NATIONAL TOXICOLOGY PROGRAM
Technical Report Series
No. 227

CARCINOGENESIS BIOASSAY OF GUM ARABIC

(CAS NO. 9000-01-5)

IN F344 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

GUM ARABIC

(CAS No. 9000-01-5)

in F344 RATS AND B6C3F$_1$ MICE

(FEED STUDY)

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

May 1982

NTP-80-81
NIH Publication No. 82-1783

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

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 ths 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

APPENDIXES

ABSTRACT

A carcinogenesis bioassay of gum arabic (81-86% pure), a widely used food stabilizer, was conducted by feeding diets containing 25,000 or 50,000 ppm of the test substance to 50 F344 rats and 50 B6C3F1 mice of each sex for 103 weeks. Groups of untreated rats and mice of each sex served as controls.

Throughout most of the study, mean body weights of dosed male and female mice and of dosed male rats were comparable with those of the controls; mean body weights of the dosed female rats were slightly lower than those of the controls. No other compound-related clinical signs or effects on survival were observed. Mean daily feed consumption by high-dose rats and mice of either sex was 85% to 94% that of the controls. The high dose (50,000 ppm) used in this bioassay is the maximum concentration (5%) currently used in feed studies.

Statistically significant ($P<0.05$) increasing trends were observed for the number of female mice with heptocellular carcinomas (1/49, 2/50, 6/50), and with total liver tumors (4/49, 2/50, 10/50). No statistically significant differences were obtained when comparing the control rates with those observed in the treated groups. These observations were not considered to be clearly associated with the dietary administration of gum arabic. Thus, no compound-related neoplastic or nonneoplastic lesions were found in rats or mice of either sex.

Under the conditions of this bioassay, gum arabic was not carcinogenic for F344 rats or B6C3F1 mice of either sex.

CONTRIBUTORS

The bioassay of gum arabic was conducted at EG&G Mason Research Institute, Worcester, Massachusetts, under a subcontract to Tracor Jitco, Inc., Rockville, Maryland, prime contractor for the NCI Carcinogenesis Testing Program. The 2-year study in mice was initiated in June 1977 and completed in June 1979, and the 2-year study in rats was begun in July 1977 and finished in July 1979.

The bioassay was conducted under the supervision of Drs. H. Lilja (1) and E. Massaro (1,2), principal investigators. Doses of the test chemical were selected by Drs. J. Robens (3,4) and C. Cueto (5). The program manager was Ms. R. Monson (1). Ms. A. Good (1) supervised the technicians in charge of animal care, and Ms. E. Zepp (1) supervised the preparation of the feed mixtures and collected samples of the diets for analysis. Ms. D. Bouthot (1) kept all daily records of the test. Dr. A. Russfield (1), pathologist, directed the necropsies and performed the histopathologic evaluations. The pathology report and selected slides were evaluated by the NCI Pathology Working Group as described in 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, which consisted of: G. Reznik (6), J. Ward (6), and P. Hildebrandt (3) who met on August 11, 1980.

Animal pathology tables and survival tables were compiled at EG&G Mason Research Institute, Rockville, Maryland (7). The statistical analyses were performed by Dr. J. R. Joiner (3) and Mr. J. Warner (3), using methods selected for the bioassay program by Dr. J. J. Gart (8). Chemicals used in this bioassay were analyzed at Midwest Research Institute (9).

This report was prepared at Tracor Jitco (3). Those responsible for the report at Tracor Jitco were Dr. C. Cueto (5), Director of the Bioassay Program; Dr. S. S. Olin, Associate Director; Dr. M. A. Stedham, pathologist; Dr. J. E. Tomaszewski, chemist; Dr. W. D. Theriault, reports manager; and Dr. A. C. Jacobs, bioscience writer.

The following scientists at NCI/NTP (6) were responsible for evaluating the bioassay experiment, interpreting the results, and reporting the findings: Dr. J. Fielding Douglas, Dr. Charles Grieshaber, Dr. James Huff (chemical manager), Dr. Joseph Haseman, Dr. Larry Hart, Dr. Ernest E. McConnell, Dr. John A. Moore, Dr. Sherman F. Stinson, Dr. R. Tennant, and Dr. Jerrold M. Ward.

---

(1) EG&G Mason Research Institute, 57 Union Street, Worcester, Massachusetts 06108.

(2) Now with Pennsylvania State University, 226 Fenske Laboratory, University Park, Pennsylvania 16802.

