas were composed of well-circumscribed solid sheets of cells which had basophilic or eosinophilic cytoplasm. Hepatocellular carcinomas had prominent trabecular areas. One control and one high-dose female mouse had a metastatic hepatocellular carcinoma in the lung.

All other microscopic abnormalities were considered to be age-associated lesions seen in B6C3F1 mice.

Histopathologic examination provided evidence that administration of C. I. Disperse Yellow 3 was associated with lung, liver, and possibly hematopoietic tumors in B6C3F1 mice under the conditions of this bioassay.

D. Statistical Analyses of Results (Mice)

Tables 14 and 15 contain the statistical analyses of those primary tumors that occurred in at least two animals of one group and with an incidence of at least 5% in one or more groups.

Alveolar/bronchiolar adenomas of the lung in male mice were observed in a statistically significant positive relation (2/50, 4% in the controls; 6/49, 12% in the low-dose; and 9/49, 18% in the high-dose). The Cochran-Armitage test for linear trend was statistically significant in the positive direction (P=0.019). The Fisher exact test between the high-dose group and the matched control group was significant (P=0.023). No significant incidence was observed in the low-dose group; however, this tumor occurred in increased incidence in the low-dose group compared with the control group. The historical control incidence of male mice with this tumor at this laboratory is 19/295 (6.4%). Fisher exact tests for male mice with adenomas or carcinomas of the lung (3/50, 6% in the control; 7/49, 14% in the low-dose; and 9/49, 18% in the high-dose) were not significant, but

the Cochran-Armitage test for linear trend was significant (P=0.046). Alveolar/bronchiolar adenomas of the lung in female mice were observed in decreased incidence in the low-dose group compared with the other two groups. The Cochran-Armitage test for linear trend was not significant, but there was a departure from linear trend due to decreased incidence in the low-dose compared with the other two dosed groups. The Fisher exact test between the low-dose group and the control group was significant (P=0.028). No significant incidence was observed in the high-dose group. Because of the higher incidences seen in other control groups at this laboratory, the negative result in the female mice, and the lack of significant Fisher exact tests between the dosed groups and the control group when the incidence of male mice with adenomas or carcinomas is analyzed, the association of these tumors in male mice with the administration of C. I. Disperse Yellow 3 is not clearly established.

Hepatocellular adenomas in female mice were observed in a statistically significant positive relation in the dosed groups compared with the control group (0/50, 0% in the controls; 6/50, 12% in the low-dose; 12/50, 24% in the high-dose). The Cochran-Armitage test for linear trend was statistically significant in the positive direction (P less than 0.001). The Fisher exact test between the control group and either of the dosed groups was significant (P less than 0.001 in the high-dose and P=0.013 in the low-dose). Adenomas in the liver have been observed in 72/3,617 (2.0%) of the control female mice in the bioassay program and in 3/298 (1.0%) of the female mice at this laboratory. Life table analysis of the time to observation of these liver tumors in female mice indicates a significant trend (P less than 0.001). The incidences of carcinomas of the liver in female mice were not statistically significant, and there were no significant increases in liver tumors in male mice.

Lymphomas of the hematopoietic system in female mice were observed in increased incidence in the dosed groups compared with the matched control group (10/50, 20% in the controls; 16/50, 32% in the low-dose; 19/50, 38% in the high-dose). The Cochran-Armitage test for linear trend was statistically significant in the positive direction (P=0.032). The Fisher

exact test between the high-dose group and the control group indicated a value of P=0.038.

The incidence of female mice with lymphomas or leukemia was increased in the dosed groups (control, 10/50, 20%; low-dose, 17/50, 34%; high-dose, 20/50, 40%). The Cochran-Armitage test for linear trend was statistically significant in the positive direction (P=0.020). The Fisher exact test between the high-dose group and the control group indicated a value of P=0.024. The high-dose incidence is also significantly ($P < 0.05$) different from the historical incidence of female mice with lymphomas or leukemia at this laboratory [70/300 (23.3%; range 10/50 to 16/50)].

One female and two male mice died before 52 weeks on study, and neither time adjusted tests nor life table analyses materially altered the results reported above.

Table 14. Analyses of the Incidence of Primary Tumors in Male Mice Fed Diets Containing C. I. Disperse Yellow 3 (a)

	Control	Low Dose	High Dose
Lung: Alveolar/Bronchiolar Adenoma (b)	2/50(4)	6/49(12)	9/49(18)
P Values (c), (d)	P=0.019	N.S.	P=0.023
Relative Risk (Control) (e)		3.061	4.592
Lower Limit		0.581	1.015
Upper Limit		29.826	41.883
Weeks to First Observed Tumor	104	98	91
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma (b)	3/50(6)	7/49(14)	9/49(18)
P Values (c), (d)	P=0.046	N.S.	N.S.
Relative Risk (Control) (e)		2.381	3.061
Lower Limit		0.581	0.820
Upper Limit		13.550	16.653
Weeks to First Observed Tumor	94	98	91
Hematopoietic System: Malignant Lymphoma, Histiocytic Type (b)	5/50(10)	3/49(6)	1/49(2)
P Values (c), (d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.612	0.204
Lower Limit		0.100	0.004
Upper Limit		2.967	1.733
Weeks to First Observed Tumor	100	86	105

Table 14. Analyses of the Incidence of Primary Tumors in Male Mice Fed Diets Containing C. I. Disperse Yellow 3 (a)

(Continued)

	Control	Low Dose	High Dose
Hematopoietic System:			
Malignant Lymphoma, NOS (b)	2/50(4)	3/49(6)	3/49(6)
P Values (c), (d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.531	1.531
Lower Limit		0.183	0.183
Upper Limit		17.671	17.671
Weeks to First Observed Tumor	96	104	100
Hematopoietic System:			
Malignant Lymphoma (b)	8/50(16)	6/49(12)	4/49(8)
P Values (c), (d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.765	0.510
Lower Limit		0.236	0.120
Upper Limit		2.325	1.771
Weeks to First Observed Tumor	96	86	100
Hematopoietic System:			
Lymphoma or Leukemia (b)	8/50(16)	6/49(12)	5/49(10)
P Values (c), (d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.765	0.638
Lower Limit		0.236	0.176
Upper Limit		2.325	2.049
Weeks to First Observed Tumor	96	86	100

Table 14. Analyses of the Incidence of Primary Tumors in Male Mice Fed Diets Containing C. I. Disperse Yellow 3 (a)

(Continued)

	Control	Low Dose	High Dose
Liver: Hepatocellular Adenoma (b)	7/50(14)	1/49(2)	7/49(14)
P Values (c), (d)	N.S.	P=0.032(N)	N.S.
Departure from Linear Trend (f)	P=0.022		
Relative Risk (Control) (e)		0.146	1.020
Lower Limit		0.003	0.330
Upper Limit		1.073	3.155
Weeks to First Observed Tumor	104	105	105
Liver: Hepatocellular Carcinoma (b)	14/50(28)	11/49(22)	12/49(24)
P Values (c), (d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.802	0.875
Lower Limit		0.367	0.413
Upper Limit		1.706	1.823
Weeks to First Observed Tumor	69	77	73
Liver: Hepatocellular Adenoma or Carcinoma (b)	20/50(40)	12/49(24)	16/49(33)
P Values (c), (d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.612	0.816
Lower Limit		0.310	0.453
Upper Limit		1.162	1.449
Weeks to First Observed Tumor	69	77	73

Table 14. Analyses of the Incidence of Primary Tumors in Male Mice Fed Diets Containing C. I. Disperse Yellow 3 (a)

(Continued)

	Control	Low Dose	High Dose
Eye/Lacrimal Gland:			
Papillary Adenoma (b)	2/50(4)	1/49(2)	3/49(6)
P Values (c), (d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.510	1.531
Lower Limit		0.009	0.183
Upper Limit		9.474	17.671
Weeks to First Observed Tumor	104	105	105

(a) Dosed groups received doses of 2,500 or 5,000 ppm in the diet.
(b) Number of tumor-bearing animals/number of animals examined at site (percent).
(c) Beneath the incidence of tumors in the control group is the probability level for the Cochran-Armitage test when P is less than 0.05; otherwise, not significant (N.S.) is indicated. Beneath the incidence of tumors in a dosed group is the probability level for the Fisher exact test for the comparison of that dosed group with the control group when P is less than 0.05; otherwise, not significant (N.S.) is indicated.
(d) A negative trend (N) indicates a lower incidence in a dosed group than in a control group.
(e) The 95 percent confidence interval of the relative risk between each dosed group and the control group.
(f) The probability level for departure from linear trend is given when P is less than 0.05 for any comparison.

Table 15. Analyses of the Incidence of Primary Tumors in Female Mice Fed Diets Containing C. I. Disperse Yellow 3 (a)

	Control	Low Dose	High Dose
Lung: Alveolar/Bronchiolar Adenoma (b)	5/50(10)	0/50(0)	3/50(6)
P Values (c), (d)	N.S.	P=0.028(N)	N.S.
Departure from Linear Trend (e)	P=0.039		
Relative Risk (Control) (f)		0.000	0.600
Lower Limit		0.000	0.098
Upper Limit		0.793	2.910
Weeks to First Observed Tumor	105	--	105
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma (b)	6/50(12)	0/50(0)	4/50(8)
P Values (c), (d)	N.S.	P=0.013(N)	N.S.
Departure from Linear Trend (e)	P=0.021		
Relative Risk (Control) (f)		0.000	0.667
Lower Limit		0.000	0.147
Upper Limit		0.625	2.635
Weeks to First Observed Tumor	105	--	105
Hematopoietic System: Malignant Lymphoma, Histiocytic Type (b)	5/50(10)	11/50(22)	9/50(18)
P Values (c), (d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		2.200	1.800
Lower Limit		0.765	0.586
Upper Limit		7.508	6.377
Weeks to First Observed Tumor	102	68	48

Table 15. Analyses of the Incidence of Primary Tumors in Female Mice Fed Diets Containing C. I. Disperse Yellow 3 (a)

(Continued)

	Control	Low Dose	High Dose
Hematopoietic System:			
Malignant Lymphoma, NOS (b)	6/50(12)	3/50(6)	7/50(14)
P Values (c), (d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.500	1.167
Lower Limit		0.085	0.361
Upper Limit		2.200	3.911
Weeks to First Observed Tumor	94	105	95
Hematopoietic System:			
Malignant Lymphoma (b)	10/50(20)	16/50(32)	19/50(38)
P Values (c), (d)	P=0.032	N.S.	P=0.038
Relative Risk (Control) (e)		1.600	1.900
Lower Limit		0.761	0.942
Upper Limit		3.540	4.074
Weeks to First Observed Tumor	94	68	48
Hematopoietic System:			
Lymphoma or Leukemia (b)	10/50(20)	17/50(34)	20/50(40)
P Values (c), (d)	P=0.020	N.S.	P=0.024
Relative Risk (Control) (e)		1.700	2.000
Lower Limit		0.821	1.004
Upper Limit		3.719	4.249
Weeks to First Observed Tumor	94	68	48

Table 15. Analyses of the Incidence of Primary Tumors in Female Mice Fed Diets Containing C. I. Disperse Yellow 3 (a)

(Continued)

	Control	Low Dose	High Dose
Liver: Hepatocellular Adenoma (b)	0/50(0)	6/50(12)	12/50(24)
P Values (c), (d)	P less than 0.001	P=0.013	P less than 0.001
Relative Risk (Control) (e)		Infinite	Infinite
Lower Limit		1.600	3.667
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	-	105	105
Liver: Hepatocellular Carcinoma (b)	2/50(4)	4/50(8)	5/50(10)
P Values (c), (d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		2.000	2.500
Lower Limit		0.301	0.432
Upper Limit		21.316	25.286
Weeks to First Observed Tumor	102	99	83
Liver: Hepatocellular Adenoma or Carcinoma (b)	2/50(4)	10/50(20)	17/50(34)
P Values (c), (d)	P less than 0.001	P=0.014	P less than 0.001
Relative Risk (Control) (e)		5.000	8.500
Lower Limit		1.140	2.180
Upper Limit		45.011	72.178
Weeks to First Observed Tumor	102	99	83

Table 15. Analyses of the Incidence of Primary Tumors in Female Mice Fed Diets Containing C. I. Disperse Yellow 3 (a)

(Continued)

	Control	Low Dose	High Dose
Pituitary: Chromophobe Adenoma (b)	1/38(3)	1/30(3)	4/42(10)
P Values (c), (d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.267	3.619
Lower Limit		0.017	0.380
Upper Limit		96.122	173.681
Weeks to First Observed Tumor	105	95	105
Eye/Lacrimal Gland: Papillary Adenoma (b)	1/50(2)	3/50(6)	1/50(2)
P Values (c), (d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		3.000	1.000
Lower Limit		0.251	0.013
Upper Limit		154.270	76.970
Weeks to First Observed Tumor	105	105	105

(a) Dosed groups received doses of 2,500 or 5,000 ppm in the diet.
(b) Number of tumor-bearing animals/number of animals examined at site (percent).
(c) Beneath the incidence of tumors in the control group is the probability level for the Cochran-Armitage test when P is less than 0.05; otherwise, not significant (N.S.) is indicated. Beneath the incidence of tumors in a dosed group is the probability level for the Fisher exact test for the comparison of that dosed group with the control group when P is less than 0.05; otherwise, not significant (N.S.) is indicated.
(d) A negative trend (N) indicates a lower incidence in a dosed group than in a control group.
(e) The 95 percent confidence interval of the relative risk between each dosed group and the control group.
(f) The probability level for departure from linear trend is given when P is less than 0.05 for any comparison.

V. DISCUSSION

During the 2-year study, body weight gains by C. I. Disperse Yellow 3 dosed rats were depressed in a dose-related fashion. Also, weight gains by dosed mice tended to be depressed, but the magnitude of the effect was less than that observed among dosed rats, and dose-response relationships were not always obvious. However, feed consumption by dosed and control groups in the chronic study were comparable (Appendix H), and the observed weight gain decrements may be attributed to consumption of the test chemical.

The NCI guidelines (NCI 1976) for chronic feeding dosage selection were not strictly adhered to during this study. These guidelines suggest that dosage levels that cause greater than 10% decrements in body weight gains during prechronic testing should not be employed in the 2-year feeding study. In the 13-week studies, 17.7% and 21.6% decrements in weight gains by male and female rats were associated with dietary levels of 10,000 ppm C. I. Disperse Yellow 3. Similarly, dietary levels of 5,000 ppm caused 18.8% and 8.2% decrements in male and female mice, whereas the 10,000 ppm levels caused a decrease in body weight gain of 15% (male) and 10% (female). These dosage levels were selected to maximize the likelihood of reproducing the thyroid lesions observed in rats during the 90-day study. Although the thyroid effects were not observed in the two-year test, the dosage levels of C. I. Disperse Yellow 3 used in this study are judged to be adequate.

Despite the effects of compound administration on body weight gains, C. I. Disperse Yellow 3 did not adversely affect either rat or mouse survival. In fact, dosed rats survived significantly longer than did control rats. The survival rate for control female rats in this study was consistent with control rates in three previous groups (190 animals) utilized in these laboratories, and control male rat survival was consistent with that in two of the three previous control groups. The excellent survival rates of dosed rats and mice indicate that the maximum tolerated doses of C. I. Disperse Yellow 3 were not exceeded during this study.

An explanation for the improved survival of rats administered C. I. Disperse Yellow 3 is not obvious. A combination of negative trends related to certain primary tumors in dosed rats (as identified below) may have influenced survival, but the effect cannot be attributed to any single decrease in tumor incidence. With the exception of the decreased incidences of lymphoma or leukemia, all negative trends were seen in either male or female animals but not in both sexes. Among males, the decreased incidence of malignant mesothelioma and C-cell carcinoma of the thyroid are not considered to be sufficient to account for a significant increase in survival rate. Among female rats, a decreased incidence of pituitary adenoma could influence survival but a decrease in endometrial stromal polyps (which was probably secondary to decreased pituitary adenomas) would not.

Although a treatment-related decrease in lymphoma or leukemia was detected in both sexes of rats, the results of earlier studies do not support a relationship between this effect and increased survival. At least four other test agents--C. I. Acid Orange 10, C. I. Acid Red 14, C. I. Solvent Yellow 14, and D & C Red No. 9 (NTP 1982, 1982a, 1982b, 1982c)—have been found to decrease the incidence of lymphoma or leukemia in F344 rats. These decreases were not associated with significant increases in survival.

Lymphomas or leukemias occurred in a dose-related trend among female mice with a statistically significant ($P < 0.05$) difference between high-dose and control groups. The high-dose incidence is also significantly ($P < 0.05$) greater than the historical control rate for female mice with lymphoma or leukemia at this laboratory (23%, range 20%-32%). However, the incidence of these tumors shows considerable variability throughout the Bioassay Program (historical control range: 8-62%); further, since the increase in this study was observed only for female mice, this induced tumor was not regarded as clearly related to the administration of C. I. Disperse Yellow 3.

Although not statistically significant, the appearance of stomach tumors among C. I. Disperse Yellow 3 dosed male rats deserves mention. These rare stomach tumors were observed in 4/50 low-dose and 1/50 high-dose F344 rats.

The historical incidence of this tumor is only 10/2,960 (0.3%) in control male rats. Despite the lack of a dose-response relationship, the occurrence of these lesions may be treatment related.

Significant increases in hepatic neoplastic nodules were detected in both dosed groups of male rats, and a significant and dose-related increase in hepatocellular adenoma was detected in female mice. The incidence of hepatocellular carcinoma was not significantly altered by administration of the test chemical, although in female mice the incidences were higher in both dosed groups compared with controls. Hepatic neoplastic nodules and adenomas are populations of lesions, some of which may regress while others may progress to hepatocellular carcinoma. At the present time, it is impossible to differentiate between lesions that will regress and those that will progress. Consequently, one should consider these nodules and adenomas to exist at some ill-defined point along a continuum between benign and malignant with various factors being capable of influencing their final disposition. Teebor and Becker (1971), working with the hepatocarcinogen N-2-fluorenylacetamide (2-AAF), presented evidence that the fate of hepatic neoplastic nodules in Sprague-Dawley rats can be influenced by the duration of carcinogen administration. Nodules induced by a 3-month exposure to the carcinogen tended to regress when the treatment was stopped. This exposure was associated with a low incidence of hepatocellular carcinomas. Nodules produced by 4 months of treatment, however, were more persistent and were associated with a high incidence of hepatocellular carcinomas. Hirota and Williams (1979) in a similar study did not report regression of the nodules in F344 rats but observed that the nodules grew progressively in size.

The National Academy of Sciences (Stewart et al., 1980) considers the hepatic neoplastic nodule (and hepatic cell adenoma) to be a manifestation of the process of hepatocarcinogenesis which is induced by a variety of hepatocarcinogens but not by noncarcinogenic agents. The NAS defined neoplastic nodules as hepatocellular carcinomas, differentiated or grade 1. National and international organizations have stated that few, if any, chemicals produce only benign tumors in any species and that agents that markedly increase the incidence of benign tumors are now viewed with as much

suspicion as they would have been had the induced tumors been malignant (IARC, 1980; IRLG, 1979; Fed. Reg., 1980). Therefore, C. I. Disperse Yellow 3 is considered to be a carcinogen in F344 male rats and in B6C3F1 female mice. It is impossible to state if this carcinogenic effect is mediated through genetic or nongenetic mechanisms. It should be pointed out, however, that this azo dye could undergo metabolic reduction to form aromatic amines. The carcinogenicity of numerous aromatic amines has been well established. Additional studies would be required to clarify this point.

Significantly decreased incidences of two primary tumors, hepatocellular adenomas in males and alveolar/bronchiolar adenomas in females, were observed in C. I. Disperse Yellow 3 dosed mice. These decreases are not considered to be associated with administration of the dye because these were evident only for mice at the low doses and were not consistent across sexes.

An increased incidence of alveolar/bronchiolar adenomas was observed among male mice, while a significantly lower incidence was detected in low-dose females. Although the increase among males was significant ($P=0.023$) and dose-related ($P=0.019$), the control incidence (2/50, 4%) was lower than the mean (6.4%) of the historical controls encountered in this laboratory. Also, when the adenomas were combined with alveolar/bronchiolar carcinomas, there were no statistically significant differences between controls and dosed groups; the dose-related trend remained significant ($P=0.046$). Because of the historical data, the significantly lower incidence among low-dose females, and the loss of statistical significance when adenomas and carcinomas were combined, relating this change to the administration of C. I. Disperse Yellow 3 lacks convincing support. However, the results cannot be dismissed and should be interpreted in light of the other experimental findings.