(3) Tracor Jitco, Inc., 1776 East Jefferson Street, Rockville, Maryland 20852.

(4) Now with Bureau of Veterinary Medicine, Food and Drug Administration, 5600 Fishers Lane, Rockville, Maryland 20857.

(5) Now with Clement Associates, 1010 Wisconsin Avenue, N.W., Washington, D.C. 20007.

(6) Bioassay Program, National Institutes of Health, Bethesda, Maryland 20205; National Toxicology Program, Research Triangle Park, Box 12233, North Carolina 27709.

(7) EG&G Mason Research Institute, 1530 East Jefferson Street, Rockville, Maryland 20852.

(8) Mathematical Statistics and Applied Mathematics Section, Biometry Branch, Field Studies and Statistics, Division of Cancer Cause and Prevention, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20205.

(9) Midwest Research Institute, 425 Volker Boulevard, Kansas City, Missouri 64110.

SUMMARY OF PEER REVIEW COMMENTS

On February 18, 1981 this carcinogenesis bioassay report on gum arabic underwent peer review and was approved by the National Toxicology Program Board of Scientific Counselors' Technical Report Review Subcommittee and associated Panel of Experts at an open meeting held in Room 31C, National Institutes of Health, Bethesda, Maryland. Members of the Subcommittee are Drs. Margaret Hitchcock (Chairperson), Curtis Harper, and Alice Whittemore. Members of the Panel are Drs. Normal Breslow, Joseph Highland, Frank Mirer, Sheldon Murphy (a principal reviewer), Svend Nielsen, Bernard Schwetz, Roy Shore, James Swenberg, and Gary Williams (a second principal reviewer). Drs. Breslow and Whittemore were unable to attend this meeting.

Dr. Murphy, a principal reviewer for the report on the carcinogenesis bioassay of gum arabic, agreed with the conclusion for a lack of carcinogenic action in rats and mice. He noted an increase in the number of hepatocellular adenomas or carcinomas in high-dose female mice which was not statistically significant by the pairwise comparison test, but was significant for a positive linear trend. These effects should not be regarded as compound related. There was a significantly decreased incidence of malignant lymphomas in high-dose male rats; yet this observation was diminished completely when the combined incidence of leukemias or lymphomas was evaluated.

As the second principal reviewer, Dr. Williams concurred with Dr. Murphy's review. Dr. Mirer said he would have liked to have seen more information included on what impurities and low molecular weight materials are found in gum arabic. Dr. Schwetz said that, as with the other food additives, the summary should clearly identify 50,000 ppm as a maximum concentration for feeding studies.

Dr. Murphy moved that the report on the bioassay of gum arabic be accepted and that statements be included to indicate 50,000 ppm as the maximum allowable concentration for feeding studies, and that the occurrence of an increase in hepatocellular neoplasms, carcinomas, or adenomas in high-dose female mice was not associated with gum arabic feeding. Dr. Williams seconded the motion, and the report was approved unanimously by the Peer Review Panel.

I. INTRODUCTION

Gum arabic (CAS No. 9000-01-5), also known as gum acacia, is the dried exudate from the branches of various species of Acacia. The major source of gum arabic used in the United States is Acacia Senegal from the Republic of Sudan (Furia, 1972). In 1971, 30 million pounds were imported into the United States (Life Sciences Research Office, 1973).

Structurally, gum arabic is a neutral or slightly acidic salt of a complex polysaccharide composed of galactose, arabinose, rhamnose, glucuronic acid, 4-O-methylglucuronic acid, calcium, magnesium, and potassium. The molecular weight has been reported to be 600,000 (Anderson and Dea, 1971). Gum arabic is distinguished from other gums by its high solubility in water; 50% solutions can be prepared, compared with maximum concentrations of 5% or less for most other gums (Furia, 1972).

Gum arabic is approved for use as a food additive by the U. S. Food and Drug Administration and is on the list of substances "generally recognized as safe" (CFR, 1974). Gum acacia is used as a flavor fixative in dry packaged food mixes, a foam stabilizer in soft drinks and beer, an adhesive for icings and toppings, and an emulsifier and stabilizer in confectionaries (Furia, 1972).