VI. CONCLUSIONS

Under the conditions of this bioassay, C. I. Disperse Yellow 3 was considered to be carcinogenic for male F344 rats, causing an increased incidence of neoplastic nodules of the liver; this dye was not carcinogenic for female F344 rats. In addition, the stomach tumors found in the male rats may have been induced by the administration of the test chemical. C. I. Disperse Yellow 3 was carcinogenic for female B6C3F1 mice, as evidenced by the increased incidence of hepatocellular adenomas. C. I. Disperse Yellow 3 was not carcinogenic for male B6C3F1 mice. Also, the increased incidence of malignant lymphoma in female mice may have been associated with the administration of C. I. Disperse Yellow 3.

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APPENDIX A

Summary of the Incidence of Neoplasms in Rats
Fed Diets Containing C. I. Disperse Yellow 3

TABLE A1.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS FED DIETS CONTAINING C.I. DISPERSE YELLOW 3

	CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA		1 (2%)	
BASAL-CELL CARCINOMA	1 (2%)		
*SUBCUT TISSUE	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA	1 (2%)		1 (2%)
BASAL-CELL CARCINOMA	1 (2%)		1 (2%)
SARCOMA, NOS			1 (2%)
FIBROMA	3 (6%)	1 (2%)	1 (2%)
FIBROSARCOMA			2 (4%)
FIBROSARCOMA, INVASIVE	1 (2%)		
LIPOMA			1 (2%)
OSTEOSARCOMA			1 (2%)
RESPIRATORY SYSTEM			
*NASAL CAVITY	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA, INVASIV	1 (2%)		
#LUNG	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA		1 (2%)	
SQUAMOUS CELL CARCINOMA, METASTA			1 (2%)
ALVEOLAR/BRONCHIOLAR ADENOMA	1 (2%)		
ALVEOLAR/BRONCHIOLAR CARCINOMA	1 (2%)		
OSTEOSARCOMA, METASTATIC			2 (4%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
LYMPHOCYTIC LEUKEMIA	13 (26%)	2 (4%)	1 (2%)
#SPLEEN	(50)	(50)	(50)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE		1 (2%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#MANDIBULAR L. NODE	(47)	(48)	(45)
SQUAMOUS CELL CARCINOMA, METASTA			1 (2%)
#PRETRACHEAL LYMPH NO	(47)	(48)	(45)
C-CELL CARCINOMA, METASTATIC	1 (2%)		
CIRCULATORY SYSTEM			
#ENDOCARDIUM	(50)	(50)	(49)
NEURILEMOMA, MALIGNANT			1 (2%)
*MIDDLE MENINGEAL ART	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA, METASTA	1 (2%)		
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(46)	(50)	(49)
FIBROSARCOMA	1 (2%)		
#LIVER	(49)	(50)	(50)
NEOPLASTIC NODULE	1 (2%)	15 (30%)	10 (20%)
HEPATOCELLULAR CARCINOMA	1 (2%)		2 (4%)
#STOMACH	(49)	(50)	(50)
ADENOCARCINOMA, NOS			1 (2%)
MUCINOUS ADENOCARCINOMA		1 (2%)	
SARCOMA, NOS			1 (2%)
#CARDIAC STOMACH	(49)	(50)	(50)
SQUAMOUS CELL PAPILLOMA		1 (2%)	
FIBROSARCOMA		1 (2%)	
#PYLORUS	(49)	(50)	(50)
ADENOMA, NOS		1 (2%)	
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(50)
TUBULAR-CELL ADENOMA			1 (2%)
TUBULAR-CELL ADENOCARCINOMA			1 (2%)
#URINARY BLADDER	(45)	(50)	(48)
LEIOMYOMA			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
ENDOCRINE SYSTEM			
#PITUITARY	(47)	(49)	(46)
ADENOMA, NOS	1 (2%)		
CHROMOPHOBE ADENOMA	5 (11%)	7 (14%)	4 (9%)
CHROMOPHOBE CARCINOMA	1 (2%)		
ACIDOPHIL ADENOMA			1 (2%)
#ADRENAL	(50)	(50)	(49)
PHEOCHROMOCYTOMA	6 (12%)	8 (16%)	3 (6%)
PHEOCHROMOCYTOMA, MALIGNANT	1 (2%)	3 (6%)	2 (4%)
#THYROID	(49)	(50)	(48)
PAPILLARY ADENOMA		1 (2%)	
FOLLICULAR-CELL ADENOMA		1 (2%)	
C-CELL ADENOMA		1 (2%)	
C-CELL CARCINOMA	4 (8%)	1 (2%)	
#PANCREATIC ISLETS	(48)	(50)	(49)
ISLET-CELL ADENOMA		2 (4%)	
ISLET-CELL CARCINOMA	2 (4%)	1 (2%)	2 (4%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
FIBROADENOMA			1 (2%)
*PREPUTIAL GLAND	(50)	(50)	(50)
CARCINOMA,NOS		2 (4%)	
ADENOMA, NOS			2 (4%)
#TESTIS	(49)	(49)	(50)
INTERSTITIAL-CELL TUMOR	46 (94%)	48 (98%)	43 (86%)
NERVOUS SYSTEM			
#BRAIN	(50)	(50)	(50)
GRANULAR-CELL TUMOR, BENIGN			1 (2%)
GLIOMA, NOS			1 (2%)
ASTROCYTOMA		1 (2%)	2 (4%)
#OLFACTORY BULB	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA, INVASIV	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
SPECIAL SENSE ORGANS			
*EAR CANAL	(50)	(50)	(50)
SQUAMOUS CELL PAPILLOMA	1 (2%)		
SQUAMOUS CELL CARCINOMA	1 (2%)		
*ZYMBAL'S GLAND	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA	1 (2%)		
MUSCULOSKELETAL SYSTEM			
*SKULL	(50)	(50)	(50)
OSTEOMA			1 (2%)
BODY CAVITIES			
*MEDIASTINUM	(50)	(50)	(50)
NONCHROMAFFIN PARAGANGLIOMA			1 (2%)
*PELVIS	(50)	(50)	(50)
OSTEOSARCOMA			1 (2%)
*TUNICA VAGINALIS	(50)	(50)	(50)
MESOTHELIOMA, NOS	1 (2%)	3 (6%)	1 (2%)
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
MESOTHELIOMA, MALIGNANT	4 (8%)	2 (4%)	
TAIL			
SQUAMOUS CELL PAPILLOMA		1	
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	15	4	8
MORIBUND SACRIFICE	4	1	3
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	31	45	39
ANIMAL MISSING			

@ INCLUDES AUTOLYZED ANIMALS

\# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	50	50	47
TOTAL PRIMARY TUMORS	98	107	93
TOTAL ANIMALS WITH BENIGN TUMORS	48	49	46
TOTAL BENIGN TUMORS	63	72	61
TOTAL ANIMALS WITH MALIGNANT TUMORS	28	15	16
TOTAL MALIGNANT TUMORS	33	17	21
TOTAL ANIMALS WITH SECONDARY TUMORS#	3		3
TOTAL SECONDARY TUMORS	5		4
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	2	17	11
TOTAL UNCERTAIN TUMORS	2	18	11
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS
\# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE A2.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS FED DIETS CONTAINING C. I. DISPERSE YELLOW 3

	CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SUBCUT TISSUE	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA		1 (2%)	
C-CELL CARCINOMA, INVASIVE			1 (2%)
SARCOMA, NOS		1 (2%)	
FIBROMA		1 (2%)	
FIBROSARCOMA	1 (2%)		
LEIOMYOSARCOMA		1 (2%)	
RESPIRATORY SYSTEM			
*NASAL CAVITY	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA, INVASIV		1 (2%)	
#LUNG	(49)	(50)	(50)
C-CELL CARCINOMA, METASTATIC			1 (2%)
GANGLIONEUROBLASTOMA, METASTATIC		1 (2%)	
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	1 (2%)	2 (4%)	2 (4%)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	1 (2%)		
LYMPHOCYTIC LEUKEMIA	7 (14%)	2 (4%)	
#SPLEEN	(48)	(50)	(50)
FIBROSARCOMA			1 (2%)
LYMPHOCYTIC LEUKEMIA	1 (2%)		1 (2%)
#LYMPH NODE	(48)	(44)	(44)
FIBROSARCOMA, METASTATIC	1 (2%)		
#BRONCHIAL LYMPH NODE	(48)	(44)	(44)
FIBROSARCOMA, METASTATIC			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#MEDIASTINAL L.NODE	(48)	(44)	(44)
C-CELL CARCINOMA, METASTATIC			1 (2%)
CIRCULATORY SYSTEM			
#HEART	(50)	(50)	(49)
NEURILEMOMA		1 (2%)	
DIGESTIVE SYSTEM			
#LIVER	(50)	(49)	(50)
NEOPLASTIC NODULE	2 (4%)	1 (2%)	2 (4%)
HEPATOCELLULAR CARCINOMA			1 (2%)
FIBROSARCOMA, METASTATIC			1 (2%)
#PANCREAS	(48)	(50)	(50)
FIBROSARCOMA, INVASIVE			1 (2%)
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(50)
TUBULAR-CELL ADENOCARCINOMA	1 (2%)		
ENDOCRINE SYSTEM			
#PITUITARY	(44)	(48)	(49)
CARCINOMA,NOS			1 (2%)
ADENOMA, NOS		1 (2%)	
CHROMOPHOBE ADENOMA	15 (34%)	15 (31%)	8 (16%)
CHROMOPHOBE CARCINOMA	1 (2%)		
#ADRENAL	(50)	(50)	(50)
CORTICAL ADENOMA		1 (2%)	
CORTICAL CARCINOMA	1 (2%)		
PHEOCHROMOCYTOMA	2 (4%)	3 (6%)	
PHEOCHROMOCYTOMA, MALIGNANT		1 (2%)	
GANGLIONEUROMA	1 (2%)	1 (2%)	
GANGLIONEUROBLASTOMA		1 (2%)	
#ZONA FASCICULATA	(50)	(50)	(50)
ADENOMA, NOS			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#THYROID	(49)	(49)	(50)
C-CELL CARCINOMA	1 (2%)	2 (4%)	3 (6%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
ADENOMA, NOS	1 (2%)	1 (2%)	
ADENOCARCINOMA, NOS		1 (2%)	
CARCINOSARCOMA		1 (2%)	
FIBROADENOMA	7 (14%)	11 (22%)	3 (6%)
*MAMMARY DUCT	(50)	(50)	(50)
ADENOCARCINOMA, NOS		1 (2%)	
*PREPUTIAL GLAND	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA	1 (2%)		
*CLITORAL GLAND	(50)	(50)	(50)
ADENOCARCINOMA, NOS	1 (2%)		
#UTERUS	(50)	(48)	(50)
ENDOMETRIAL STROMAL POLYP	14 (28%)	7 (15%)	3 (6%)
CARCINOSARCOMA		1 (2%)	
#OVARY	(50)	(49)	(50)
GRANULOSA-CELL TUMOR		1 (2%)	1 (2%)
FIBROSARCOMA			1 (2%)
NERVOUS SYSTEM			
#BRAIN	(50)	(50)	(49)
GRANULAR-CELL TUMOR, BENIGN		1 (2%)	
ASTROCYTOMA	1 (2%)		
SPECIAL SENSE ORGANS			
NONE			
MUSCULOSKELETAL SYSTEM			
NONE			

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
BODY CAVITIES			
NONE			
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA, METASTA	1 (2%)		
LEIOMYOSARCOMA		1 (2%)	
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	11	7	3
MORIBUND SACRIFICE	6	3	1
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	33	40	46
ANIMAL MISSING			
@ INCLUDES AUTOLYZED ANIMALS			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	38	40	25
TOTAL PRIMARY TUMORS	60	61	28
TOTAL ANIMALS WITH BENIGN TUMORS	29	30	15
TOTAL BENIGN TUMORS	40	43	15
TOTAL ANIMALS WITH MALIGNANT TUMORS	17	15	9
TOTAL MALIGNANT TUMORS	18	16	10
TOTAL ANIMALS WITH SECONDARY TUMORS#	2	2	2
TOTAL SECONDARY TUMORS	2	2	6
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	2	2	3
TOTAL UNCERTAIN TUMORS	2	2	3
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS
# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE A3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY TABLES OF MALE RATS IN THE 2-YEAR STUDY OF C.I. DISPERSE YELLOW 3

CONTROL

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	104	104	104	093	081	104	104	104	104	104	104	104	101	104	094	099	104	077	104	099	104	104	075	104	104
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	N	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+
BASAL-CELL CARCINOMA																									
SUBCUTANEOUS TISSUE	+	+	+	N	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA																									
BASAL-CELL CARCINOMA																									
FIBROMA				X																					
FIBROSARCOMA, INVASIVE																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA																									
ALVEOLAR/BRONCHIOLAR CARCINOMA																									
TRACHEA	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
NASAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL CARCINOMA, INVASIVE																									
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
C-CELL CARCINOMA, METASTATIC																									
THYMUS	+	+	+	-	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BLOOD VESSELS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL CARCINOMA, METASTAT																									
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
FIBROSARCOMA																									
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE																									X
HEPATOCELLULAR CARCINOMA																									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+
LARGE INTESTINE	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+
ADENOMA, NOS											X														
CHROMOPHOBE ADENOMA																									
CHROMOPHOBE CARCINOMA																									
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA							X			X					X									X	
PHEOCHROMOCYTOMA, MALIGNANT																									
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
C-CELL CARCINOMA										X									X			X			
PARATHYROID	-	+	+	+	-	-	+	-	+	+	-	+	-	+	+	+	+	+	-	+	+	-	+	-	+
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL CARCINOMA																									
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	+	+	N	N	+	N	N	+	+	+	+	N	+	N	N	+	N	+	N	+	+	+	+	+
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PROSTATE	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA, INVASIVE																									
SPECIAL SENSE ORGANS																									
EAR	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL PAPILLOMA																									
SQUAMOUS CELL CARCINOMA																									
ZYMBAL'S GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL CARCINOMA																						X			
BODY CAVITIES																									
TUNICA VAGINALIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MESOTHELIOMA, NOS																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MESOTHELIOMA, MALIGNANT								X																	
LYMPHOCYTIC LEUKEMIA			X	X	X	X				X				X						X					

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A3. MALE RATS: TUMOR PATHOLOGY (CONTINUED) CONTROL

ANIMAL NUMBER	026	027	028	029	031	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL
WEEKS ON STUDY	104	104	104	104	096	102	104	104	104	081	104	104	102	090	080	104	104	096	093	104	104	093	101	081	104	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SKIN	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	50*
BASAL-CELL CARCINOMA												X														1
SUBCUTANEOUS TISSUE	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	50*
SQUAMOUS CELL CARCINOMA																						X				1
BASAL-CELL CARCINOMA													X													1
FIBROMA					X		X																			3
FIBROSARCOMA, INVASIVE																					X					1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALVEOLAR/BRONCHIOLAR ADENOMA																							X			1
ALVEOLAR/BRONCHIOLAR CARCINOMA				X																						1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
NASAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
SQUAMOUS CELL CARCINOMA, INVASIVE																						X				1
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	48
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	47
C-CELL CARCINOMA, METASTATIC																		X								1
THYMUS	-	+	+	+	-	-	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	40
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
BLOOD VESSELS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
SQUAMOUS CELL CARCINOMA, METASTAT																						X				1
DIGESTIVE SYSTEM																										
SALIVARY GLAND	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	46
FIBROSARCOMA																					X					1
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	49
NEOPLASTIC NODULE																										1
HEPATOCELLULAR CARCINOMA				X																						1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	49
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
PANCREAS	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SMALL INTESTINE	+	+	+	+	-	-	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	43
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	45
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ADENOMA, NOS		X																								1
CHROMOPHOBE ADENOMA								X		X		X														5
CHROMOPHOBE CARCINOMA																		X							X	1
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
PHEOCHROMOCYTOMA								X													X					6
PHEOCHROMOCYTOMA, MALIGNANT																									X	1
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
C-CELL CARCINOMA																		X								4
PARATHYROID	-	+	+	+	+	-	+	+	-	+	+	+	-	+	+	-	-	-	+	+	+	+	+	+	+	34
PANCREATIC ISLETS	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ISLET-CELL CARCINOMA									X										X							2
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	N	+	+	N	+	N	+	+	N	+	+	N	N	N	N	+	N	N	+	+	N	+	+	+	50*
TESTIS	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
INTERSTITIAL-CELL TUMOR	X	X	X	X	X		X		X		X	X	X	X	X	X	X	X	X	X	X	X	X		X	46
PROSTATE	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	45
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SQUAMOUS CELL CARCINOMA, INVASIVE																						X				1
SPECIAL SENSE ORGANS																										
EAR	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N	50*
SQUAMOUS CELL PAPILLOMA																							X			1
SQUAMOUS CELL CARCINOMA														X												1
ZYMBAL'S GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N	50*
SQUAMOUS CELL CARCINOMA																										1
BODY CAVITIES																										
TUNICA VAGINALIS	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
MESOTHELIOMA, NOS											X															1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
MESOTHELIOMA, MALIGNANT	X				X										X											4
LYMPHOCYTIC LEUKEMIA		X				X							X						X				X	X		13

* ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY TABLES OF MALE RATS IN THE 2-YEAR STUDY OF C.I. DISPERSE YELLOW 3

LOW DOSE

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	104	104	098	104	104	104	077	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	095	104
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA																							X		
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROMA																									X
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA																									
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																									
LYMPH NODES	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE					X			X	X					X		X			X	X					
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL PAPILLOMA											X														
ADENOMA, NOS															X										
MUCINOUS ADENOCARCINOMA						X																			
FIBROSARCOMA																									
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	-	+	+	-	-	+	+	+	+	+	+	+	-	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CHROMOPHOBE ADENOMA		X			X			X	X		X		X												
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA															X		X								
PHEOCHROMOCYTOMA, MALIGNANT							X												X						
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PAPILLARY ADENOMA																									
FOLLICULAR-CELL ADENOMA			X																						
C-CELL ADENOMA																									
C-CELL CARCINOMA																			X						
PARATHYROID	+	+	+	+	-	-	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL ADENOMA											X														
ISLET-CELL CARCINOMA																									
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	N	+	+	+	N	+	N	+	+	+	N	+	+	N	+	N	+	+	+	+	N	N	+
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PROSTATE	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
CARCINOMA,NOS				X																					
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ASTROCYTOMA						X																			
BODY CAVITIES																									
TUNICA VAGINALIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MESOTHELIOMA, NOS																				X					
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MESOTHELIOMA, MALIGNANT																									
LYMPHOCYTIC LEUKEMIA			X											X											
TAIL																									
SQUAMOUS CELL PAPILLOMA																									

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A3. MALE RATS: TUMOR PATHOLOGY (CONTINUED) LOW DOSE

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL TISSUES TUMORS
WEEKS ON STUDY	089	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	093	104	104	104	104	
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SQUAMOUS CELL CARCINOMA																										1
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
FIBROMA																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SQUAMOUS CELL CARCINOMA																								X		1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																					X					1
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
THYMUS	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	45
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NEOPLASTIC NODULE					X						X	X		X		X						X		X	X	15
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SQUAMOUS CELL PAPILLOMA																										1
ADENOMA, NOS																										1
MUCINOUS ADENOCARCINOMA																										1
FIBROSARCOMA		X																								1
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LARGE INTESTINE	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	49
CHROMOPHOBE ADENOMA																					X					7
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
PHEOCHROMOCYTOMA		X			X					X			X						X				X			8
PHEOCHROMOCYTOMA, MALIGNANT																						X				3
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
PAPILLARY ADENOMA																						X				1
FOLLICULAR-CELL ADENOMA																										1
C-CELL ADENOMA														X												1
C-CELL CARCINOMA																										1
PARATHYROID	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	43
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ISLET-CELL ADENOMA																						X				2
ISLET-CELL CARCINOMA			X																							1
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	50
TESTIS	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
INTERSTITIAL-CELL TUMOR	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	48
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
CARCINOMA,NOS																			X							2
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ASTROCYTOMA																										1
BODY CAVITIES																										
TUNICA VAGINALIS	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
MESOTHELIOMA, NOS			X	X																						3
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
MESOTHELIOMA, MALIGNANT							X									X										2
LYMPHOCYTIC LEUKEMIA																										2
TAIL																										
SQUAMOUS CELL PAPILLOMA										X																1

N ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY TABLES OF MALE RATS IN THE 2-YEAR STUDY OF C.I. DISPERSE YELLOW 3

HIGH DOSE

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	104	104	104	071	104	101	104	079	104	078	104	102	104	104	098	104	104	104	104	104	104	104	104	104	104
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA																									
BASAL-CELL CARCINOMA																									
SARCOMA, NOS																									
FIBROMA																	X								
FIBROSARCOMA																									
LIPOMA																						X			
OSTEOSARCOMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA, METASTAT																									
OSTEOSARCOMA, METASTATIC						X																			
TRACHEA	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+
SQUAMOUS CELL CARCINOMA, METASTAT																									
THYMUS	+	+	+	+	-	-	-	-	+	A	+	-	+	+	+	+	+	+	-	+	-	-	+	+	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEURILEMOMA, MALIGNANT														X											
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE	X						X									X	X			X			X		
HEPATOCELLULAR CARCINOMA																X									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS	X																								
SARCOMA, NOS	X																								
SMALL INTESTINE	+	+	+	+	+	-	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	A	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TUBULAR-CELL ADENOMA														X											
TUBULAR-CELL ADENOCARCINOMA																									
URINARY BLADDER	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LEIOMYOMA																		X							
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+
CHROMOPHOBE ADENOMA																						X			
ACIDOPHIL ADENOMA												X													
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA									X																
PHEOCHROMOCYTOMA, MALIGNANT																	X								
THYROID	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
PARATHYROID	+	+	+	-	+	+	-	-	+	+	-	-	+	-	+	+	+	+	-	+	+	+	+	+	+
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL CARCINOMA	X																								X
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	+	+	+	+	N	+	N	+	+	+	N	N	+	N	+	N	+	+	+	N	N	N	+	+
FIBROADENOMA																									
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR	X	X	X	X	X	X	X		X		X		X	X	X	X	X	X	X	X	X	X	X	X	X
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS							X																		
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GRANULAR-CELL TUMOR, BENIGN																									
GLIOMA, NOS																									
ASTROCYTOMA				X																					
MUSCULOSKELETAL SYSTEM																									
BONE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
OSTEOMA								X																	
BODY CAVITIES																									
MEDIASTINUM	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
NONCHROMAFFIN PARAGANGLIOMA																									
PERITONEUM	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
OSTEOSARCOMA						X																			
TUNICA VAGINALIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MESOTHELIOMA, NOS																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
LYMPHOCYTIC LEUKEMIA															X										

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A3. MALE RATS: TUMOR PATHOLOGY (CONTINUED) HIGH DOSE

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL
WEEKS ON STUDY	104	104	041	000	087	041	041	098	041	041	041	041	041	041	041	041	041	041	041	043	041	041	062	041	041	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	N	+	+	+	+	+	+	+	50M	
SQUAMOUS CELL CARCINOMA					X																				1	
BASAL-CELL CARCINOMA				X																					1	
SARCOMA, NOS								X																	1	
FIBROMA																									1	
FIBROSARCOMA					X														X						2	
LIPOMA																									1	
OSTEOSARCOMA													X												1	
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
SQUAMOUS CELL CARCINOMA, METASTAT					X																				1	
OSTEOSARCOMA, METASTATIC													X												2	
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
LYMPH NODES	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	45	
SQUAMOUS CELL CARCINOMA, METASTAT					X																				1	
THYMUS	+	+	+	-	-	+	+	-	+	+	+	-	-	+	+	+	+	-	+	+	+	+	+	+	34	
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
NEURILEMOMA, MALIGNANT																									1	
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
NEOPLASTIC NODULE						X				X			X											X	1	0
HEPATOCELLULAR CARCINOMA														X											1	2
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M	
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
ADENOCARCINOMA, NOS																									1	
SARCOMA, NOS																									1	
SMALL INTESTINE	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	46	
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47	
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
TUBULAR-CELL ADENOMA																									1	
TUBULAR-CELL ADENOCARCINOMA								X																	1	
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	48	
LEIOMYOMA																									1	
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46	
CHROMOPHOBE ADENOMA							X						X						X						4	
ACIDOPHIL ADENOMA																									1	
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	49	
PHEOCHROMOCYTOMA		X																	X						3	
PHEOCHROMOCYTOMA, MALIGNANT																			X						2	
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48	
PARATHYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	-	-	+	39	
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
ISLET-CELL CARCINOMA																									2	
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	N	N	N	N	+	+	N	+	+	+	N	+	+	N	N	+	+	N	N	+	50M	
FIBROADENOMA																	X								1	
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
INTERSTITIAL-CELL TUMOR	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	43	
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M	
ADENOMA, NOS	X																								2	
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
GRANULAR-CELL TUMOR, BENIGN												X													1	
GLIOMA, NOS																								X	1	
ASTROCYTOMA						X																			2	
MUSCULOSKELETAL SYSTEM																										
BONE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M	
OSTEOMA																									1	
BODY CAVITIES																										
MEDIASTINUM	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M	
NONCHROMAFFIN PARAGANGLIOMA																	X								1	
PERITONEUM	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M	
OSTEOSARCOMA																									1	
TUNICA VAGINALIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M	
MESOTHELIOMA, NOS													X												1	
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M	
LYMPHOCYTIC LEUKEMIA																									1	

M ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY TABLES OF FEMALE RATS IN THE 2-YEAR STUDY OF C.I. DISPERSE YELLOW 3

CONTROL

ANIMAL NUMBER	0012	0028	0034	0046	0052	0068	0074	0088	0094	0110	0114	0122	0134	0141	0155	0166	0178	0184	0190	0206	0212	0226	0234	0251
WEEKS ON STUDY	1104	1104	1104	1104	0988	0889	0104	1104	1101	1104	1104	1104	1104	1104	0080	0699	1104	1104	0664	0994	1104	1104	0882	1104	1104
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROSARCOMA																			X						
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPHOCYTIC LEUKEMIA																									
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROSARCOMA, METASTATIC																			X						
THYMUS	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	-	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE	X																								
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TUBULAR-CELL ADENOCARCINOMA																									
URINARY BLADDER	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	-	+	+	+	-	+	+	+	+	+	+	-	+	-	+	-	+	+	+	+	+	+
CHROMOPHOBE ADENOMA						X			X	X										X	X				
CHROMOPHOBE CARCINOMA																									
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CORTICAL CARCINOMA						X																			
PHEOCHROMOCYTOMA					X																				
GANGLIONEUROMA						X																			
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+
C-CELL CARCINOMA																									
PARATHYROID	-	+	+	+	+	-	-	+	-	-	-	+	+	+	+	-	+	+	+	+	+	+	-	+	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	N	+	+
ADENOMA, NOS	X								X															X	
FIBROADENOMA				X																					
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL CARCINOMA																X									
ADENOCARCINOMA, NOS																									
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOMETRIAL STROMAL POLYP					X				X							X				X		X		X	
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ASTROCYTOMA																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL CARCINOMA, METASTAT																X									
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																									
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																									
LYMPHOCYTIC LEUKEMIA			X	X			X												X				X		

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

.: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A4. FEMALE RATS: TUMOR PATHOLOGY (CONTINUED) CONTROL

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL
WEEKS ON STUDY	104	083	104	104	104	073	104	103	104	104	104	104	104	098	104	117	101	098	104	104	104	103	104	104	099	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
FIBROSARCOMA																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	49
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	–	+	+	+	48
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPLEEN	+	–	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
LYMPHOCYTIC LEUKEMIA											X															1
LYMPH NODES	+	+	+	+	+	+	–	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	48
FIBROSARCOMA, METASTATIC																										1
THYMUS	+	–	–	+	+	+	+	–	+	+	+	+	+	A	+	–	+	–	–	–	+	+	+	+	–	37
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	49
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NEOPLASTIC NODULE																									X	2
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
PANCREAS	+	+	+	+	+	–	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	48
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
STOMACH	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SMALL INTESTINE	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
TUBULAR-CELL ADENOCARCINOMA									X																	1
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
CHROMOPHOBE ADENOMA							X			X	X	X						X	X	X	X	X		X		15
CHROMOPHOBE CARCINOMA																									X	1
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CORTICAL CARCINOMA																										1
PHEOCHROMOCYTOMA																		X								2
GANGLIONEUROMA																										1
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
C-CELL CARCINOMA																								X		1
PARATHYROID	+	+	+	+	+	+	+	+	–	+	+	+	+	+	–	–	+	+	–	–	+	+	+	+	+	37
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	N	+	+	+	N	N	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
ADENOMA, NOS															X											1
FIBROADENOMA				X					X				X													7
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
SQUAMOUS CELL CARCINOMA																										1
ADENOCARCINOMA, NOS																									X	1
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOMETRIAL STROMAL POLYP			X	X	X			X				X	X										X	X		14
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ASTROCYTOMA		X																								1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
SQUAMOUS CELL CARCINOMA, METASTAT																	X									1
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																										1
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																X										1
LYMPHOCYTIC LEUKEMIA																				X			X			7

* ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
–: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY TABLES OF FEMALE RATS IN THE 2-YEAR STUDY OF C.I. DISPERSE YELLOW 3

LOW DOSE

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	071	104	104	651	041	093	041	041	041	041	041	041	041	041	041	041	041	089	041	001	041	041	041	041	041
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA																		X							
SARCOMA, NOS	X																								
FIBROMA																									
LEIOMYOSARCOMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GANGLIONEUROBLASTOMA, METASTATIC																						X			
TRACHEA	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NASAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N
SQUAMOUS CELL CARCINOMA, INVASIVE																		X							
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
THYMUS	+	-	+	-	+	-	+	+	+	-	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEURILEMOMA								X																	
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+
NEOPLASTIC NODULE										X															
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+
ADENOMA, NOS																									
CHROMOPHOBE ADENOMA			X			X	X									X	X		X					X	
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CORTICAL ADENOMA																									X
PHEOCHROMOCYTOMA									X														X		
PHEOCHROMOCYTOMA, MALIGNANT																									
GANGLIONEUROMA																									
GANGLIONEUROBLASTOMA																						X			
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+
C-CELL CARCINOMA			X																						
PARATHYROID	-	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	-	-	-	-	+	+	+	-	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS									X																
ADENOCARCINOMA, NOS																								X	
CARCINOSARCOMA											X														
FIBROADENOMA			X											X			X						X		X
UTERUS	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOMETRIAL STROMAL POLYP					X				X													X			
CARCINOSARCOMA											X														
OVARY	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GRANULOSA-CELL TUMOR																									
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GRANULAR-CELL TUMOR, BENIGN																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
LEIOMYOSARCOMA																									
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																									
LYMPHOCYTIC LEUKEMIA				X																X					

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A4. FEMALE RATS: TUMOR PATHOLOGY (CONTINUED) LOW DOSE

ANIMAL NUMBER	02 6	02 7	02 8	02 9	03 0	03 1	03 2	03 3	03 4	03 5	03 6	03 7	03 8	03 9	04 0	04 1	04 2	04 3	04 4	04 5	04 6	04 7	04 8	04 9	05 0	TOTAL
WEEKS ON STUDY	10 4	10 4	10 4	08 6	10 4	10 4	10 4	10 4	10 4	09 5	10 4	10 3	10 0	10 4	10 4	10 4	10 4	10 4	10 4	06 3	10 4	10 4	10 4	10 4	10 4	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SQUAMOUS CELL CARCINOMA																										1
SARCOMA, NOS																										1
FIBROMA												X														1
LEIOMYOSARCOMA																	X									1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GANGLIONEUROBLASTOMA, METASTATIC																										1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
NASAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
SQUAMOUS CELL CARCINOMA, INVASIVE																										1
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LYMPH NODES	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	44
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	-	41
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NEURILEMOMA																										1
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
NEOPLASTIC NODULE																										1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ADENOMA, NOS													X													1
CHROMOPHOBE ADENOMA	X						X		X		X	X			X		X							X		15
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CORTICAL ADENOMA																										1
PHEOCHROMOCYTOMA												X														3
PHEOCHROMOCYTOMA, MALIGNANT													X													1
GANGLIONEUROMA																				X						1
GANGLIONEUROBLASTOMA																										1
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
C-CELL CARCINOMA		X																								2
PARATHYROID	+	-	-	+	-	+	+	+	+	+	-	+	+	-	-	+	-	+	+	-	+	+	+	+	-	33
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	N	+	N	+	+	+	+	+	50
ADENOMA, NOS																										1
ADENOCARCINOMA, NOS				X																						2
CARCINOSARCOMA																										1
FIBROADENOMA		X					X	X	X					X						X						11
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ENDOMETRIAL STROMAL POLYP									X				X					X			X					7
CARCINOSARCOMA																										1
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
GRANULOSA-CELL TUMOR																				X						1
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GRANULAR-CELL TUMOR, BENIGN														X												1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
LEIOMYOSARCOMA										X																1
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																X									X	2
LYMPHOCYTIC LEUKEMIA																										2

* ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: *TUMOR INCIDENCE*
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: *AUTOLYSIS*
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY TABLES OF FEMALE RATS IN THE 2-YEAR STUDY OF C.I. DISPERSE YELLOW 3

HIGH DOSE

ANIMAL NUMBER	0011	0012	0013	0014	0015	0016	0017	0018	0019	0110	0111	0112	0113	0114	0115	0116	0117	0118	0119	0120	0121	0122	0123	0124	0125
WEEKS ON STUDY	104	104	104	104	104	104	111	104	104	104	104	104	104	104	104	104	103	104	104	104	104	104	104	104	104
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+
C-CELL CARCINOMA, INVASIVE														X											
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-CELL CARCINOMA, METASTATIC														X											
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROSARCOMA																	X								
LYMPHOCYTIC LEUKEMIA																									
LYMPH NODES	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	-	+	+	+
C-CELL CARCINOMA, METASTATIC														X											
FIBROSARCOMA, METASTATIC																	X								
THYMUS	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE			X																						
HEPATOCELLULAR CARCINOMA																									
FIBROSARCOMA, METASTATIC																	X								
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROSARCOMA, INVASIVE																	X								
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA,NOS														X											
CHROMOPHOBE ADENOMA								X			X		X											X	
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS																									
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-CELL CARCINOMA														X				X							
PARATHYROID	-	+	+	+	+	+	-	+	+	+	+	+	+	-	+	-	+	-	+	+	+	+	+	+	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	+	N	+	+	+	+	+	N	+	+	+	+	+	+	+	+	X	+	+	+
FIBROADENOMA																						X			
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOMETRIAL STROMAL POLYP						X				X												X			
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GRANULOSA-CELL TUMOR																									
FIBROSARCOMA																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																									

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A4. FEMALE RATS: TUMOR PATHOLOGY (CONTINUED) HIGH DOSE

ANIMAL NUMBER	02 26	02 27	02 28	02 29	03 01	03 11	03 12	03 33	03 34	03 35	03 36	03 37	03 38	03 39	04 01	04 11	04 12	04 43	04 44	04 45	04 46	04 47	04 48	04 49	05 01	TOTAL TISSUES TUMORS
WEEKS ON STUDY	10 49	10 49	01 13	10 49	10 49	10 49	10 49	10 49	10 49	05 56	10 49	10 49	10 49	10 49	10 49	10 49	10 49	10 49	10 49	10 49	10 49	10 49	10 49	10 49	10 49	
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	+	N	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
C-CELL CARCINOMA, INVASIVE																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-CELL CARCINOMA, METASTATIC																										1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
FIBROSARCOMA																										1
LYMPHOCYTIC LEUKEMIA																				X						1
LYMPH NODES	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	44
C-CELL CARCINOMA, METASTATIC																										1
FIBROSARCOMA, METASTATIC																										1
THYMUS	+	+	-	+	+	+	+	+	-	-	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	42
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NEOPLASTIC NODULE																X										2
HEPATOCELLULAR CARCINOMA															X											1
FIBROSARCOMA, METASTATIC																										1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
FIBROSARCOMA, INVASIVE																										1
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	49
CARCINOMA, NOS																										1
CHROMOPHOBE ADENOMA				X		X			X	X																8
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOMA, NOS															X											1
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-CELL CARCINOMA							X																			3
PARATHYROID	+	+	-	-	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	-	+	-	+	+	39
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	N	N	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
FIBROADENOMA	X																	X								3
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOMETRIAL STROMAL POLYP																										3
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GRANULOSA-CELL TUMOR	X																									1
FIBROSARCOMA											X															1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE			X											X												2

* ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

APPENDIX B

Summary of the Incidence of Neoplasms in Mice Fed Diets Containing C. I. Disperse Yellow 3

TABLE B1.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE FED DIETS CONTAINING C. I. DISPERSE YELLOW 3

	CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS MISSING			1
ANIMALS NECROPSIED	50	49	49
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	49	49
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(49)	(49)
FIBROSARCOMA		2 (4%)	
*SUBCUT TISSUE	(50)	(49)	(49)
FIBROMA		1 (2%)	
LEIOMYOSARCOMA	1 (2%)		1 (2%)
RESPIRATORY SYSTEM			
#LUNG	(50)	(49)	(49)
NEOPLASM, NOS, METASTATIC			1 (2%)
HEPATOCELLULAR CARCINOMA, METAST	3 (6%)	3 (6%)	
ALVEOLAR/BRONCHIOLAR ADENOMA	2 (4%)	6 (12%)	9 (18%)
ALVEOLAR/BRONCHIOLAR CARCINOMA	1 (2%)	1 (2%)	
TUBULAR-CELL ADENOCARCINOMA, MET			1 (2%)
SARCOMA, NOS, METASTATIC		1 (2%)	
FIBROSARCOMA, METASTATIC	1 (2%)		
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(49)	(49)
MALIGNANT LYMPHOMA, NOS	2 (4%)	1 (2%)	1 (2%)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	1 (2%)		
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	4 (8%)	2 (4%)	1 (2%)
MAST-CELL LEUKEMIA			1 (2%)
*SUBCUT TISSUE	(50)	(49)	(49)
MAST-CELL TUMOR			1 (2%)
#SPLEEN	(50)	(49)	(48)
MALIGNANT LYMPHOMA, NOS			2 (4%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#LYMPH NODE	(37)	(39)	(36)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	1 (3%)		
#MESENTERIC L. NODE	(37)	(39)	(36)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE		1 (3%)	
#PANCREAS	(50)	(48)	(47)
MALIGNANT LYMPHOMA, NOS		1 (2%)	
#PEYER'S PATCH	(47)	(49)	(46)
MALIGNANT LYMPHOMA, NOS		1 (2%)	
CIRCULATORY SYSTEM			
#SPLEEN	(50)	(49)	(48)
HEMANGIOSARCOMA	1 (2%)		
#MESENTERIC L. NODE	(37)	(39)	(36)
ANGIOMA		1 (3%)	1 (3%)
#HEART	(50)	(49)	(49)
TUBULAR-CELL ADENOCARCINOMA, MET			1 (2%)
#LEFT VENTRICLE	(50)	(49)	(49)
ANGIOSARCOMA			1 (2%)
#LIVER	(50)	(49)	(49)
ANGIOMA		1 (2%)	1 (2%)
DIGESTIVE SYSTEM			
#LIVER	(50)	(49)	(49)
HEPATOCELLULAR ADENOMA	7 (14%)	1 (2%)	7 (14%)
HEPATOCELLULAR CARCINOMA	14 (28%)	11 (22%)	12 (24%)
#LIVER/KUPFFER CELL	(50)	(49)	(49)
SARCOMA, NOS		1 (2%)	
URINARY SYSTEM			
#KIDNEY	(50)	(49)	(49)
ALVEOLAR/BRONCHIOLAR CA, METASTA	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
TUBULAR-CELL ADENOCARCINOMA			1 (2%)
#KIDNEY/CORTEX	(50)	(49)	(49)
TUBULAR-CELL ADENOMA			1 (2%)
ENDOCRINE SYSTEM			
#PITUITARY	(43)	(34)	(32)
CHROMOPHOBE CARCINOMA	1 (2%)		
#ADRENAL	(50)	(47)	(47)
PHEOCHROMOCYTOMA	1 (2%)	2 (4%)	1 (2%)
#ADRENAL/CAPSULE	(50)	(47)	(47)
ADENOMA, NOS	1 (2%)		
#THYROID	(49)	(48)	(47)
FOLLICULAR-CELL ADENOMA			1 (2%)
REPRODUCTIVE SYSTEM			
NONE			
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
*EYE/LACRIMAL GLAND	(50)	(49)	(49)
PAPILLARY ADENOMA	2 (4%)	1 (2%)	3 (6%)
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*MEDIASTINUM	(50)	(49)	(49)
FIBROSARCOMA, METASTATIC	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
ALL OTHER SYSTEMS			
NONE			
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	5	9	7
MORIBUND SACRIFICE	2	2	
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	43	39	42
ANIMAL MISSING			1
@ INCLUDES AUTOLYZED ANIMALS			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	33	26	33
TOTAL PRIMARY TUMORS	39	34	45
TOTAL ANIMALS WITH BENIGN TUMORS	13	11	20
TOTAL BENIGN TUMORS	13	13	24
TOTAL ANIMALS WITH MALIGNANT TUMORS	23	18	20
TOTAL MALIGNANT TUMORS	26	21	20
TOTAL ANIMALS WITH SECONDARY TUMORS#	4	4	2
TOTAL SECONDARY TUMORS	6	4	3
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT			1
TOTAL UNCERTAIN TUMORS			1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS
\# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE B2.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE FED DIETS CONTAINING C. I. DISPERSE YELLOW 3

	CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
MALIGNANT MELANOMA			1 (2%)
*SUBCUT TISSUE	(50)	(50)	(50)
SARCOMA, NOS		1 (2%)	
FIBROSARCOMA	1 (2%)		
RESPIRATORY SYSTEM			
*NASAL CAVITY	(50)	(50)	(50)
ADENOCARCINOMA, NOS, INVASIVE			1 (2%)
#LUNG	(50)	(50)	(50)
ADENOCARCINOMA, NOS, METASTATIC			1 (2%)
HEPATOCELLULAR CARCINOMA, METAST	1 (2%)		1 (2%)
ALVEOLAR/BRONCHIOLAR ADENOMA	5 (10%)		3 (6%)
ALVEOLAR/BRONCHIOLAR CARCINOMA	1 (2%)		1 (2%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
MALIGNANT LYMPHOMA, NOS	5 (10%)	2 (4%)	3 (6%)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE		2 (4%)	1 (2%)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	4 (8%)	10 (20%)	7 (14%)
MALIGNANT LYMPHOMA, MIXED TYPE			1 (2%)
LYMPHOCYTIC LEUKEMIA			1 (2%)
GRANULOCYTIC LEUKEMIA		1 (2%)	
#SPLEEN	(50)	(50)	(49)
MALIGNANT LYMPHOMA, NOS	1 (2%)		1 (2%)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#LYMPH NODE	(40)	(43)	(42)
MALIGNANT LYMPHOMA, NOS			2 (5%)
#SUBMANDIBULAR L.NODE	(40)	(43)	(42)
ADENOCARCINOMA, NOS, METASTATIC			1 (2%)
#PANCREATIC L.NODE	(40)	(43)	(42)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE			1 (2%)
#MESENTERIC L. NODE	(40)	(43)	(42)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE			1 (2%)
#PANCREAS	(50)	(47)	(50)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	1 (2%)		
#PEYER'S PATCH	(48)	(46)	(46)
MALIGNANT LYMPHOMA, NOS		1 (2%)	
#UTERUS	(50)	(50)	(50)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE		1 (2%)	
#THYMUS	(41)	(43)	(42)
MALIGNANT LYMPHOMA, NOS			1 (2%)
CIRCULATORY SYSTEM			
*SUBCUT TISSUE	(50)	(50)	(50)
ANGIOSARCOMA			1 (2%)
#SPLEEN	(50)	(50)	(49)
HEMANGIOMA			1 (2%)
HEMANGIOSARCOMA		1 (2%)	
#LUNG	(50)	(50)	(50)
ANGIOSARCOMA, METASTATIC			1 (2%)
#LIVER	(50)	(50)	(50)
ANGIOMA		1 (2%)	1 (2%)
#URINARY BLADDER	(50)	(46)	(49)
HEMANGIOMA		1 (2%)	
#UTERUS	(50)	(50)	(50)
ANGIOMA		1 (2%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#OVARY	(46)	(48)	(47)
HEMANGIOMA		1 (2%)	
DIGESTIVE SYSTEM			
#LIVER	(50)	(50)	(50)
HEPATOCELLULAR ADENOMA		6 (12%)	12 (24%)
HEPATOCELLULAR CARCINOMA	2 (4%)	4 (8%)	5 (10%)
#STOMACH	(50)	(48)	(50)
SQUAMOUS CELL PAPILLOMA		1 (2%)	
#COLON	(49)	(45)	(48)
LEIOMYOSARCOMA, INVASIVE		1 (2%)	
URINARY SYSTEM			
NONE			
ENDOCRINE SYSTEM			
#PITUITARY	(38)	(30)	(42)
CHROMOPHOBE ADENOMA	1 (3%)	1 (3%)	4 (10%)
#ADRENAL	(46)	(47)	(49)
HEPATOCELLULAR CARCINOMA, METAST	1 (2%)		
#PANCREATIC ISLETS	(50)	(47)	(50)
ISLET-CELL ADENOMA		1 (2%)	
ISLET-CELL CARCINOMA	1 (2%)		
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
ADENOCARCINOMA, NOS			1 (2%)
*VAGINA	(50)	(50)	(50)
SARCOMA, NOS			1 (2%)
#UTERUS	(50)	(50)	(50)
SARCOMA, NOS		1 (2%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
LEIOMYOMA	1 (2%)		1 (2%)
LEIOMYOSARCOMA		1 (2%)	1 (2%)
ENDOMETRIAL STROMAL POLYP	1 (2%)		1 (2%)
#OVARY	(46)	(48)	(47)
NEOPLASM, NOS			1 (2%)
NERVOUS SYSTEM			
#CEREBRUM	(50)	(49)	(50)
OLIGODENDROGLIOMA		1 (2%)	
SPECIAL SENSE ORGANS			
*EYE/LACRIMAL GLAND	(50)	(50)	(50)
ADENOMA, NOS	1 (2%)		
ADENOCARCINOMA, NOS			1 (2%)
PAPILLARY ADENOMA	1 (2%)	3 (6%)	1 (2%)
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
NONE			
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
FIBROSARCOMA, METASTATIC	1 (2%)		
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	5	11	7
MORIBUND SACRIFICE	1		1
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	44	39	42
ANIMAL MISSING			

@ INCLUDES AUTOLYZED ANIMALS

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	20	33	36
TOTAL PRIMARY TUMORS	26	42	57
TOTAL ANIMALS WITH BENIGN TUMORS	9	13	17
TOTAL BENIGN TUMORS	10	16	24
TOTAL ANIMALS WITH MALIGNANT TUMORS	14	25	26
TOTAL MALIGNANT TUMORS	16	26	32
TOTAL ANIMALS WITH SECONDARY TUMORS#	2	1	3
TOTAL SECONDARY TUMORS	3	1	5
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT			1
TOTAL UNCERTAIN TUMORS			1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS
# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE B3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY TABLES OF MALE MICE IN THE 2-YEAR STUDY OF C.I. DISPERSE YELLOW 3

CONTROL

ANIMAL NUMBER	0011	0012	0013	0014	0015	0016	0017	0018	0019	0020	0021	0022	0023	0024	0025	0026	0027	0028	0029	0030	0031	0032	0033	0034	0035
WEEKS ON STUDY	104	104	104	104	101	071	104	094	104	104	104	104	104	104	104	104	104	101	079	104	104	104	104	096	104
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LEIOMYOSARCOMA																			X						
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA, METASTA						X																	X		
ALVEOLAR/BRONCHIOLAR ADENOMA				X									X												
ALVEOLAR/BRONCHIOLAR CARCINOMA								X																	
FIBROSARCOMA, METASTATIC								X																	
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOSARCOMA																									
LYMPH NODES	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	-	
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																				X					
THYMUS	+	+	+	-	+	+	-	+	+	+	-	-	+	+	+	+	+	-	+	+	+	+	-	+	
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA												X											X		X
HEPATOCELLULAR CARCINOMA			X			X		X															X		
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	N	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR CA, METASTAT								X																	
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	-	+	-	+	+	+	-	+	+	+	+	-	+	+	+	-	+	
CHROMOPHOBE CARCINOMA																									
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS																		X							
PHEOCHROMOCYTOMA																									
THYROID	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PARATHYROID	+	-	-	+	+	-	+	-	-	+	-	+	+	-	-	-	-	+	-	-	+	-	+	+	-
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
TESTIS	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
LACRIMAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PAPILLARY ADENOMA										X				X											
BODY CAVITIES																									
MEDIASTINUM	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
FIBROSARCOMA, METASTATIC								X																	
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIGNANT LYMPHOMA, NOS																								X	
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																									
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	X																	X							

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B3. MALE MICE: TUMOR PATHOLOGY (CONTINUED) CONTROL

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL
WEEKS ON STUDY	104	104	104	104	104	104	100	104	104	069	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	N	+	+	+	50M
LEIOMYOSARCOMA																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR CARCINOMA, METASTA																						X				3
ALVEOLAR/BRONCHIOLAR ADENOMA																										2
ALVEOLAR/BRONCHIOLAR CARCINOMA																										1
FIBROSARCOMA, METASTATIC																										1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	49
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMANGIOSARCOMA	X																									1
LYMPH NODES	+	-	-	-	+	+	-	-	+	-	+	+	+	+	+	-	+	+	+	+	-	-	+	+	+	37
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																										1
THYMUS	-	-	+	-	-	+	-	+	+	-	+	+	-	-	+	+	+	+	+	+	+	-	+	+	+	35
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR ADENOMA					X																	X			X	7
HEPATOCELLULAR CARCINOMA		X				X			X	X		X	X	X	X					X			X		X	14
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
LARGE INTESTINE	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALVEOLAR/BRONCHIOLAR CA, METASTAT																										1
URINARY BLADDER	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	43
CHROMOPHOBE CARCINOMA										X																1
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOMA, NOS																										1
PHEOCHROMOCYTOMA		X																								1
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
PARATHYROID	-	-	+	-	-	-	+	-	+	-	-	-	-	+	-	-	+	-	-	-	-	+	+	-	-	18
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
LACRIMAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
PAPILLARY ADENOMA																										2
BODY CAVITIES																										
MEDIASTINUM	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
FIBROSARCOMA, METASTATIC																										1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
MALIGNANT LYMPHOMA, NOS																		X								2
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE														X												1
MALIG.LYMPHOMA, HISTIOCYTIC TYPE							X																		X	4

M ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY TABLES OF MALE MICE IN THE 2-YEAR STUDY OF C.I. DISPERSE YELLOW 3

LOW DOSE

ANIMAL NUMBER	0011	0012	0013	0014	0015	0016	0017	0018	0019	0020	0021	0022	0023	0024	0025	0026	0027	0028	0029	0030	0031	0032	0033	0034	0035
WEEKS ON STUDY	098	077	051	051	051	051	051	051	051	086	051	073	086	051	051	051	051	051	051	051	051	051	051	051	051
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROSARCOMA									X																
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROMA												X													
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA, METASTA		X						X											X						
ALVEOLAR/BRONCHIOLAR ADENOMA	X				X									X							X				
ALVEOLAR/BRONCHIOLAR CARCINOMA								X																	
SARCOMA, NOS, METASTATIC													X												
TRACHEA	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	-	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	-	+	-	+	+	+	-	+
ANGIOMA					X																				
MALIG.LYMPHOMA, HISTIOCYTIC TYPE							X																		
THYMUS	+	-	-	-	+	-	+	+	-	+	+	-	+	+	-	+	+	+	+	+	-	+	-	+	
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA																						X			
HEPATOCELLULAR CARCINOMA		X					X	X										X	X						
SARCOMA, NOS												X													
ANGIOMA								X																	
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MALIGNANT LYMPHOMA, NOS																									
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MALIGNANT LYMPHOMA, NOS																		X							
LARGE INTESTINE	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA																									
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PARATHYROID	-	+	+	-	+	-	-	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	-	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
LACRIMAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PAPILLARY ADENOMA																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIGNANT LYMPHOMA, NOS																									
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	X									X															

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B3. MALE MICE: TUMOR PATHOLOGY (CONTINUED) LOW DOSE

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL TISSUES TUMORS
WEEKS ON STUDY	105	105	091	105	105	105	105	105	085	105	087	095	105	105	105	030	105	105	105	105	105	105	105	104	105	
INTEGUMENTARY SYSTEM																										
SKIN	+	+	A	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	49*
FIBROSARCOMA																				X						2
SUBCUTANEOUS TISSUE	+	+	A	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	49*
FIBROMA																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEPATOCELLULAR CARCINOMA, METASTA																										3
ALVEOLAR/BRONCHIOLAR ADENOMA					X																	X				6
ALVEOLAR/BRONCHIOLAR CARCINOMA																										1
SARCOMA, NOS, METASTATIC																										1
TRACHEA	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SPLEEN	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LYMPH NODES	+	+	A	+	-	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+	39
ANGIOMA																										1
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																										1
THYMUS	-	-	A	+	-	+	+	-	-	+	+	+	-	+	+	-	+	-	+	-	+	+	+	-	-	29
CIRCULATORY SYSTEM																										
HEART	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LIVER	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEPATOCELLULAR ADENOMA																										1
HEPATOCELLULAR CARCINOMA	X	X			X				X						X			X								11
SARCOMA, NOS																										1
ANGIOMA																										1
BILE DUCT	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
GALLBLADDER & COMMON BILE DUCT	+	+	A	+	+	+	+	+	N	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49*
PANCREAS	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	48
MALIGNANT LYMPHOMA, NOS																	X									1
ESOPHAGUS	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
STOMACH	+	+	A	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
SMALL INTESTINE	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
MALIGNANT LYMPHOMA, NOS																										1
LARGE INTESTINE	+	+	A	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
URINARY SYSTEM																										
KIDNEY	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY BLADDER	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ENDOCRINE SYSTEM																										
PITUITARY	-	+	A	+	-	-	-	+	-	-	+	+	-	+	-	-	+	-	-	-	+	+	-	+		34
ADRENAL	+	+	A	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
PHEOCHROMOCYTOMA				X																		X				2
THYROID	+	+	A	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
PARATHYROID	-	+	A	+	-	-	-	+	-	-	-	-	-	+	+	-	+	-	-	-	+	-	+	-	-	26
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	49*
TESTIS	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
PROSTATE	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPECIAL SENSE ORGANS																										
LACRIMAL GLAND	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	49*
PAPILLARY ADENOMA																						X				1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	49*
MALIGNANT LYMPHOMA, NOS																								X		1
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																										2

* ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY TABLES OF MALE MICE IN THE 2-YEAR STUDY OF C.I. DISPERSE YELLOW 3

HIGH DOSE

ANIMAL NUMBER	0011	0029	0031	0045	0055	0066	0077	0088	0099	0110	0111	0122	0133	0146	0155	0166	0177	0188	0199	0200	0211	0222	0233	0244	0255
WEEKS ON STUDY	091	105	051	055	055	051	055	055	058	873	055	055	055	078	055	055	055	051	055	055	055	055	055	055	055
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+
LEIOMYOSARCOMA																									
MAST-CELL TUMOR						X																			
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASM, NOS, METASTATIC														X											
ALVEOLAR/BRONCHIOLAR ADENOMA	X				X												X				X	X			
TUBULAR-CELL ADENOCARCINOMA, META																			X						
TRACHEA	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	M	+	+	+	-	-	+	+	+	+	+	-	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MALIGNANT LYMPHOMA, NOS					X																				
LYMPH NODES	-	-	+	+	-	+	+	+	M	+	+	+	-	+	-	+	+	-	+	+	-	+	+	+	-
ANGIOMA								X																	
THYMUS	-	+	+	+	-	+	+	+	M	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TUBULAR-CELL ADENOCARCINOMA, META																			X						
ANGIOSARCOMA																									
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA						X							X												
HEPATOCELLULAR CARCINOMA				X						X		X	X	X						X					
ANGIOMA																									
BILE DUCT	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	+	+	M	+	+	+	N	N	+	+	+	+	+	+	+	+	+	+	+
PANCREAS	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	
STOMACH	+	+	+	+	+	+	+	+	M	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	M	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	M	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TUBULAR-CELL ADENOMA				X																					
TUBULAR-CELL ADENOCARCINOMA																			X						
URINARY BLADDER	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	-	-	-	+	-	+	-	M	-	+	+	+	-	-	+	+	+	+	+	+	+	+	-	+
ADRENAL	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA															X										
THYROID	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
FOLLICULAR-CELL ADENOMA																									
PARATHYROID	-	-	+	-	+	+	+	-	M	-	+	+	+	-	+	-	-	+	-	+	+	+	+	-	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	N	N	N	N	N	M	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
TESTIS	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PROSTATE	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
LACRIMAL GLAND	N	N	N	N	N	N	N	N	M	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PAPILLARY ADENOMA																									X
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	M	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIGNANT LYMPHOMA, NOS																									
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																X									
MAST-CELL LEUKEMIA																									

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B3. MALE MICE: TUMOR PATHOLOGY (CONTINUED) HIGH DOSE

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL
WEEKS ON STUDY	012	050	000	055	055	055	055	095	085	055	055	055	055	055	055	093	085	055	055	055	055	055	055	055	085	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	49M
LEIOMYOSARCOMA								X																		1
MAST-CELL TUMOR																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
NEOPLASM, NOS, METASTATIC																										1
ALVEOLAR/BRONCHIOLAR ADENOMA		X				X							X				X									9
TUBULAR-CELL ADENOCARCINOMA, META																										1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	48
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	48
MALIGNANT LYMPHOMA, NOS																									X	2
LYMPH NODES	-	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-		36
ANGIOMA																										1
THYMUS	+	+	+	+	+	+	+	-	-	-	+	+	+	+	-	A	+	+	-	+	+	-	+	+.	+	38
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
TUBULAR-CELL ADENOCARCINOMA, META																										1
ANGIOSARCOMA		X																								1
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEPATOCELLULAR ADENOMA		X		X		X	X			X																7
HEPATOCELLULAR CARCINOMA						X	X												X	X		X		X		12
ANGIOMA																				X						1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
GALLBLADDER & COMMON BILE DUCT	+	+	N	+	+	+	+	N	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	49M
PANCREAS	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	47
ESOPHAGUS	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	46
STOMACH	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	46
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	46
LARGE INTESTINE	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
TUBULAR-CELL ADENOMA																										1
TUBULAR-CELL ADENOCARCINOMA																										1
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ENDOCRINE SYSTEM																										
PITUITARY	-	-	+	+	+	+	+	+	+	+	-	-	+	-	-	A	+	+	+	+	+	+	+	-	+	32
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	-	+	+	+	+	+	+	+	47
PHEOCHROMOCYTOMA																										1
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	47
FOLLICULAR-CELL ADENOMA										X																1
PARATHYROID	-	+	+	-	-	+	-	-	+	+	-	-	+	+	-	A	+	+	+	-	-	-	+	+	-	26
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	49M
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPECIAL SENSE ORGANS																										
LACRIMAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	49M
PAPILLARY ADENOMA						X									X											3
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	49M
MALIGNANT LYMPHOMA, NOS			X																							1
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																										1
MAST-CELL LEUKEMIA					X																					1

* ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY TABLES OF FEMALE MICE IN THE 2-YEAR STUDY OF C.I. DISPERSE YELLOW 3