The following products may contain gum arabic at approximately the concentrations indicated: candy (28%); chewing gum (2.8%); imitation dairy products, frostings, fats and oils, and grain products (1%); sugar substitutes, fruit ices, nut products, and gelatin puddings (0.5% - 0.06%); baked goods, meat products, and alcoholic beverages (0.15% - 0.06%); instant coffee and tea (0.08% - 0.01%); nonalcoholic beverages (0.06% - 0.04%), processed fruit, frozen dairy products, and breakfast cereals (0.02% - 0.007%) (Life Sciences Research Office, 1973).

Gum arabic is used as an excipient for pills and tablets, a syrup for the suspension of insoluble drugs, an emulsion stabilizer for lotions and protective creams, and a pigment binder in face powders and rouges (Kirk and Othmer, 1966).

Gum arabic may be added to various glues, pastes, and binding cements, to paint and pigment formulations, and to inks. This gum is also used as a sizing and finishing agent in the textile industry, a corrosion inhibitor in storage batteries, and a binder for insecticides (Kirk and Othmer, 1966).

The oral LD_{50} of gum arabic in rats and mice is greater than 16 g/kg body weight (Bailey and Morgareidge, 1976).

Gum arabic was not mutagenic when tested without metabolic activation in several short-term mutagenicity assay systems, including Salmonella typhimurium TA 1530 and G-46 and Saccharomyces cerevisiae D-3. Gum arabic was not tested with metabolic activation (Green, 1977).

Gum arabic was tested by the NCI/NTP because of its widespread use as a food additive and therefore, the widespread exposure of the human population and because of the absence of carcinogenicity data.

II. MATERIALS AND METHODS

A. Chemical

Gum arabic (CAS No. 9000-01-5) was obtained in two batches from the Stein Hall Company, a division of Celanese Polymer Specialties Company (Louisville, KY). Lot No. 54-36431 was used for the subchronic studies and the first 3 months of the chronic studies. Lot No. 54-77890 was used for the rest of the chronic studies.

Purity and identity analyses were conducted at Midwest Research Institute (Appendixes E and F). Results of titration by periodate oxidation indicated that Lot No. 54-36431 was 80.8% pure and that Lot No. 54-77890 was 85.5% pure based on an assay for mannitol as compared with a glucose standard. Results of the Karl Fisher titrations indicated 12.3% water in Lot No. 5436431 and 9.0% water in Lot No. 54-77890. Four components in the hydrolysates of each batch of gum arabic were separated by thin-layer chromatography; three were identified as D-galactose, L-rhamnose, and L-arabinose. The fourth component may have been glucuronic acid. The infrared spectra of both batches were consistent with the literature spectra. The infrared spectra of both lots of gum arabic taken on a periodic basis at the bioassay laboratory showed no change over the course of the study.

B. Dietary Preparation

Each test diet was prepared by mixing the chemical and an aliquot of Wayne Lab Blox® meal with a mortar and pestle and then adding this premix to the rest of the feed and mixing in a Patterson-Kelly® twin-shell V-blender for 15 minutes. Test diets were sealed in labelled plastic bags and stored at 4°C for no longer than 14 days.

Due to some similar components in the test substance and feed, the quantitative method available could not measure concentration levels used in

the chronic study reproducibly within ±10%. Thus, formulated diets were not analyzed for concentrations of gum arabic during the study.

C. Animals

Four-week old F344 rats and B6C3F1 mice were obtained from the NCI Frederick Cancer Research Center (Frederick, MD) and observed for the presence of parasites and other diseases (8 days for rats and 9 days for mice). The animals were then randomly assigned to cages, and the cages were randomly assigned to control or dosed groups.

D. Animal Maintenance

Rats and mice were housed five per cage in suspended polycarbonate cages equipped with disposable nonwoven fiber filter sheets (Table 1). Cages and hardwood chip bedding were changed twice weekly, and cage racks were changed every 2 weeks. Water was supplied by an Edstrom automatic watering system, and Wayne Lab Blox® meal in stainless-steel, gang-style hoppers was available *ad libitum*.

The temperature in the animals rooms ranged from 19° to 32°C (average 23.8°C), and relative humidity was uncontrolled (average 43%). Incoming air was filtered through Tri-Dek 15/40 denier Dacron filters. Room air was changed 10 to 12 times per hour. Fluorescent lighting was provided 12 hours per day.

For the first 4 months of the chronic study, rats and mice were housed by species in separate rooms in which chronic feed studies were being conducted for locust bean gum (CAS No. 9000-40-2). For the remainder of the chronic study, rats and mice fed gum arabic were housed in the same room, and no other chemicals were on test in that room.

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

Item	Description	Source
Animal Feed	Wayne® Lab Blox Meal	Allied Mills (Chicago, IL)
Feed Hoppers	Stainless steel, gang style	Scientific Cages, (Bryan, TX)
Cages	Polycarbonate	Lab Products, Inc. (Garfield, NJ)
Filter Sheets	Disposable, non-woven fiber	Lab Products, Inc. (Rochelle, Park, NJ)
Bedding	Hardwood chips: Aspen bed®	American Excelsior (Baltimore, MD)
	Beta® chips	Agway Corp. (Syracuse, NY)
Cage and Hopper Washer	Adamation Cage Washer	Adamation (Newton, MA)
Rack Washer	Kleen-King Jet-Spray Washer	Britt-Tech Corp. (Britt, IA)

E. Repeated-Dose Studies

Repeated-dose feed studies were conducted using F344 rats and B6C3F1 mice to determine the concentrations of gum arabic to be used in the subchronic studies.

In the repeated dose study, groups of five males and five females of each species were fed diets containing 0, 6,300, 12,500, 25,000, 50,000, or 100,000 ppm gum arabic for 14 days. One male rat receiving 100,000 ppm died. All surviving animals were killed on day 15. No compound-related effects were observed.

F. Subchronic Studies

Subchronic studies were conducted to determine the concentrations to be used in the chronic studies. Diets containing 0, 6,300, 12,500, 25,000, 50,000, or 100,000 ppm were fed for 13 weeks to groups of 10 males and 10 females of each species. Mortality checks were made twice daily, and animals were weighed weekly (Tables 2 and 3). Feed consumption was measured during weeks 4, 8, and 12 (Table 4). At the end of the 91-day study, survivors were killed, necropsies were performed on all animals, and tissues (see Section H) were taken for histopathologic analysis.

Rats: No compound-related effects were observed, except for a reduction in feed consumption at the two highest doses in males and at all doses in females as compared with control animals.

Doses selected for the rats for the chronic study were 25,000 and 50,000 ppm gum arabic in feed, since the maximum concentration recommended for chronic feeding studies is 50,000 ppm (NCI, 1976).

Mice: No compound-related effects were observed. Doses selected for the mice for the chronic study were 25,000 and 50,000 ppm gum arabic in feed.

Table 2. Dosage, Survival, and Mean Body Weights of Rats Fed Diets Containing Gum Arabic for 13 Weeks

Dose (ppm)	Survival (a)	Mean Body Weights (grams)			Weight Change Relative to Controls (b) (Percent)
		Initial	Final	Change	
MALE					
0	10/10	85.3	350.8	+265.5	
6,300	10/10	85.1	337.4	+252.3	-5
12,500	10/10	85.5	336.1	+250.6	-6
25,000	10/10	85.9	340.4	+254.5	-4
50,000	10/10	85.4	337.5	+252.1	-5
100,000	10/10	85.6	332.4	+246.8	-7
FEMALE					
0	10/10	79.0	202.1	+123.1	
6,300	10/10	78.7	199.0	+120.3	-2
12,500	10/10	76.2	200.3	+124.1	+1
25,000	10/10	78.6	198.5	+119.9	-3
50,000	10/10	78.4	198.7	+120.3	-2
100,000	10/10	77.8	190.5	+112.7	-8

(a) Number surviving/number per group.

(b) Weight Change Relative to Controls =

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

Table 3. Dosage, Survival, and Mean Body Weights of Mice Fed Diets Containing Gum Arabic for 13 weeks

Dose (ppm)	Survival (a)	Mean Body Weights (grams)			Weight Change Relative to Controls (b) (Percent)
		Initial	Final	Change	
MALE					
0	10/10	20.9	34.2	+13.3	
6,300	10/10	20.9	34.3	+13.4	+1
12,500	10/10	20.9	33.1	+12.2	-8
25,000	10/10	20.9	34.2	+13.3	0
50,000	10/10	20.9	35.0	+14.1	+6
100,000	10/10	20.9	32.9	+12.0	-10
FEMALE					
0	10/10	17.9	27.6	+9.7	
6,300	10/10	18.2	26.7	+8.5	-8
12,500	10/10	18.1	25.5	+7.4	-23
25,000	10/10	17.9	25.7	+7.8	-20
50,000	10/10	17.9	28.2	+10.3	+6
100,000	10/10	17.8	25.7	+7.9	-19