CONTROL

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	105	105	105	105	105	105	105	094	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	102	105
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	N	+	+	+	+	+	N	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	N	+
FIBROSARCOMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA, METASTA																								X	
ALVEOLAR/BRONCHIOLAR ADENOMA																									
ALVEOLAR/BRONCHIOLAR CARCINOMA																									
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MALIGNANT LYMPHOMA, NOS																									
LYMPH NODES	+	+	+	-	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	-	+
THYMUS	+	-	+	-	+	+	+	-	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	-	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA																								X	
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																									
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	-	+	+	+	+	+	-	-	+	-	-	+	+	-	+	+	+	+	+	+	+	+	+	+
CHROMOPHOBE ADENOMA																							X		
ADRENAL	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA, METASTA																								X	
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PARATHYROID	+	+	+	+	-	+	+	-	-	+	+	+	-	+	+	+	-	+	-	-	-	+	+	+	+
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL CARCINOMA				X																					
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	N	N	+	+	+	N	N	+	+	+	+	+	+	+	N	N	+	+	+	+	+	+	N	+
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LEIOMYOMA																									
ENDOMETRIAL STROMAL POLYP																							X		
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
LACRIMAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS								X																	
PAPILLARY ADENOMA																				X					
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
FIBROSARCOMA, METASTATIC																									
MALIGNANT LYMPHOMA, NOS								X	X									X							
MALIG.LYMPHOMA, HISTIOCYTIC TYPE			X																						

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B4. FEMALE MICE: TUMOR PATHOLOGY (CONTINUED) CONTROL

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL
WEEKS ON STUDY	105	089	105	105	105	105	105	105	105	105	105	105	105	095	105	105	105	105	105	105	105	105	102	105	101	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	50*
FIBROSARCOMA								X																		1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR CARCINOMA, METASTA																										1
ALVEOLAR/BRONCHIOLAR ADENOMA			X			X			X		X													X		5
ALVEOLAR/BRONCHIOLAR CARCINOMA															X											1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
MALIGNANT LYMPHOMA, NOS								X																		1
LYMPH NODES	-	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	-		40
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	-		41
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-		48
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR CARCINOMA																	X									2
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																			X							1
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	49
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	48
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																										
PITUITARY	-	+	+	+	-	+	+	+	+	+	+	+	+	-	-	+	-	+	+	+	+	+	+	+	+	38
CHROMOPHOBE ADENOMA																										1
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	46
HEPATOCELLULAR CARCINOMA, METASTA																										1
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
PARATHYROID	-	+	-	-	+	-	-	-	+	+	+	-	-	-	-	+	+	+	-	-	+	+	+	-	-	28
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ISLET-CELL CARCINOMA																										1
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	N	+	+	+	+	+	+	+	+	+	+	N	N	+	+	+	+	N	N	+	+	+	+	N	50*
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LEIOMYOMA																							X			1
ENDOMETRIAL STROMAL POLYP																										1
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	-	+	+	+	+	-	+	46
SPECIAL SENSE ORGANS																										
LACRIMAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
ADENOMA, NOS																										1
PAPILLARY ADENOMA																										1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
FIBROSARCOMA, METASTATIC								X																		1
MALIGNANT LYMPHOMA, NOS							X			X																5
MALIG.LYMPHOMA, HISTIOCYTIC TYPE								X															X	X		4

* ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY TABLES OF FEMALE MICE IN THE 2-YEAR STUDY OF C.I. DISPERSE YELLOW 3

LOW DOSE

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	098	083	105	105	090	105	105	105	099	105	095	105	079
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE SARCOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	−	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−
SPLEEN HEMANGIOSARCOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	−	+	+	+	+	−	+	+	+	−	−	+	+	+	+	+	+	+	+	+	+	−
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	−	+	+	+	+	−	+	+	−
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+
LIVER HEPATOCELLULAR ADENOMA				X			X	X		X															
HEPATOCELLULAR CARCINOMA																				X		X			
ANGIOMA			X																						
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	−	+	+	+	−
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	−	+	+	+	+
STOMACH SQUAMOUS CELL PAPILLOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−
SMALL INTESTINE MALIGNANT LYMPHOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	−
					X																				
LARGE INTESTINE LEIOMYOSARCOMA, INVASIVE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	−	+	+
																	X								
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER HEMANGIOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	−	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY CHROMOPHOBE ADENOMA	+	+	+	+	+	−	+	+	+	+	+	+	−	−	+	−	+	+	+	−	−	+	+	+	−
																							X		
ADRENAL	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+
PARATHYROID	−	+	+	−	−	−	+	+	+	−	−	−	+	+	−	−	+	+	+	−	−	+	+	−	
PANCREATIC ISLETS ISLET-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	−	+	+	−	
									X																
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	N	N	+	+	+	N	+	+	+	+	+	N	+	+	+	+	N	+	N	+	+	N	
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SARCOMA, NOS																	X								
LEIOMYOSARCOMA																									
ANGIOMA																									
MALIG.LYMPHOMA, HISTIOCYTIC TYPE													X												
OVARY HEMANGIOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
																	X								
NERVOUS SYSTEM																									
BRAIN OLIGODENDROGLIOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−
													X												
SPECIAL SENSE ORGANS																									
LACRIMAL GLAND PAPILLARY ADENOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
		X					X												X						
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIGNANT LYMPHOMA, NOS			X				X																		
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																									
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	X																					X	X	X	X
GRANULOCYTIC LEUKEMIA														X											

+: TISSUE EXAMINED MICROSCOPICALLY
−: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B4. FEMALE MICE: TUMOR PATHOLOGY (CONTINUED) LOW DOSE

ANIMAL NUMBER	02 26	02 27	02 28	02 29	03 30	03 31	03 32	03 33	03 34	03 35	03 36	03 37	03 38	03 39	04 40	04 41	04 42	04 43	04 44	04 45	04 46	04 47	04 48	04 49	05 00	TOTAL TISSUES TUMORS
WEEKS ON STUDY	11 05	11 05	01 05	01 05	11 05	10 05	10 68	11 05	10 05	10 80	10 91	09 99	11 05	10 05	10 05	11 05	10 05	11 05	11 05	10 05	10 05	10 05	11 05	11 05	10 95	
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
SARCOMA, NOS						X																				1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
TRACHEA	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMANGIOSARCOMA	X																									1
LYMPH NODES	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	43
THYMUS	+	+	+	+	+	-	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR ADENOMA																							X	X		6
HEPATOCELLULAR CARCINOMA			X												X											4
ANGIOMA																										1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ESOPHAGUS	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
STOMACH	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SQUAMOUS CELL PAPILLOMA																						X				1
SMALL INTESTINE	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	46
MALIGNANT LYMPHOMA, NOS																										1
LARGE INTESTINE	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	45
LEIOMYOSARCOMA, INVASIVE																										1
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	46
HEMANGIOMA																						X				1
ENDOCRINE SYSTEM																										
PITUITARY	+	-	-	-	-	+	-	-	+	-	-	+	+	+	+	-	+	-	-	-	+	+	-	+	+	30
CHROMOPHOBE ADENOMA																										1
ADRENAL	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
PARATHYROID	+	-	-	+	+	-	-	-	+	-	+	-	-	-	-	+	+	-	+	-	+	-	+	+	-	24
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ISLET-CELL ADENOMA																										1
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	N	+	+	+	N	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SARCOMA, NOS																	X									1
LEIOMYOSARCOMA																										1
ANGIOMA																										1
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																										1
OVARY	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	48
HEMANGIOMA																										1
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
OLIGODENDROGLIOMA																										1
SPECIAL SENSE ORGANS																										
LACRIMAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
PAPILLARY ADENOMA																										3
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
MALIGNANT LYMPHOMA, NOS																										2
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE										X															X	2
MALIG.LYMPHOMA, HISTIOCYTIC TYPE							X				X	X		X						X						10
GRANULOCYTIC LEUKEMIA																										1

* ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY TABLES OF FEMALE MICE IN THE 2-YEAR STUDY OF C.I. DISPERSE YELLOW 3

HIGH DOSE

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	105	105	105	105	105	051	083	105	048	051	105	105	105	105	105	105	058	105	105	105	051	105	105	105	105
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+ X	+	+	+	N	+	+	+	+
MALIGNANT MELANOMA																	X								
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+
ANGIOSARCOMA							X																		
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+ X	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS, METASTATIC																	X								
HEPATOCELLULAR CARCINOMA, METASTA		X																							
ALVEOLAR/BRONCHIOLAR ADENOMA													X												
ALVEOLAR/BRONCHIOLAR CARCINOMA																									
ANGIOSARCOMA, METASTATIC							X																		
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+
NASAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N X	N	N	N	N	N	N	N	N
ADENOCARCINOMA, NOS, INVASIVE																	X								
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+
HEMANGIOMA					X																				
MALIGNANT LYMPHOMA, NOS																									
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																									
LYMPH NODES	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+ X	+	-	-	+	+	+	+	+
ADENOCARCINOMA, NOS, METASTATIC																	X								
MALIGNANT LYMPHOMA, NOS																									X
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE													X												
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																									
THYMUS	+	-	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MALIGNANT LYMPHOMA, NOS																									
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA	X				X			X			X			X	X	X							X		
HEPATOCELLULAR CARCINOMA		X					X																		
ANGIOMA																									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	-	+	+	+	+	-	+	-	+	-	+	+	+	+	+ X	+	+	+	-	+	-	+	+	+	+
CHROMOPHOBE ADENOMA															X										
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PARATHYROID	-	+	+	+	+	-	+	+	-	-	-	+	-	+	-	+	+	-	-	-	-	-	+	-	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	N	+	+	+	N	N	+	+	+	N	+	N	+	+	N	N	+	N	+	N	+	N	+	+
ADENOCARCINOMA, NOS																									
VAGINA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SARCOMA, NOS																									X
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+ X	+	+	+	+	+	+	+
LEIOMYOMA																									
LEIOMYOSARCOMA																									
ENDOMETRIAL STROMAL POLYP																									
OVARY	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASM, NOS																									
SPECIAL SENSE ORGANS																									
LACRIMAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N X	N	N	N	N	N	N	N	N
ADENOCARCINOMA, NOS																	X								
PAPILLARY ADENOMA																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N X	N	N	N	N	N	N	N	N	N	N	N	N	N	N X	N	N
MALIGNANT LYMPHOMA, NOS																									
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE		X																							
MALIG.LYMPHOMA, HISTIOCYTIC TYPE									X																
MALIGNANT LYMPHOMA, MIXED TYPE																									
LYMPHOCYTIC LEUKEMIA																									

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B4. FEMALE MICE: TUMOR PATHOLOGY (CONTINUED) HIGH DOSE

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL
WEEKS ON STUDY	105	085	105	105	105	105	105	105	088	075	095	105	105	076	105	105	105	105	105	105	105	105	105	105	105	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	50M
MALIGNANT MELANOMA																										1
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	50M
ANGIOSARCOMA																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOCARCINOMA, NOS, METASTATIC																										1
HEPATOCELLULAR CARCINOMA, METASTA																										1
ALVEOLAR/BRONCHIOLAR ADENOMA							X					X														3
ALVEOLAR/BRONCHIOLAR CARCINOMA					X																					1
ANGIOSARCOMA, METASTATIC																										1
TRACHEA	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
NASAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
ADENOCARCINOMA, NOS, INVASIVE																										1
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMANGIOMA																										1
MALIGNANT LYMPHOMA, NOS											X															1
MALIG.LYMPHOMA, HISTIOCYTIC TYPE												X														1
LYMPH NODES	+	+	+	-	-	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	42
ADENOCARCINOMA, NOS, METASTATIC																										1
MALIGNANT LYMPHOMA, NOS						X																				2
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																										1
MALIG.LYMPHOMA, HISTIOCYTIC TYPE							X																			1
THYMUS	+	-	+	+	-	+	+	+	+	-	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	42
MALIGNANT LYMPHOMA, NOS																				X						1
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR ADENOMA								X					X						X						X	12
HEPATOCELLULAR CARCINOMA	X			X														X								5
ANGIOMA								X																		1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	+	N	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	50M
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ESOPHAGUS	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SMALL INTESTINE	+	+	+	+	+	+	+	+	-	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	46
LARGE INTESTINE	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	48
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	42
CHROMOPHOBE ADENOMA																X				X					X	4
ADRENAL	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
THYROID	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
PARATHYROID	-	-	+	-	-	+	+	-	-	+	+	+	+	-	-	+	-	+	+	+	+	+	+	+	+	28
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	+	+	N	+	N	N	+	+	N	N	+	+	+	+	+	+	+	+	+	+	+	50M
ADENOCARCINOMA, NOS																									X	1
VAGINA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
SARCOMA, NOS																										1
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LEIOMYOMA																										1
LEIOMYOSARCOMA																				X						1
ENDOMETRIAL STROMAL POLYP																							X			1
OVARY	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	47
NEOPLASM, NOS									X																	1
SPECIAL SENSE ORGANS																										
LACRIMAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
ADENOCARCINOMA, NOS																										1
PAPILLARY ADENOMA												X														1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
MALIGNANT LYMPHOMA, NOS					X																					3
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE		X																								1
MALIG.LYMPHOMA, HISTIOCYTIC TYPE			X											X	X					X						7
MALIGNANT LYMPHOMA, MIXED TYPE																								X		1
LYMPHOCYTIC LEUKEMIA									X																	1

M ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

APPENDIX C

Summary of the Incidence of Nonneoplastic Lesions in Rats Fed Diets Containing C. I. Disperse Yellow 3