(a) Number surviving/number per group.
(b) 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. Feed Consumption by Rats and Mice Fed Diets Containing 100,000 ppm Gum Arabic for 13 Weeks

Week No.	Control grams/kg (a)	Highest Dose (b) grams/kg (a)	Highest Dose/Control (c)
Male Rats			
4	718	696	1.0
8	467	503	1.1
12	507	430	0.8
Female Rats			
4	779	645	0.8
8	692	500	0.7
12	714	490	0.7
Male Mice			
4	1,956	1,650	0.8
8	1,650	1,394	0.8
12	1,245	1,253	1.0
Female Mice			
4	3,313	1,820	0.5
8	2,484	1,836	0.7
12	1,737	2,047	1.2

(a) Grams of feed consumed per kg of body weight
(b) Highest dose is 100,000 ppm
(c) Ratio of the grams/kg for the highest dose group to the grams/kg for the controls

G. Chronic Studies

The number of animals per group, the concentration of the test substance in the diet, and the duration of the chronic studies are shown in Table 5.

H. Clinical Examinations and Pathology

Mortality checks were made twice daily, and animals were weighed monthly. Animals that were moribund and those that survived to the end of the study were killed with carbon dioxide and necropsied.

Gross and microscopic examinations were performed on major tissues and major organs, and on all gross lesions from killed animals and from animals found dead unless precluded in whole or in part 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. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. The following were examined microscopically: skin, lungs and bronchi, trachea, bone and bone marrow, spleen, lymph nodes, heart, salivary gland, liver, pancreas, stomach, small intestine, large intestine, kidneys, urinary bladder, pituitary, adrenal, thyroid, parathyroid, mammary gland, prostate and seminal vesicles or uterus, testis or ovary, brain, thymus, larynx, and esophagus.

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).

Table 5. Experimental Design of Chronic Feeding Studies with Gum Arabic in Rats and Mice

Test Group	Initial No. of Animals	Gum Arabic (ppm)	Weeks on Study	
			Dosed	Not Dosed
Male Rats				
Control	50	0	0	105
Low-Dose	50	25,000	103	2
High-Dose	50	50,000	103	2
Female Rats				
Control	50	0	0	105
Low-Dose	50	25,000	103	2
High-Dose	50	50,000	103	2
Male Mice				
Control	50	0	0	105
Low-Dose	50	25,000	103	2
High-Dose	50	50,000	103	2
Female Mice				
Control	50	0	0	105
Low-Dose	50	25,000	103	2
High-Dose	50	50,000	103	2

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 method 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 prior to histologic sampling (e.g., skin or mammary tumors) 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 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 is 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. 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 an 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 animals 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% 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).

III. RESULTS - RATS

A. Body Weights and Clinical Signs (Rats)

Mean body weights of dosed and control male rats were comparable throughout the study. The mean body weights of dosed female rats were slightly lower than those of the controls (Figure 1 and Table 6). No compound-related clinical signs were observed. The mean daily feed consumption per animal was 94% (20.8/22.1) and 88% (19.4/22.1) for low- and high-dose male rats and 88% (16.4/18.7) and 87% (16.3/18.7) for low- and high-dose female rats, compared with controls (Appendix G).

B. Survival (Rats)

Estimates of the probabilities of survival of male and female rats fed diets containing gum arabic at the concentrations of this bioassay, together with those of the control group, are shown by the Kaplan and Meier curves in Figure 2. No significant differences in survival were found between any group of rats of either sex.

In male rats, 26/50 (52%) of the controls, 26/50 (52%) of the low-dose, and 29/50 (58%) of the high-dose group lived to the end of the study at 105 weeks. In female rats, 34/50 (68%) of the controls, 36/50 (72%) of the low-dose, and 32/50 (64%) of the high-dose group lived to the end of the study at 105 weeks.

C. Pathology (Rats)

Histopathologic findings on neoplasms in rats are summarized in Appendix A, Tables A1 and A2; findings on nonneoplastic lesions are summarized in Appendix C, Tables C1 and C2.