TABLE C1.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS FED DIETS CONTAINING C. I. DISPERSE YELLOW 3

	CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
ULCER, NOS	1 (2%)		
RESPIRATORY SYSTEM			
#TRACHEA	(48)	(50)	(49)
INFLAMMATION, CHRONIC			1 (2%)
#LUNG/BRONCHUS	(50)	(50)	(50)
INFLAMMATION, CHRONIC FOCAL			1 (2%)
#LUNG/BRONCHIOLE	(50)	(50)	(50)
HYPERPLASIA, NOS	2 (4%)	3 (6%)	
#LUNG	(50)	(50)	(50)
EDEMA, NOS			2 (4%)
HEMORRHAGE			1 (2%)
HEMORRHAGIC CYST			1 (2%)
INFLAMMATION ACUTE AND CHRONIC		1 (2%)	
PNEUMONIA INTERSTITIAL CHRONIC	1 (2%)		2 (4%)
INFLAMMATION, CHRONIC FOCAL			1 (2%)
INFLAMMATION, FOCAL GRANULOMATOU			3 (6%)
HYPERPLASIA, ALVEOLAR EPITHELIUM	2 (4%)	3 (6%)	
HISTIOCYTOSIS	1 (2%)	2 (4%)	
HEMATOPOIETIC SYSTEM			
#BONE MARROW	(48)	(50)	(50)
INFLAMMATION, CHRONIC			1 (2%)
DEPLETION		1 (2%)	
HYPERPLASIA, HEMATOPOIETIC	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
HYPERPLASIA, RETICULUM CELL			1 (2%)
HYPOPLASIA, HEMATOPOIETIC	2 (4%)		2 (4%)
#SPLEEN	(50)	(50)	(50)
FIBROSIS, FOCAL	2 (4%)		
HEMOSIDEROSIS	1 (2%)		4 (8%)
LYMPHOID DEPLETION		2 (4%)	
LIPOMATOSIS	2 (4%)		
#SPLENIC RED PULP	(50)	(50)	(50)
INFLAMMATION, CHRONIC DIFFUSE		1 (2%)	
FIBROSIS, FOCAL	1 (2%)		1 (2%)
#MANDIBULAR L. NODE	(47)	(48)	(45)
INFLAMMATION, ACUTE	1 (2%)		
LYMPHOID DEPLETION			1 (2%)
PLASMACYTOSIS	1 (2%)		
HYPERPLASIA, LYMPHOID	1 (2%)		
#HEPATIC LYMPH NODE	(47)	(48)	(45)
EDEMA, NOS			1 (2%)
#MESENTERIC L. NODE	(47)	(48)	(45)
HEMORRHAGE	1 (2%)		
HEMOSIDEROSIS		1 (2%)	
LYMPHOID DEPLETION	1 (2%)		4 (9%)
#THYMUS	(40)	(45)	(34)
ATROPHY, DIFFUSE	1 (3%)		
CIRCULATORY SYSTEM			
#BRAIN	(50)	(50)	(50)
PERIVASCULITIS		1 (2%)	
*THORAX	(50)	(50)	(50)
PERIARTERITIS	1 (2%)		
*SUBCUT TISSUE	(50)	(50)	(50)
PERIARTERITIS			1 (2%)
*MAMMARY GLAND	(50)	(50)	(50)
PERIVASCULITIS			1 (2%)
#MANDIBULAR L. NODE	(47)	(48)	(45)
LYMPHANGIECTASIS	1 (2%)	1 (2%)	1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#MESENTERIC L. NODE	(47)	(48)	(45)
LYMPHANGIECTASIS	1 (2%)	1 (2%)	1 (2%)
#LUNG	(50)	(50)	(50)
PERIVASCULITIS			1 (2%)
*EPICARDIUM	(50)	(50)	(50)
PERIVASCULITIS			1 (2%)
#HEART	(50)	(50)	(49)
PERIARTERITIS		1 (2%)	
DEGENERATION, NOS	18 (36%)	27 (54%)	29 (59%)
#HEART/ATRIUM	(50)	(50)	(49)
THROMBOSIS, NOS		1 (2%)	
#LEFT ATRIUM	(50)	(50)	(49)
THROMBOSIS, NOS	2 (4%)	1 (2%)	1 (2%)
#MYOCARDIUM	(50)	(50)	(49)
INFLAMMATION, CHRONIC FOCAL		2 (4%)	
DEGENERATION, NOS			2 (4%)
NECROSIS, FOCAL		1 (2%)	1 (2%)
#ENDOCARDIUM	(50)	(50)	(49)
INFLAMMATION, CHRONIC			2 (4%)
INFLAMMATION, CHRONIC FOCAL		1 (2%)	
#CARDIAC VALVE	(50)	(50)	(49)
INFLAMMATION, CHRONIC		1 (2%)	1 (2%)
*ARTERY	(50)	(50)	(50)
PERIVASCULITIS			1 (2%)
*PULMONARY ARTERY	(50)	(50)	(50)
ARTERIOSCLEROSIS, NOS		1 (2%)	
*TESTICULAR ARTERY	(50)	(50)	(50)
INFLAMMATION, CHRONIC NECROTIZIN			1 (2%)
#PANCREAS	(48)	(50)	(49)
PERIARTERITIS		5 (10%)	1 (2%)
*MESENTERY	(50)	(50)	(50)
PERIARTERITIS	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#KIDNEY	(50)	(50)	(50)
PERIARTERITIS			1 (2%)
DIGESTIVE SYSTEM			
*TONGUE	(50)	(50)	(50)
ACANTHOSIS		1 (2%)	
#SALIVARY GLAND	(46)	(50)	(49)
CELL-SHAPE, ALTERATION			1 (2%)
ATROPHY, FOCAL		1 (2%)	2 (4%)
#LIVER	(49)	(50)	(50)
CONGESTION, CHRONIC PASSIVE	1 (2%)	1 (2%)	
INFLAMMATION, ACUTE/CHRONIC			1 (2%)
GRANULOMA, NOS		1 (2%)	
DEGENERATION, NOS		1 (2%)	
DEGENERATION, CYSTIC		1 (2%)	
NECROSIS, FOCAL	1 (2%)		3 (6%)
CYTOPLASMIC VACUOLIZATION		2 (4%)	2 (4%)
BASOPHILIC CYTO CHANGE	26 (53%)	26 (52%)	25 (50%)
FOCAL CELLULAR CHANGE	1 (2%)	4 (8%)	17 (34%)
ANGIECTASIS			2 (4%)
#HEPATIC CAPSULE	(49)	(50)	(50)
INFLAMMATION, CHRONIC		1 (2%)	
#LIVER/CENTRILOBULAR	(49)	(50)	(50)
CONGESTION, NOS	1 (2%)		
CONGESTION, ACUTE PASSIVE			1 (2%)
DEGENERATION, NOS		2 (4%)	
NECROSIS, NOS	1 (2%)	1 (2%)	1 (2%)
NECROSIS, FOCAL	2 (4%)	2 (4%)	1 (2%)
CYTOPLASMIC VACUOLIZATION			1 (2%)
#LIVER/PERIPORTAL	(49)	(50)	(50)
FIBROSIS, FOCAL	1 (2%)		
#LIVER/HEPATOCYTES	(49)	(50)	(50)
NECROSIS, FOCAL			2 (4%)
#BILE DUCT	(49)	(50)	(50)
HYPERPLASIA, NOS	10 (20%)		1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
HYPERPLASIA, FOCAL	4 (8%)	8 (16%)	1 (2%)
#PANCREATIC ACINUS	(48)	(50)	(49)
ATROPHY, NOS	2 (4%)	2 (4%)	2 (4%)
ATROPHY, FOCAL	6 (13%)	7 (14%)	12 (24%)
#STOMACH	(49)	(50)	(50)
ULCER, CHRONIC	1 (2%)		
#GASTRIC MUCOSA	(49)	(50)	(50)
MINERALIZATION		1 (2%)	
#GASTRIC SUBMUCOSA	(49)	(50)	(50)
EDEMA, NOS	1 (2%)		
#CARDIAC STOMACH	(49)	(50)	(50)
EDEMA, NOS			1 (2%)
HYPERPLASIA, EPITHELIAL		1 (2%)	2 (4%)
#GASTRIC FUNDUS	(49)	(50)	(50)
NECROSIS, FOCAL	1 (2%)		
#PYLORUS	(49)	(50)	(50)
ECTOPIA			1 (2%)
#COLON	(49)	(45)	(47)
NEMATODIASIS	2 (4%)	3 (7%)	1 (2%)
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(50)
HYDRONEPHROSIS			1 (2%)
CYST, NOS			1 (2%)
POLYCYSTIC KIDNEY		1 (2%)	
NEPHROPATHY	38 (76%)	41 (82%)	42 (84%)
PIGMENTATION, NOS		1 (2%)	3 (6%)
HYPERPLASIA, TUBULAR CELL		1 (2%)	
#KIDNEY/CORTEX	(50)	(50)	(50)
CYST, NOS		2 (4%)	2 (4%)
PIGMENTATION, NOS	3 (6%)		
#KIDNEY/PELVIS	(50)	(50)	(50)
MINERALIZATION	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
HYPERPLASIA, EPITHELIAL		4 (8%)	7 (14%)
HYPERPLASIA, PAPILLARY	1 (2%)	1 (2%)	1 (2%)
*URETER	(50)	(50)	(50)
HYPERPLASIA, EPITHELIAL			1 (2%)
#URINARY BLADDER	(45)	(50)	(48)
HEMORRHAGE	1 (2%)		
HYPERPLASIA, EPITHELIAL			1 (2%)
METAPLASIA, SQUAMOUS			1 (2%)
#U. BLADDER/MUCOSA	(45)	(50)	(48)
NECROSIS, NOS	1 (2%)		
POLYPOID HYPERPLASIA			1 (2%)
ENDOCRINE SYSTEM			
#PITUITARY	(47)	(49)	(46)
CYTOLOGIC DEGENERATION	1 (2%)		
HYPERPLASIA, CHROMOPHOBE-CELL	3 (6%)	3 (6%)	4 (9%)
#PITUITARY ACIDOPHIL	(47)	(49)	(46)
HYPERPLASIA, FOCAL		2 (4%)	
#ADRENAL	(50)	(50)	(49)
NECROSIS, NOS			1 (2%)
HYPERPLASIA, NODULAR			2 (4%)
#ADRENAL CORTEX	(50)	(50)	(49)
CYST, NOS			1 (2%)
LIPOIDOSIS	2 (4%)		5 (10%)
HYPERPLASIA, NODULAR	2 (4%)	2 (4%)	6 (12%)
HYPERPLASIA, FOCAL	5 (10%)		
#ZONA FASCICULATA	(50)	(50)	(49)
HEMORRHAGE		1 (2%)	
LIPOIDOSIS		1 (2%)	
HYPERTROPHY, NOS			1 (2%)
HYPERPLASIA, NODULAR	1 (2%)	12 (24%)	7 (14%)
#ADRENAL MEDULLA	(50)	(50)	(49)
HYPERPLASIA, NOS	2 (4%)	1 (2%)	
HYPERPLASIA, FOCAL	1 (2%)	3 (6%)	4 (8%)
ANGIECTASIS	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#THYROID	(49)	(50)	(48)
THYROGLOSSAL DUCT CYST		2 (4%)	
COLLOID CYST		3 (6%)	1 (2%)
INFLAMMATION, FOCAL GRANULOMATOU			1 (2%)
HYPERPLASIA, C-CELL	9 (18%)	9 (18%)	9 (19%)
#PARATHYROID	(34)	(43)	(39)
HYPERPLASIA, NOS		2 (5%)	
HYPERPLASIA, FOCAL	1 (3%)		
#PANCREATIC ISLETS	(48)	(50)	(49)
HYPERPLASIA, NOS	1 (2%)		2 (4%)
HYPERPLASIA, FOCAL			3 (6%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
HYPERPLASIA, EPITHELIAL		5 (10%)	
HYPERPLASIA, CYSTIC	2 (4%)	2 (4%)	1 (2%)
*MAMMARY ACINUS	(50)	(50)	(50)
DILATATION, NOS	1 (2%)		
CYST, NOS	2 (4%)		
#PROSTATE	(45)	(49)	(49)
INFLAMMATION, INTERSTITIAL	1 (2%)		
INFLAMMATION, ACUTE NECROTIZING		1 (2%)	
INFLAMMATION ACUTE AND CHRONIC	2 (4%)	2 (4%)	2 (4%)
INFLAMMATION, CHRONIC	2 (4%)	1 (2%)	1 (2%)
INFLAMMATION, CHRONIC FOCAL	1 (2%)		1 (2%)
HYPERPLASIA, EPITHELIAL	1 (2%)		
HYPERPLASIA, CYSTIC	1 (2%)		
#TESTIS	(49)	(49)	(50)
FIBROSIS, DIFFUSE		1 (2%)	
ATROPHY, NOS	32 (65%)	40 (82%)	36 (72%)
ATROPHY, DIFFUSE	7 (14%)		
HYPERPLASIA, INTERSTITIAL CELL		1 (2%)	1 (2%)
NERVOUS SYSTEM			
#BRAIN	(50)	(50)	(50)
HYDROCEPHALUS, NOS	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
HEMORRHAGE	1 (2%)		
NECROSIS, HEMORRHAGIC	1 (2%)		
ATROPHY, PRESSURE	2 (4%)	1 (2%)	
#HYPOTHALAMUS	(50)	(50)	(50)
ATROPHY, PRESSURE	2 (4%)		2 (4%)
SPECIAL SENSE ORGANS			
*EYE	(50)	(50)	(50)
INFLAMMATION, ACUTE/CHRONIC			1 (2%)
MUSCULOSKELETAL SYSTEM			
*BONE	(50)	(50)	(50)
FIBROUS OSTEODYSTROPHY		1 (2%)	
HYPERPLASIA, NOS			1 (2%)
BODY CAVITIES			
*ABDOMINAL CAVITY	(50)	(50)	(50)
NECROSIS, FAT	1 (2%)		
*MESENTERY	(50)	(50)	(50)
INFLAMMATION, GRANULOMATOUS	1 (2%)	1 (2%)	1 (2%)
INFLAMMATION, FOCAL GRANULOMATOU	1 (2%)	1 (2%)	2 (4%)
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
MINERALIZATION		1 (2%)	
ADIPOSE TISSUE			
INFLAMMATION, FOCAL GRANULOMATOU	1		1
CRANIOBUCCAL POUCH			
CYSTIC DUCTS	1	1	5
SPECIAL MORPHOLOGY SUMMARY			
AUTO/NECROPSY/HISTO PERF			1

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS FED DIETS CONTAINING C.I. DISPERSE YELLOW 3

	CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
EDEMA, NOS		1 (2%)	
*SUBCUT TISSUE	(50)	(50)	(50)
THYROGLOSSAL DUCT CYST		1 (2%)	
EDEMA, NOS	2 (4%)		
RESPIRATORY SYSTEM			
#LUNG	(49)	(50)	(50)
EDEMA, NOS	2 (4%)		
INFLAMMATION, INTERSTITIAL	1 (2%)	1 (2%)	
GRANULOMA, NOS	1 (2%)	1 (2%)	1 (2%)
INFLAMMATION, FOCAL GRANULOMATOU			1 (2%)
GRANULOMA, FOREIGN BODY			1 (2%)
HEMOSIDEROSIS	1 (2%)	1 (2%)	
HISTIOCYTOSIS			4 (8%)
HEMATOPOIETIC SYSTEM			
#BONE MARROW	(49)	(49)	(50)
HYPERPLASIA, HEMATOPOIETIC	1 (2%)	2 (4%)	
HYPERPLASIA, RETICULUM CELL			2 (4%)
HYPOPLASIA, HEMATOPOIETIC	1 (2%)		
#SPLEEN	(48)	(50)	(50)
CONGESTION, NOS			1 (2%)
PIGMENTATION, NOS		1 (2%)	
HEMOSIDEROSIS	1 (2%)		1 (2%)
LYMPHOID DEPLETION			2 (4%)
HYPERPLASIA, RETICULUM CELL	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
HEMATOPOIESIS	2 (4%)	3 (6%)	
#MANDIBULAR L. NODE	(48)	(44)	(44)
HEMORRHAGE	1 (2%)	1 (2%)	1 (2%)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
GRANULOMA, NOS			1 (2%)
HYPERPLASIA, LYMPHOID	1 (2%)		
#MESENTERIC L. NODE	(48)	(44)	(44)
HEMORRHAGE	1 (2%)	1 (2%)	
GRANULOMA, NOS	1 (2%)		7 (16%)
NECROSIS, DIFFUSE	1 (2%)		
HEMOSIDEROSIS			1 (2%)
LYMPHOID DEPLETION			1 (2%)
#LUNG	(49)	(50)	(50)
HYPERPLASIA, LYMPHOID			3 (6%)
#THYMUS	(37)	(41)	(42)
HEMORRHAGE			1 (2%)
ATROPHY, DIFFUSE	1 (3%)		
#THYMIC CORTEX	(37)	(41)	(42)
HYPERPLASIA, LYMPHOID	1 (3%)		
CIRCULATORY SYSTEM			
#MANDIBULAR L. NODE	(48)	(44)	(44)
LYMPHANGIECTASIS	1 (2%)		
#MESENTERIC L. NODE	(48)	(44)	(44)
LYMPHANGIECTASIS	1 (2%)		
#HEART	(50)	(50)	(49)
THROMBOSIS, NOS		1 (2%)	
DEGENERATION, NOS	10 (20%)	20 (40%)	3 (6%)
#HEART/ATRIUM	(50)	(50)	(49)
THROMBOSIS, NOS	1 (2%)		
#RIGHT ATRIUM	(50)	(50)	(49)
THROMBOSIS, NOS	1 (2%)		
#LEFT ATRIUM	(50)	(50)	(49)
THROMBOSIS, NOS		1 (2%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
THROMBUS, ORGANIZED	1 (2%)		
#MYOCARDIUM	(50)	(50)	(49)
MINERALIZATION	1 (2%)		
INFLAMMATION, CHRONIC FOCAL	2 (4%)	1 (2%)	1 (2%)
#CARDIAC VALVE	(50)	(50)	(49)
INFLAMMATION, CHRONIC			1 (2%)
INFLAMMATION, CHRONIC FOCAL		1 (2%)	
*CORONARY ARTERY	(50)	(50)	(50)
INFLAMMATION, CHRONIC		2 (4%)	1 (2%)
DEGENERATION, NOS		1 (2%)	
*PULMONARY VEIN	(50)	(50)	(50)
MINERALIZATION			1 (2%)
#LIVER	(50)	(49)	(50)
THROMBOSIS, NOS	1 (2%)		
*MESENTERY	(50)	(50)	(50)
PERIARTERITIS			1 (2%)
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(49)	(49)	(47)
EDEMA, NOS	1 (2%)		
LYMPHOCYTIC INFLAMMATORY INFILTR	1 (2%)		
ATROPHY, FOCAL		1 (2%)	1 (2%)
#LIVER	(50)	(49)	(50)
MINERALIZATION		1 (2%)	
CYST, NOS	1 (2%)		
CONGESTION, CHRONIC PASSIVE	1 (2%)	1 (2%)	
INFLAMMATION, CHRONIC FOCAL	1 (2%)	2 (4%)	
GRANULOMA, NOS	4 (8%)	4 (8%)	4 (8%)
INFLAMMATION, FOCAL GRANULOMATOU	1 (2%)		
DEGENERATION, NOS	1 (2%)		2 (4%)
NECROSIS, FOCAL		7 (14%)	
CYTOPLASMIC VACUOLIZATION	1 (2%)		2 (4%)
BASOPHILIC CYTO CHANGE	30 (60%)	40 (82%)	38 (76%)
FOCAL CELLULAR CHANGE	1 (2%)	1 (2%)	2 (4%)
ANGIECTASIS		1 (2%)	
#PORTAL TRACT	(50)	(49)	(50)
INFLAMMATION, CHRONIC			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
INFLAMMATION, CHRONIC FOCAL		1 (2%)	
#LIVER/CENTRILOBULAR	(50)	(49)	(50)
CONGESTION, ACUTE	1 (2%)		
DEGENERATION, NOS	2 (4%)		
NECROSIS, NOS	1 (2%)	1 (2%)	
NECROSIS, FOCAL	1 (2%)		1 (2%)
METAMORPHOSIS FATTY	1 (2%)		
#BILE DUCT	(50)	(49)	(50)
HYPERPLASIA, FOCAL	4 (8%)	1 (2%)	1 (2%)
HYPERPLASIA, DIFFUSE	1 (2%)		
#PANCREAS	(48)	(50)	(50)
INFLAMMATION, CHRONIC FOCAL	1 (2%)		
#PANCREATIC ACINUS	(48)	(50)	(50)
NECROSIS, FOCAL			1 (2%)
ATROPHY, NOS	2 (4%)		
ATROPHY, FOCAL	3 (6%)	2 (4%)	4 (8%)
ATROPHY, DIFFUSE			1 (2%)
#STOMACH	(49)	(49)	(50)
HYPERPLASIA, EPITHELIAL	1 (2%)		
#COLON	(49)	(49)	(47)
NEMATODIASIS	3 (6%)	1 (2%)	
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(50)
MINERALIZATION	1 (2%)	1 (2%)	1 (2%)
INFLAMMATION, INTERSTITIAL		1 (2%)	2 (4%)
NEPHROPATHY	3 (6%)	4 (8%)	7 (14%)
INFARCT, FOCAL		1 (2%)	
PIGMENTATION, NOS	1 (2%)	1 (2%)	2 (4%)
BASOPHILIC CYTO CHANGE			1 (2%)
#KIDNEY/CORTEX	(50)	(50)	(50)
CYST, NOS		1 (2%)	
PIGMENTATION, NOS		8 (16%)	34 (68%)
#KIDNEY/TUBULE	(50)	(50)	(50)
PIGMENTATION, NOS	2 (4%)	1 (2%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#KIDNEY/PELVIS	(50)	(50)	(50)
MINERALIZATION	2 (4%)		
INFLAMMATION, FOCAL GRANULOMATOU			1 (2%)
HYPERPLASIA, EPITHELIAL			1 (2%)
#URINARY BLADDER	(49)	(48)	(48)
INFLAMMATION, ACUTE	1 (2%)		
ENDOCRINE SYSTEM			
#PITUITARY	(44)	(48)	(49)
CONGESTION, NOS			1 (2%)
HEMORRHAGE			1 (2%)
HYPERPLASIA, CHROMOPHOBE-CELL	9 (20%)	7 (15%)	8 (16%)
ANGIECTASIS			1 (2%)
#ADRENAL	(50)	(50)	(50)
ANGIECTASIS			1 (2%)
#ADRENAL CORTEX	(50)	(50)	(50)
HEMORRHAGE	1 (2%)		
NECROSIS, FOCAL		1 (2%)	
LIPOIDOSIS	1 (2%)	1 (2%)	2 (4%)
HYPERPLASIA, NODULAR			2 (4%)
ANGIECTASIS		2 (4%)	3 (6%)
#ZONA FASCICULATA	(50)	(50)	(50)
LIPOIDOSIS	4 (8%)	5 (10%)	2 (4%)
BASOPHILIC CYTO CHANGE			1 (2%)
HYPERPLASIA, NODULAR	15 (30%)	11 (22%)	9 (18%)
HYPERPLASIA, FOCAL			1 (2%)
ANGIECTASIS			1 (2%)
#ZONA RETICULARIS	(50)	(50)	(50)
HYPERPLASIA, NODULAR			1 (2%)
#ADRENAL MEDULLA	(50)	(50)	(50)
HYPERPLASIA, NOS	1 (2%)	1 (2%)	1 (2%)
HYPERPLASIA, FOCAL			1 (2%)
#THYROID	(49)	(49)	(50)
COLLOID CYST	1 (2%)	1 (2%)	2 (4%)
HYPERPLASIA, C-CELL	10 (20%)	12 (24%)	10 (20%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#PARATHYROID	(37)	(33)	(39)
DEGENERATION, NOS	1 (3%)		
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
DILATATION/DUCTS	1 (2%)		
CYST, NOS	2 (4%)	1 (2%)	
MULTIPLE CYSTS	2 (4%)	1 (2%)	
FIBROSIS		1 (2%)	
HYPERPLASIA, NODULAR		2 (4%)	3 (6%)
HYPERPLASTIC NODULE	1 (2%)		
HYPERPLASIA, NOS			2 (4%)
HYPERPLASIA, EPITHELIAL			1 (2%)
HYPERPLASIA, CYSTIC	12 (24%)	12 (24%)	5 (10%)
ADENOSIS	1 (2%)		
*MAMMARY ACINUS	(50)	(50)	(50)
CYST, NOS	1 (2%)		
#UTERUS	(50)	(48)	(50)
DILATATION, NOS	2 (4%)	2 (4%)	6 (12%)
#CERVIX UTERI	(50)	(48)	(50)
INFLAMMATION, CHRONIC FOCAL		1 (2%)	
HYPERPLASIA, STROMAL		1 (2%)	
#UTERUS/ENDOMETRIUM	(50)	(48)	(50)
FIBROSIS	1 (2%)		
#ENDOMETRIAL GLAND	(50)	(48)	(50)
CYST, NOS	1 (2%)		3 (6%)
MULTIPLE CYSTS		7 (15%)	1 (2%)
INFLAMMATION, ACUTE FOCAL	1 (2%)		
HYPERPLASIA, NOS		1 (2%)	
HYPERPLASIA, EPITHELIAL		1 (2%)	
#OVARY	(50)	(49)	(50)
CYST, NOS	1 (2%)		
CORPUS LUTEUM CYST	1 (2%)		1 (2%)
PAROVARIAN CYST		1 (2%)	
HYPERPLASIA, GRANULOSA-CELL	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
NERVOUS SYSTEM			
#BRAIN/MENINGES	(50)	(50)	(49)
INFLAMMATION, CHRONIC FOCAL		1 (2%)	
#BRAIN	(50)	(50)	(49)
NECROSIS, HEMORRHAGIC		1 (2%)	
ATROPHY, PRESSURE			1 (2%)
#HYPOTHALAMUS	(50)	(50)	(49)
ATROPHY, PRESSURE	2 (4%)	6 (12%)	2 (4%)
SPECIAL SENSE ORGANS			
*EYE/RETINA	(50)	(50)	(50)
ATROPHY, NOS	2 (4%)		4 (8%)
*EYE/CRYSTALLINE LENS	(50)	(50)	(50)
MINERALIZATION	1 (2%)		1 (2%)
*LENS CAPSULE	(50)	(50)	(50)
MINERALIZATION			1 (2%)
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*PERITONEUM	(50)	(50)	(50)
INFLAMMATION, FIBRINOUS	1 (2%)		
*MESENTERY	(50)	(50)	(50)
CYST, NOS		1 (2%)	
LYMPHOCYTIC INFLAMMATORY INFILTR		1 (2%)	
INFLAMMATION, CHRONIC FOCAL		1 (2%)	
INFLAMMATION, FOCAL GRANULOMATOU		1 (2%)	
NECROSIS, FAT	2 (4%)		
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
TAIL			
HYPERKERATOSIS		1	
CRANIOBUCCAL POUCH			
CYSTIC DUCTS		3	
SPECIAL MORPHOLOGY SUMMARY			
AUTO/NECROPSY/HISTO PERF	1		

\# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

APPENDIX D

Summary of the Incidence of Nonneoplastic Lesions in Mice Fed Diets Containing C. I. Disperse Yellow 3

TABLE D1.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE FED DIETS CONTAINING C. I. DISPERSE YELLOW 3

	CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS MISSING			1
ANIMALS NECROPSIED	50	49	49
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	49	49
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(49)	(49)
ULCER, ACUTE		2 (4%)	
INFLAMMATION, ACUTE/CHRONIC		1 (2%)	
INFLAMMATION, CHRONIC DIFFUSE			1 (2%)
FIBROSIS	1 (2%)		
FIBROSIS, FOCAL	2 (4%)		1 (2%)
FIBROSIS, DIFFUSE		2 (4%)	
ACANTHOSIS	1 (2%)		
PARAKERATOSIS	1 (2%)		
*SUBCUT TISSUE	(50)	(49)	(49)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
INFLAMMATION, GRANULOMATOUS	1 (2%)		
RESPIRATORY SYSTEM			
#LUNG/BRONCHIOLE	(50)	(49)	(49)
HYPERPLASIA, NOS	13 (26%)	24 (49%)	16 (33%)
#LUNG	(50)	(49)	(49)
LYMPHOCYTIC INFLAMMATORY INFILTR			1 (2%)
INFLAMMATION, INTERSTITIAL	5 (10%)	10 (20%)	8 (16%)
INFLAMMATION, FOCAL GRANULOMATOU		2 (4%)	1 (2%)
GRANULOMA, PYOGENIC			1 (2%)
HYPERPLASIA, ALVEOLAR EPITHELIUM	13 (26%)	24 (49%)	16 (33%)
HISTIOCYTOSIS	2 (4%)	1 (2%)	1 (2%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(49)	(49)
HYPERPLASIA, LYMPHOID	1 (2%)	1 (2%)	3 (6%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#BONE MARROW	(49)	(48)	(45)
DEPLETION	1 (2%)	1 (2%)	
ANGIECTASIS			1 (2%)
HYPERPLASIA, HEMATOPOIETIC		4 (8%)	
HYPERPLASIA, GRANULOCYTIC	1 (2%)		2 (4%)
#SPLEEN	(50)	(49)	(48)
INFLAMMATION, FOCAL GRANULOMATOU		1 (2%)	
LYMPHOID DEPLETION	1 (2%)	1 (2%)	
HYPERPLASIA, LYMPHOID	4 (8%)	1 (2%)	4 (8%)
HEMATOPOIESIS		2 (4%)	1 (2%)
#SPLENIC RED PULP	(50)	(49)	(48)
HEMATOPOIESIS	4 (8%)	5 (10%)	5 (10%)
#MANDIBULAR L. NODE	(37)	(39)	(36)
HYPERPLASIA, LYMPHOID			2 (6%)
#MESENTERIC L. NODE	(37)	(39)	(36)
HYPERPLASIA, LYMPHOID			1 (3%)
HEMATOPOIESIS	12 (32%)	3 (8%)	3 (8%)
#LUNG	(50)	(49)	(49)
HYPERPLASIA, LYMPHOID	9 (18%)	3 (6%)	5 (10%)
#SALIVARY GLAND	(50)	(49)	(49)
HYPERPLASIA, LYMPHOID	8 (16%)	7 (14%)	4 (8%)
#LIVER	(50)	(49)	(49)
LEUKEMOID REACTION	1 (2%)		
HYPERPLASIA, LYMPHOID	1 (2%)		
HEMATOPOIESIS	1 (2%)	2 (4%)	
*MUCOSA OF GALLBLADDE	(50)	(49)	(49)
HYPERPLASIA, LYMPHOID		1 (2%)	
#BILE DUCT	(50)	(49)	(49)
HYPERPLASIA, LYMPHOID	1 (2%)		
#PEYER'S PATCH	(47)	(49)	(46)
HYPERPLASIA, LYMPHOID		1 (2%)	3 (7%)
#KIDNEY	(50)	(49)	(49)
LEUKEMOID REACTION	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
HYPERPLASIA, LYMPHOID	30 (60%)	28 (57%)	35 (71%)
#U.BLADDER/SUBMUCOSA	(48)	(49)	(49)
HYPERPLASIA, LYMPHOID	4 (8%)	5 (10%)	
*URETHRA	(50)	(49)	(49)
HYPERPLASIA, LYMPHOID		1 (2%)	
#THYMIC CORTEX	(35)	(29)	(38)
LYMPHOID DEPLETION		1 (3%)	2 (5%)
CIRCULATORY SYSTEM			
#SPLEEN	(50)	(49)	(48)
THROMBOSIS, NOS		1 (2%)	
#MESENTERIC L. NODE	(37)	(39)	(36)
LYMPHANGIECTASIS		1 (3%)	2 (6%)
#LUNG	(50)	(49)	(49)
PERIVASCULITIS	1 (2%)	1 (2%)	
#MYOCARDIUM	(50)	(49)	(49)
INFLAMMATION, CHRONIC FOCAL		1 (2%)	1 (2%)
#CARDIAC VALVE	(50)	(49)	(49)
HEMOSIDEROSIS		2 (4%)	6 (12%)
*RENAL VEIN	(50)	(49)	(49)
CONGESTION, NOS		1 (2%)	
#U.BLADDER/SUBMUCOSA	(48)	(49)	(49)
PERIARTERITIS			1 (2%)
DIGESTIVE SYSTEM			
#LIVER	(50)	(49)	(49)
HEMORRHAGIC CYST			1 (2%)
INFLAMMATION, ACUTE/CHRONIC		1 (2%)	1 (2%)
INFLAMMATION, FOCAL GRANULOMATOU	4 (8%)	1 (2%)	
INFLAMMATION, PYOGRANULOMATOUS			1 (2%)
NECROSIS, FOCAL	1 (2%)	2 (4%)	
NECROSIS, ISCHEMIC		2 (4%)	2 (4%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
BASOPHILIC CYTO CHANGE	1 (2%)		
FOCAL CELLULAR CHANGE	4 (8%)		4 (8%)
ANGIECTASIS		1 (2%)	
#LIVER/CENTRILOBULAR	(50)	(49)	(49)
LYMPHOCYTIC INFLAMMATORY INFILTR	1 (2%)		
*GALLBLADDER	(50)	(49)	(49)
INFLAMMATION, MULTIFOCAL		1 (2%)	
INFLAMMATION, ACUTE		1 (2%)	
#BILE DUCT	(50)	(49)	(49)
DILATATION, NOS	1 (2%)		
CYST, NOS			2 (4%)
HYPERPLASIA, NOS		1 (2%)	
HYPERPLASIA, CYSTIC		1 (2%)	
#PANCREAS	(50)	(48)	(47)
CYST, NOS			1 (2%)
FIBROSIS, DIFFUSE	1 (2%)		
NECROSIS, NOS	1 (2%)		
#PANCREATIC ACINUS	(50)	(48)	(47)
ATROPHY, NOS	2 (4%)		1 (2%)
ATROPHY, FOCAL	1 (2%)		
ATROPHY, DIFFUSE	1 (2%)		
#STOMACH	(50)	(47)	(46)
INFLAMMATION, ACUTE FOCAL			1 (2%)
#GASTRIC FUNDAL GLAND	(50)	(47)	(46)
POLYP			1 (2%)
#GASTRIC SUBMUCOSA	(50)	(47)	(46)
INFLAMMATION, ACUTE FOCAL			2 (4%)
#PEYER'S PATCH	(47)	(49)	(46)
HYPERPLASIA, NOS	1 (2%)		
#COLON	(47)	(44)	(46)
NEMATODIASIS	1 (2%)		
URINARY SYSTEM			
#KIDNEY	(50)	(49)	(49)
MINERALIZATION		1 (2%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
INFLAMMATION, INTERSTITIAL	1 (2%)		
NEPHROPATHY	1 (2%)		2 (4%)
NEPHROSIS, NOS	1 (2%)	3 (6%)	
METAPLASIA, OSSEOUS		1 (2%)	
#KIDNEY/CORTEX	(50)	(49)	(49)
INFLAMMATION, INTERSTITIAL	3 (6%)		1 (2%)
NEPHROPATHY	1 (2%)		3 (6%)
NEPHROSIS, NOS		8 (16%)	
METAPLASIA, OSSEOUS	1 (2%)		
#KIDNEY/TUBULE	(50)	(49)	(49)
CYST, NOS	2 (4%)		
NEPHROPATHY	1 (2%)		
REGENERATION, NOS	18 (36%)	27 (55%)	30 (61%)
#URETHRA	(50)	(49)	(49)
ANGIECTASIS			1 (2%)
ENDOCRINE SYSTEM			
#PITUITARY	(43)	(34)	(32)
CYST, NOS	1 (2%)		
HYPERPLASIA, CHROMOPHOBE-CELL		1 (3%)	
#ADRENAL/CAPSULE	(50)	(47)	(47)
HYPERPLASIA, FOCAL		1 (2%)	
#ADRENAL CORTEX	(50)	(47)	(47)
CYST, NOS			1 (2%)
HEMORRHAGIC CYST	1 (2%)		
FOCAL CELLULAR CHANGE			2 (4%)
HYPERPLASIA, NODULAR			1 (2%)
THYROID	(49)	(48)	(47)
FOLLICULAR CYST, NOS	1 (2%)	4 (8%)	2 (4%)
THYROID FOLLICLE	(49)	(48)	(47)
DEGENERATION, NOS		1 (2%)	
DEGENERATION, CYSTIC		1 (2%)	
HYPERPLASIA, CYSTIC		1 (2%)	
PANCREATIC ISLETS	(50)	(48)	(47)
HYPERPLASIA, FOCAL	2 (4%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
NUMBER OF ANIMALS NECROPSIED

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
REPRODUCTIVE SYSTEM			
*PREPUTIAL GLAND	(50)	(49)	(49)
INFLAMMATION, GRANULOMATOUS	1 (2%)		
INFLAMMATION, PYOGRANULOMATOUS		1 (2%)	
#TESTIS	(49)	(49)	(49)
MINERALIZATION	1 (2%)		
HYPERPLASIA, INTERSTITIAL CELL		1 (2%)	
#TESTIS/TUBULE	(49)	(49)	(49)
MINERALIZATION	4 (8%)	1 (2%)	2 (4%)
DEGENERATION, NOS	1 (2%)	2 (4%)	
*EPIDIDYMIS	(50)	(49)	(49)
INFLAMMATION, ACUTE/CHRONIC	2 (4%)		
INFLAMMATION, FOCAL GRANULOMATOU			1 (2%)
NERVOUS SYSTEM			
#CEREBRUM	(50)	(48)	(48)
MINERALIZATION	19 (38%)	9 (19%)	17 (35%)
#BRAIN	(50)	(48)	(48)
HEMORRHAGE		1 (2%)	
ATROPHY, PRESSURE	1 (2%)		
SPECIAL SENSE ORGANS			
NONE			
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*MEDIASTINUM	(50)	(49)	(49)
HEMORRHAGE	1 (2%)		
*MESENTERY	(50)	(49)	(49)
INFLAMMATION, FOCAL GRANULOMATOU			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
ALL OTHER SYSTEMS			
NONE			
SPECIAL MORPHOLOGY SUMMARY			
ANIMAL MISSING/NO NECROPSY			1
AUTO/NECROPSY/HISTO PERF			1
AUTOLYSIS/NO NECROPSY		1	

\# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE FED DIETS CONTAINING C. I. DISPERSE YELLOW 3

	CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
HYPERPLASIA, FOCAL		1 (2%)	
*SUBCUT TISSUE	(50)	(50)	(50)
EPIDERMAL INCLUSION CYST		1 (2%)	
RESPIRATORY SYSTEM			
#LUNG/BRONCHIOLE	(50)	(50)	(50)
HYPERPLASIA, NOS	1 (2%)	11 (22%)	8 (16%)
#LUNG	(50)	(50)	(50)
CONGESTION, PASSIVE		1 (2%)	
LYMPHOCYTIC INFLAMMATORY INFILTR	1 (2%)		
INFLAMMATION, INTERSTITIAL	1 (2%)	3 (6%)	4 (8%)
HYPERPLASIA, ALVEOLAR EPITHELIUM	1 (2%)	11 (22%)	8 (16%)
HISTIOCYTOSIS			1 (2%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
HYPERPLASIA, LYMPHOID	13 (26%)	10 (20%)	10 (20%)
#BONE MARROW	(49)	(49)	(48)
HYPERPLASIA, GRANULOCYTIC	4 (8%)	2 (4%)	2 (4%)
HYPERPLASIA, RETICULUM CELL	2 (4%)		
#SPLEEN	(50)	(50)	(49)
FIBROSIS, FOCAL			1 (2%)
LYMPHOID DEPLETION	1 (2%)		
HYPERPLASIA, LYMPHOID	7 (14%)	2 (4%)	6 (12%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#SPLENIC RED PULP	(50)	(50)	(49)
HEMATOPOIESIS	9 (18%)	2 (4%)	2 (4%)
#LYMPH NODE	(40)	(43)	(42)
INFLAMMATION, GRANULOMATOUS	1 (3%)		
#PANCREATIC L.NODE	(40)	(43)	(42)
HYPERPLASIA, NOS	1 (3%)		
#MESENTERIC L. NODE	(40)	(43)	(42)
HEMATOPOIESIS	1 (3%)		
#LUNG	(50)	(50)	(50)
HYPERPLASIA, LYMPHOID	3 (6%)	13 (26%)	11 (22%)
#SALIVARY GLAND	(48)	(49)	(47)
HYPERPLASIA, LYMPHOID	2 (4%)	7 (14%)	3 (6%)
#LIVER	(50)	(50)	(50)
HYPERPLASIA, LYMPHOID	5 (10%)		2 (4%)
HEMATOPOIESIS	2 (4%)		
#PANCREAS	(50)	(47)	(50)
HYPERPLASIA, LYMPHOID	2 (4%)		
#KIDNEY	(50)	(50)	(50)
HYPERPLASIA, LYMPHOID	22 (44%)	20 (40%)	26 (52%)
#URINARY BLADDER	(50)	(46)	(49)
HYPERPLASIA, LYMPHOID	1 (2%)		
#U.BLADDER/SUBMUCOSA	(50)	(46)	(49)
HYPERPLASIA, LYMPHOID	17 (34%)	14 (30%)	18 (37%)
#THYMUS	(41)	(43)	(42)
HYPERPLASIA, EPITHELIAL		2 (5%)	
HYPERPLASIA, RETICULUM CELL		1 (2%)	
HYPERPLASIA, LYMPHOID	1 (2%)		
#THYMIC CORTEX	(41)	(43)	(42)
ATROPHY, NOS	1 (2%)		
#THYMIC MEDULLA	(41)	(43)	(42)
HYPERPLASIA, FOCAL		1 (2%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
CIRCULATORY SYSTEM			
#LUNG	(50)	(50)	(50)
PERIVASCULITIS	1 (2%)	1 (2%)	
#HEART	(50)	(50)	(50)
MINERALIZATION		1 (2%)	
PERIARTERITIS			1 (2%)
#LEFT VENTRICLE	(50)	(50)	(50)
PERIARTERITIS	1 (2%)		
#MYOCARDIUM	(50)	(50)	(50)
INFLAMMATION, ACUTE/CHRONIC		1 (2%)	
#CARDIAC VALVE	(50)	(50)	(50)
HEMOSIDEROSIS	4 (8%)	4 (8%)	3 (6%)
#KIDNEY/MEDULLA	(50)	(50)	(50)
PERIARTERITIS			1 (2%)
#THYROID	(50)	(49)	(49)
PERIARTERITIS	1 (2%)		
DIGESTIVE SYSTEM			
#LIVER	(50)	(50)	(50)
INFLAMMATION, FOCAL GRANULOMATOU	9 (18%)	2 (4%)	10 (20%)
NECROSIS, FOCAL			2 (4%)
FOCAL CELLULAR CHANGE	1 (2%)	2 (4%)	7 (14%)
#LIVER/CENTRILOBULAR	(50)	(50)	(50)
NECROSIS, FOCAL			1 (2%)
CYTOPLASMIC VACUOLIZATION			1 (2%)
#LIVER/KUPFFER CELL	(50)	(50)	(50)
HYPERPLASIA, DIFFUSE	1 (2%)		
*GALLBLADDER	(50)	(50)	(50)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
*MUCOSA OF GALLBLADDE	(50)	(50)	(50)
CYST, NOS			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#BILE DUCT	(50)	(50)	(50)
DILATATION, NOS	1 (2%)		2 (4%)
CYST, NOS			2 (4%)
#PANCREAS	(50)	(47)	(50)
DILATATION/DUCTS	1 (2%)	2 (4%)	
CYSTIC DUCTS	1 (2%)	1 (2%)	
INFLAMMATION, NOS	1 (2%)		
INFLAMMATION, FOCAL	1 (2%)		
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
NECROSIS, FOCAL		1 (2%)	
NECROSIS, FAT	1 (2%)		
#PANCREATIC ACINUS	(50)	(47)	(50)
ATROPHY, NOS		1 (2%)	1 (2%)
ATROPHY, FOCAL	2 (4%)	1 (2%)	
ATROPHY, DIFFUSE	1 (2%)	1 (2%)	
#STOMACH	(50)	(48)	(50)
INFLAMMATION, ACUTE FOCAL	1 (2%)		
#PEYER'S PATCH	(48)	(46)	(46)
ULCER, NOS	1 (2%)		
FIBROSIS	1 (2%)		
#ILEUM	(48)	(46)	(46)
INFLAMMATION, NECROTIZING	1 (2%)		
#COLON	(49)	(45)	(48)
NEMATODIASIS	1 (2%)	5 (11%)	
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(50)
HYDRONEPHROSIS	1 (2%)	1 (2%)	
NEPHROSIS, NOS	3 (6%)	1 (2%)	
#KIDNEY/CORTEX	(50)	(50)	(50)
NEPHROSIS, NOS	1 (2%)		
#KIDNEY/GLOMERULUS	(50)	(50)	(50)
NEPHROSIS, NOS			1 (2%)
#KIDNEY/TUBULE	(50)	(50)	(50)
DEGENERATION, NOS		1 (2%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
DEGENERATION, HYALINE			1 (2%)
HEMOSIDEROSIS	1 (2%)	1 (2%)	
REGENERATION, NOS	11 (22%)	13 (26%)	18 (36%)
#URINARY BLADDER	(50)	(46)	(49)
INFLAMMATION, CHRONIC SUPPURATIV			1 (2%)
HYPERPLASIA, EPITHELIAL	1 (2%)		
ENDOCRINE SYSTEM			
#PITUITARY	(38)	(30)	(42)
HYPERPLASIA, CHROMOPHOBE-CELL	4 (11%)		
#ADRENAL	(46)	(47)	(49)
METAMORPHOSIS FATTY			1 (2%)
#ADRENAL CORTEX	(46)	(47)	(49)
CYST, NOS		1 (2%)	
#ADRENAL MEDULLA	(46)	(47)	(49)
HYPERPLASIA, NOS	3 (7%)		
HYPERPLASIA, FOCAL	1 (2%)		
#THYROID	(50)	(49)	(49)
CYSTIC FOLLICLES			1 (2%)
FOLLICULAR CYST, NOS	4 (8%)	6 (12%)	5 (10%)
HYPERPLASIA, FOLLICULAR-CELL	1 (2%)		
#THYROID FOLLICLE	(50)	(49)	(49)
MULTILOCULAR CYST	1 (2%)	1 (2%)	
DEGENERATION, NOS	1 (2%)		
REPRODUCTIVE SYSTEM			
#UTERUS	(50)	(50)	(50)
DILATATION, NOS	1 (2%)	1 (2%)	4 (8%)
ANGIECTASIS	3 (6%)		1 (2%)
#UTERUS/ENDOMETRIUM	(50)	(50)	(50)
HEMORRHAGE		1 (2%)	
INFLAMMATION, SUPPURATIVE	1 (2%)		
CYTOPLASMIC VACUOLIZATION			1 (2%)
#ENDOMETRIAL GLAND	(50)	(50)	(50)
CYST, NOS	1 (2%)		1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
HYPERPLASIA, CYSTIC	41 (82%)	43 (86%)	40 (80%)
METAPLASIA, SQUAMOUS	1 (2%)	2 (4%)	
#OVARY	(46)	(48)	(47)
CYST, NOS	7 (15%)	9 (19%)	7 (15%)
FOLLICULAR CYST, NOS			1 (2%)
CORPUS HEMORRHAGICUM CYST		1 (2%)	
MULTIPLE CYSTS	1 (2%)		
PAROVARIAN CYST	1 (2%)		
HEMORRHAGIC CYST			1 (2%)
HYPERPLASIA, PAPILLARY	1 (2%)		
HYPERPLASIA, STROMAL	1 (2%)		
NERVOUS SYSTEM			
#CEREBRUM	(50)	(49)	(50)
MINERALIZATION	25 (50%)	11 (22%)	15 (30%)
#BRAIN	(50)	(49)	(50)
INFLAMMATION, NOS	1 (2%)		
PERIVASCULAR CUFFING		1 (2%)	
SPECIAL SENSE ORGANS			
NONE			
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*EPICARDIUM	(50)	(50)	(50)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
*MESENTERY	(50)	(50)	(50)
INFLAMMATION, FOCAL GRANULOMATOU	1 (2%)		
NECROSIS, FAT	1 (2%)		
ALL OTHER SYSTEMS			
CRANIOBUCCAL POUCH			
CYST, NOS			1

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
SPECIAL MORPHOLOGY SUMMARY			
NONE			

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

APPENDIX E

Analysis of C. I. Disperse Yellow 3

(Lot No. 19-007630)

Midwest Research Institute

Appendix E

Analysis of C. I. Disperse Yellow 3
(Lot No. 19-007630)
Midwest Research Institute

A. ELEMENTAL ANALYSIS

Element	C	H	N	Cl^-	$CO_3^=$
Theory	66.90	5.61	15.60	0.0	0.0
Determined	59.57	6.10	13.48	3.58	0.65
	59.31	5.98	13.50	3.36	0.66

B. WATER ANALYSIS

(Karl Fisher)

$6.62 \pm 0.02(\delta)\%$

C. TITRATION

$TiCl_3$ reduction of azo group

87.6 ± 1.1 $(\delta)\%$ (4 electrons per mole)

D. MELTING POINT

Determined	Literature Values
m.p. Endotherms at 57° to 65°C, 67° to 81°C, 91° to 99°C, 99° to 106°C, 127° to 148°C, 170° to 180°C, 185° to 191°C; exotherm at 180° to 185°C (Dupont 900 DTA) m.p. 192° to 193.5°C (decomposition visual, capillary)	m.p. 195°C (Patterson and Sheldon, 1960)

E. THIN-LAYER CHROMATOGRAPHY

Plates: Silica Gel 60F-254
Amount spotted: 100 and 300 μg
Ref. standard: Methyl Red
Visualization: UV (254 and 366 nm)

System 1: 2-Propanol

R_f: 0.85 (trace)
0.74 (major)
0.028 (slight trace)
Origin (trace)

R_{st}: 1.89, 1.64, 0.062, and origin

System 2: Chloroform

R_f: 0.85 (trace)
0.52 (slight trace)
0.21 (slight trace)
0.11 (major)

R_{st}: Origin (minor)
9.34, 5.71, 2.31, 1.21 and origin

F. HIGH PRESSURE-LIQUID CHROMATOGRAPHY

Instrument: Waters ALC202
Detector: Ultraviolet, 254 nm
Column: C^{18} μBondapak (300 x 4 mm ID)
Solvent: Methanol:water (70:30) with 0.005 M tetrabutylammonium hydroxide and 1% acetic acid
Flow: 1.5 ml/min
Results: Major peak, one multicomponent impurity peak and two single impurity peaks

Peak 3	Retention Time (min)	Retention Time Relative to C. I. Disperse Yellow 3	Area Relative to C. I. Disperse Yellow 3
minor (multicomponent)	2.5-4.4	0.32-0.57	2.15
minor	6.2	0.81	0.28
major	7.7	1.00	100.00
minor	13.5	1.75	0.28

G. SPECTRAL DATA

(1) Infrared

Instrument: Beckman IR 12
Cell: 1% KBr pellet
Results: See Figure 5.

Literature Values

Identical to literature spectrum (Sadtler Standard Spectra)

(2) Ultraviolet/Visible

Instrument: Cary 118

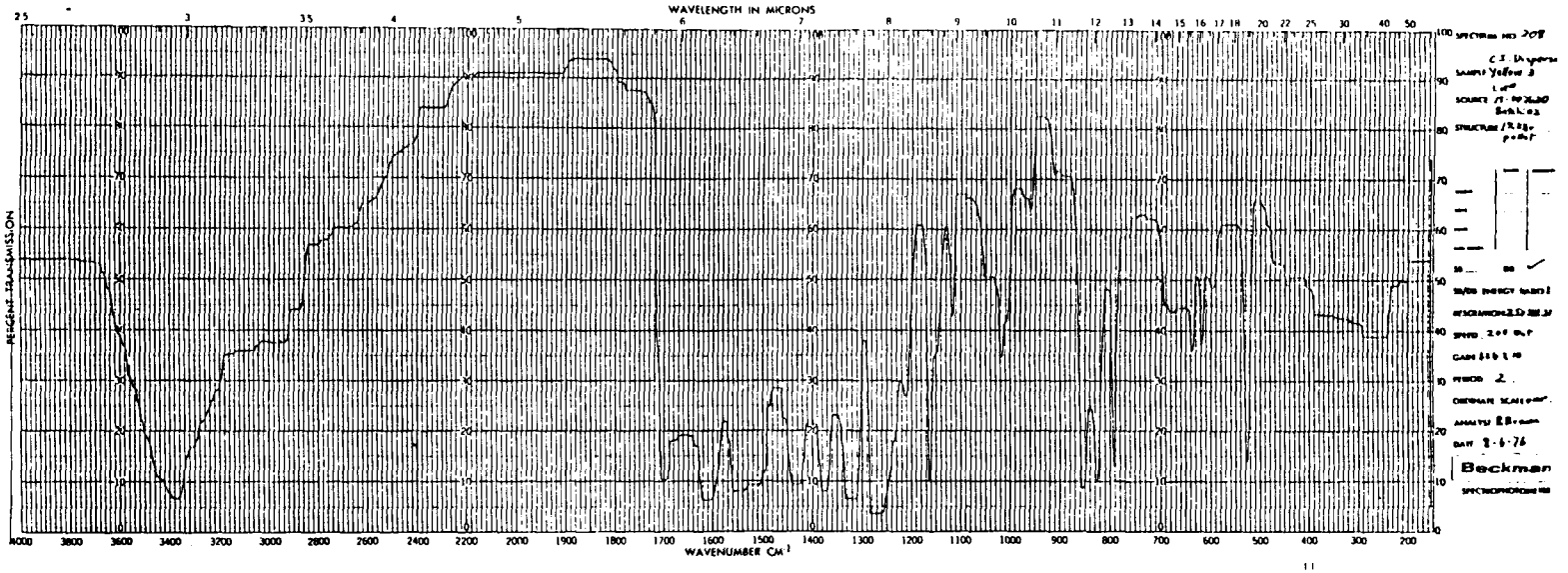

Figure 5. Infrared Absorption Spectrum of C.I. Disperse Yellow 3 (Lot No. 19-007630)

λmax (nm)	ε x 10^{-2}
392	120.7 ± 0.6 (δ)
345	169 ± 2 (δ)
249	102 ± 2 (δ)

Solvent: Methanol: concentrated sulfuric acid (95:5)

λ max (nm)	ε x 10^{-2}
360	188.50 (Patterson and Sheldon, 1960)

Solvent: 50% aqueous acetone

Determined

(3) Nuclear magnetic resonance

Unable to obtain adequate solvent

Literature Values

No literature reference found

APPENDIX F

Analysis of Formulated Diets for Stability of C. I. Disperse Yellow 3

Appendix F

Analysis of Formulated Diets For Stability of
C. I. Disperse Yellow 3

HEAT STABILITY

1. Mixing and Storage

C. I. Disperse Yellow 3 (2.500 g) and Wayne Lab Blox® Rodent Feed (22.500 g) were mixed in a mortar. Samples of the mixture were removed and stored for 2 weeks at -20°, 5°, 25°, and 45°C, respectively. These samples were then analyzed by high-pressure liquid chromatography as described below.

2. Extraction

One-gram samples of each of the above stability mixtures were mixed with 50 ml of 75% aqueous methanol in an ultrasonic vibratory bath for 1 minute and then were triturated for 1 minute using a Polytron® high-speed blender. The mixture was centrifuged, and the supernatant solution was decanted into a 100-ml volumetric flask. This extraction was repeated on the feed residue, and the combined supernatant solutions were brought to volume with fresh 75% aqueous methanol.

3. Analysis

Instrument: Waters ALC 202 with Model 660 Solvent Programmer
Column: $C^{18}\mu$ Bondapak, 300 x 4 mm I.D.
Solvent: 25% A + 75% B
A - 0.005M tetrabutylammonium hydroxide and 1% acetic acid in water
B - 0.005M tetrabutylammonium hydroxide and 1% acetic acid in methanol
Detector: Ultraviolet, 254 nm
Flow rate: 1.5 ml/min

Sample (°C)	Average Percentage Compound (a)
-20	9.9±0.6
5	10.4±0.6
25	9.0±0.6 (b)
45	8.8±0.6 (b)

(a) Corrected for a spiked recovery value of 95.2%; theoretical 100% value = 10.0%
(b) Within experimental error.

4. Conclusion

C. I. Disperse Yellow 3 mixed with feed is stable for 2 weeks at temperatures up to 45°C.

APPENDIX G

Analysis of Formulated Diets for Concentrations of C. I. Disperse Yellow 3

Appendix G

Analysis of Formulated Diets for Concentrations of
C. I. Disperse Yellow 3

1. For the first 18 months, samples (100 mg) of the formulated diets were extracted with 20 ml of a 1:1 acetone:water mixture. The absorbance of the extract at 473 nm was then measured in a spectrophotometer. The results of these analyses are summarized in the following table.

2. For the final 6 months, samples (1g) of the formulated diets were extracted twice with 50 ml acidic methanol. The combined extract (100 ml) was then diluted five-fold with solvent and the absorbance at 390 nm was measured on a spectrophotometer. This second extraction method was found to give a lower feed blank absorbance value (0.062) than that obtained from the aqueous acetone extraction (0.520).

Table G1. Analyses of Formulated Diets

Date Mixed (a)	Date Used	Concentration (b) of C. I. Disperse Yellow 3 in feed for target concentration of		
		2,500 ppm	5,000 ppm	10,000 ppm
3/10/77	week of 3/14 and 3/20		5,070	10,750
4/17/77	week of 4/21 and 4/27	2,680	5,100	
6/03/77	week of 6/7 and 6/13	2,500	5,260	9,500
			5,260	10,010
8/24/77	week of 8/28 and 9/2	2,450	4,980	10,600
			4,990	9,900
10/21/77	week of 10/24 and 10/31	2,530	4,980	10,400
			4,740	10,100
1/28/78	week of 1/31 and 2/7	2,360	4,980	9,820
			5,050	9,220
4/07/78	week of 4/10 and 4/17	2,495	5,010	10,100
			4,980	9,980
6/21/78	week of 6/24 and 6/31	2,510	5,030	10,180
			4,970	10,230
			4,950	
7/06/78	week of 7/9 and 7/16	2,700	5,000	9,890
			5,010	10,800
			4,800	
9/13/78	week of 9/15 and 9/23	2,310	4,660	9,510
			4,720	9,880
			4,970	
11/14/78	week of 11/17 and 11/24	2,480	5,220	10,100
			5,040	9,990
			4,930	
1/22/79	week of 1/24 and 1/31	2,720	5,300	10,500
			5,310	10,200
			5,290	
3/12/79	week of 3/15 and 3/22	2,490	5,180	
Mean (ppm)		2,519	5,028	10,079
Standard deviation		127	172	398
Coefficient of Variation (%)		5	3	4
Number of Samples		12	28	21
Range (ppm)		2,310-2,720	4,660-5,310	9,220-10,800

(a) The start dates for male and for female rats were 3/10/77 and 3/23/77. The start dates for male and for female mice were 4/8/77 and 4/13/77.
(b) The data presented are the average of duplicate analyses.

Appendix H

Feed Consumption by Rats and Mice Fed C. I. Disperse Yellow 3

Table H1. Feed Consumption by Male Rats Receiving C. I. Disperse Yellow 3

Week	Control GRAMS FEED/ DAY (a)	Low GRAMS FEED/ DAY (a)	Low LOW/ CONTROL (b)	High GRAMS FEED/ DAY (a)	High HIGH/ CONTROL (b)
5	19.3	18.6	1.0	17.3	0.9
10	17.6	17.1	1.0	17.7	1.0
14	19.1	17.5	0.9	19.0	1.0
18	20.0	17.9	0.9	21.3	1.1
22	18.7	18.1	1.0	18.3	1.0
26	20.1	19.6	1.0	18.9	0.9
30	19.7	20.0	1.0	19.0	1.0
36	21.7	19.4	0.9	20.9	1.0
41	18.0	20.0	1.1	20.9	1.2
46	24.1	22.1	0.9	26.1	1.1
50	22.6	20.7	0.9	21.1	0.9
54	21.3	19.7	0.9	23.0	1.1
58	22.9	23.9	1.0	23.6	1.0
62	21.1	18.4	0.9	20.3	1.0
67	27.4	23.9	0.9	26.7	1.0
70	22.4	25.9	1.2	25.0	1.1
75	19.3	19.9	1.0	25.9	1.3
81	20.0	18.1	0.9	18.1	0.9
84	22.4	22.4	1.0	23.9	1.1
88	22.9	22.6	1.0	24.4	1.1
92	18.7	20.1	1.1	23.7	1.3
97	18.4	18.7	1.0	15.3	0.8
101	19.7	19.1	1.0	18.0	0.9
Mean	20.8	20.2	1.0	21.2	1.0
SD (c)	2.3	2.3	0.1	3.2	0.1
CV (d)	11.1	11.4	10.0	15.1	10.0

(a) Grams of feed consumed per animal per day.
(b) Ratio of feed consumed per day for the dosed group to that for the controls.
(c) Standard Deviation
(d) (Standard Deviation/Mean) x 100.

Table H2. Feed Consumption by Female Rats Receiving C. I. Disperse Yellow 3

Week	Control GRAMS FEED/ DAY (a)	Low GRAMS FEED/ DAY (a)	Low LOW/ CONTROL (b)	High GRAMS FEED/ DAY (a)	High HIGH/ CONTROL (b)
3	13.9	15.7	1.1	12.3	0.9
8	9.0	13.3	1.5	8.0	0.9
12	13.7	11.6	0.8	11.9	0.9
16	14.0	12.6	0.9	13.9	1.0
20	14.3	13.3	0.9	13.3	0.9
24	13.4	11.9	0.9	14.0	1.0
28	14.4	14.9	1.0	15.6	1.0
34	13.0	14.1	1.1	14.0	1.1
39	12.0	12.6	1.1	13.9	1.2
44	20.6	19.3	0.9	21.0	1.0
48	12.0	11.7	1.0	13.6	1.1
52	15.1	15.7	1.0	16.0	1.1
56	19.3	20.1	1.0	21.6	1.1
60	14.1	13.6	1.0	14.3	1.0
65	21.3	16.4	0.8	19.0	0.9
68	14.9	18.7	1.3	15.9	1.1
73	15.7	15.1	1.0	15.0	1.0
79	12.1	11.9	1.0	11.1	0.9
82	15.6	14.9	1.0	14.3	0.9
86	16.6	15.4	0.9	14.0	0.8
90	16.0	14.4	0.9	17.1	1.1
95	13.0	14.4	1.1	15.9	1.2
99	15.4	13.1	0.9	15.9	1.0
Mean	14.8	14.6	1.0	14.8	1.0
SD (c)	2.8	2.4	0.1	3.0	0.1
CV (d)	18.9	16.4	10.0	20.3	10.0

(a) Grams of feed consumed per animal per day.
(b) Ratio of feed consumed per day for the dosed group to that for the controls.
(c) Standard Deviation.
(d) (Standard Deviation/Mean) x 100.

Table H3. Feed Consumption by Male Mice Receiving C. I. Disperse Yellow 3

Week	Control GRAMS FEED/ DAY (a)	Low GRAMS FEED/ DAY (a)	Low LOW/ CONTROL (b)	High GRAMS FEED/ DAY (a)	High HIGH/ CONTROL (b)
1	7.7	7.7	1.0	8.1	1.1
5	7.7	7.7	1.0	8.1	1.1
10	3.7	3.4	1.0	3.4	0.9
14	5.9	3.9	0.7	3.9	0.7
19	8.0	8.4	1.1	8.7	1.1
23	8.1	8.4	1.1	8.7	1.1
27	8.3	8.7	1.1	8.9	1.1
33	8.1	7.9	1.0	8.7	1.1
37	8.1	8.3	1.1	8.4	1.1
42	8.1	8.3	1.0	8.0	1.0
46	8.4	8.3	1.0	8.6	1.1
50	8.3	8.6	1.1	9.0	1.1
54	8.1	8.4	1.1	9.0	1.2
58	7.9	8.1	1.1	8.9	1.2
62	8.6	8.6	1.1	9.3	1.2
66	8.3	8.4	1.1	9.3	1.1
71	8.6	9.0	1.1	10.0	1.2
76	8.3	8.6	1.1	8.9	1.1
79	10.1	10.0	1.0	11.9	1.2
84	8.4	10.9	1.3	8.9	1.1
88	9.0	9.4	1.1	10.6	1.2
92	9.1	9.6	1.2	10.1	1.1
96	8.6	9.9	1.2	9.9	1.2
100	11.0	12.4	1.2	12.6	1.2
Mean	8.2	8.5	1.0	8.8	1.1
SD (c)	1.3	1.8	0.1	1.9	0.1
CV (d)	15.9	21.2	10.0	21.6	9.1

(a) Grams of feed consumed per animal per day.
(b) Ratio of feed consumed per day for the dosed group to that for the controls.
(c) Standard Deviation.
(d) (Standard Deviation/Mean) x 100.

Table H4. Feed Consumption by Female Mice Receiving C. I. Disperse Yellow 3

Week	Control GRAMS FEED/ DAY (a)	Low GRAMS FEED/ DAY (a)	Low LOW/ CONTROL (b)	High GRAMS FEED/ DAY (a)	High HIGH/ CONTROL (b)
1	7.0	7.0	0.9	7.4	1.0
4	7.0	7.0	1.0	7.4	1.0
9	2.1	2.1	1.0	2.1	1.0
13	4.6	2.0	0.4	1.7	0.4
18	8.0	8.1	1.1	7.6	1.0
22	7.4	8.4	1.1	7.7	1.0
26	7.9	8.3	1.1	8.3	1.1
32	8.3	7.4	0.9	8.4	1.0
36	8.1	8.4	1.1	8.3	1.1
41	8.1	7.9	1.0	7.9	1.0
45	8.1	8.1	1.1	7.9	1.0
49	8.7	8.1	1.0	8.4	1.0
53	8.0	8.0	1.0	8.3	1.1
57	7.9	8.7	1.2	6.4	0.9
61	8.4	8.4	1.1	9.1	1.2
65	7.6	8.6	1.2	8.9	1.2
70	8.7	9.0	1.1	8.9	1.0
75	8.0	8.4	1.1	8.7	1.1
78	10.7	10.3	1.0	11.0	1.0
83	7.7	8.9	1.2	9.1	1.2
87	8.6	9.7	1.2	10.3	1.2
91	8.4	9.0	1.2	9.6	1.2
95	8.4	10.0	1.3	10.1	1.2
99	9.6	11.6	1.2	11.0	1.2
Mean	7.8	8.1	1.0	8.1	1.0
SD (c)	1.6	2.1	0.1	2.2	0.2
CV (d)	20.5	25.9	10.0	27.2	20.0

(a) Grams of feed consumed per animal per day.
(b) Ratio of feed consumed per day for the dosed group to that for the controls.
(c) Standard Deviation.
(d) (Standard Deviation/Mean) x 100.

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