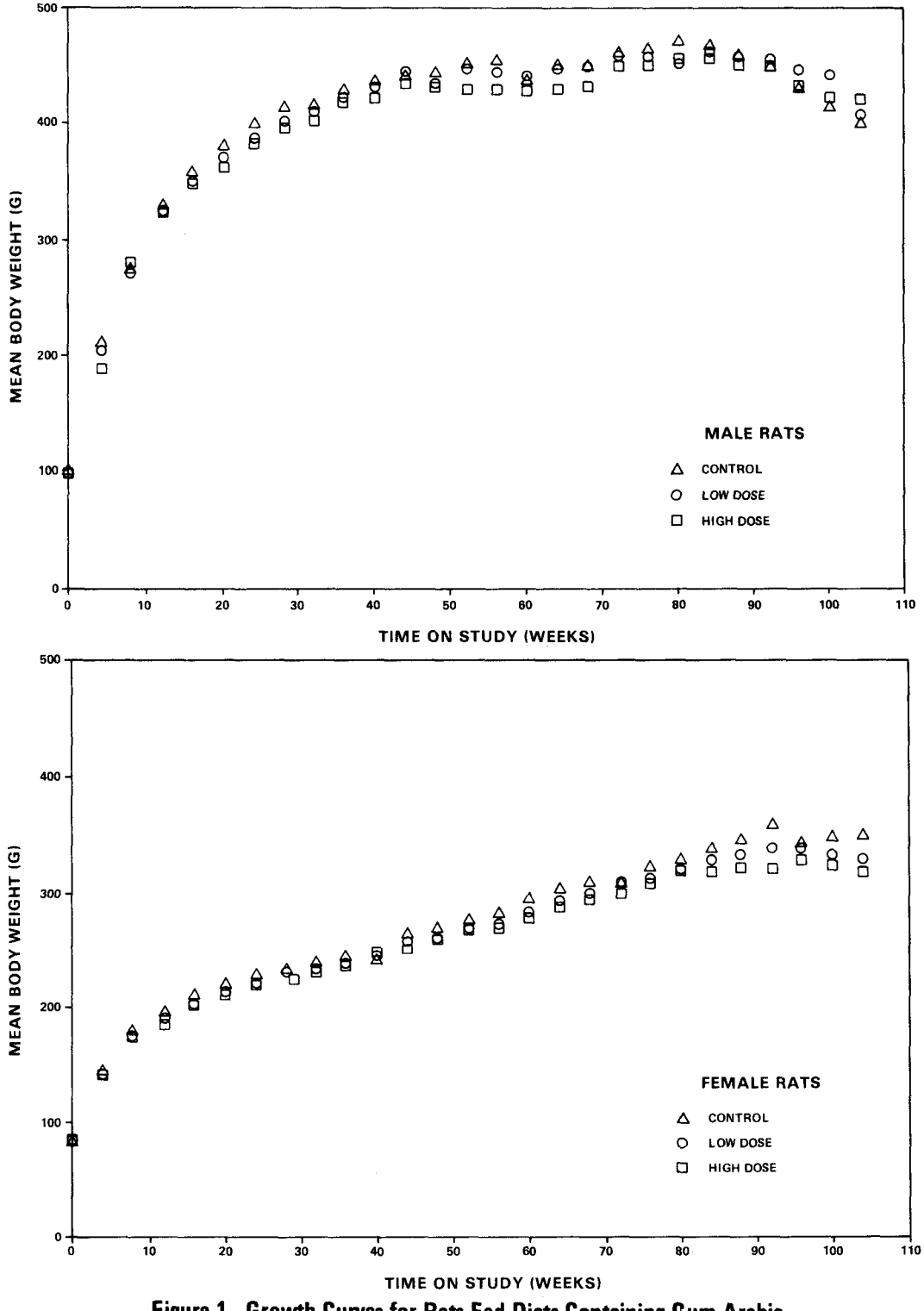

Figure 1. Growth Curves for Rats Fed Diets Containing Gum Arabic

Table 6. Mean Body Weight Change (Relative to Controls) of Rats Fed Diets Containing Gum Arabic

	Week No.	Mean Body Weight Change (grams)			Weight Change Relative to Controls (a) (Percent)	
		Control	Low Dose	High Dose	Low Dose	High Dose
Male	0	100(b)	97(b)	97(b)		
	4	113	107	90	-5	-20
	24	298	289	285	-3	-4
	44	342	348	337	+2	-1
	64	352	349	331	-1	-6
	84	367	365	359	-1	-2
	104	298	315	323	+6	+8
Female	0	84(b)	85(b)	85(b)		
	4	62	58	57	-6	-8
	24	144	136	134	-6	-7
	44	182	172	167	-5	-8
	64	221	209	202	-5	-9
	84	254	242	234	-5	-8
	104	267	236	237	-12	-11

(d) Weight Change Relative to Controls =

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

(b) Initial weight

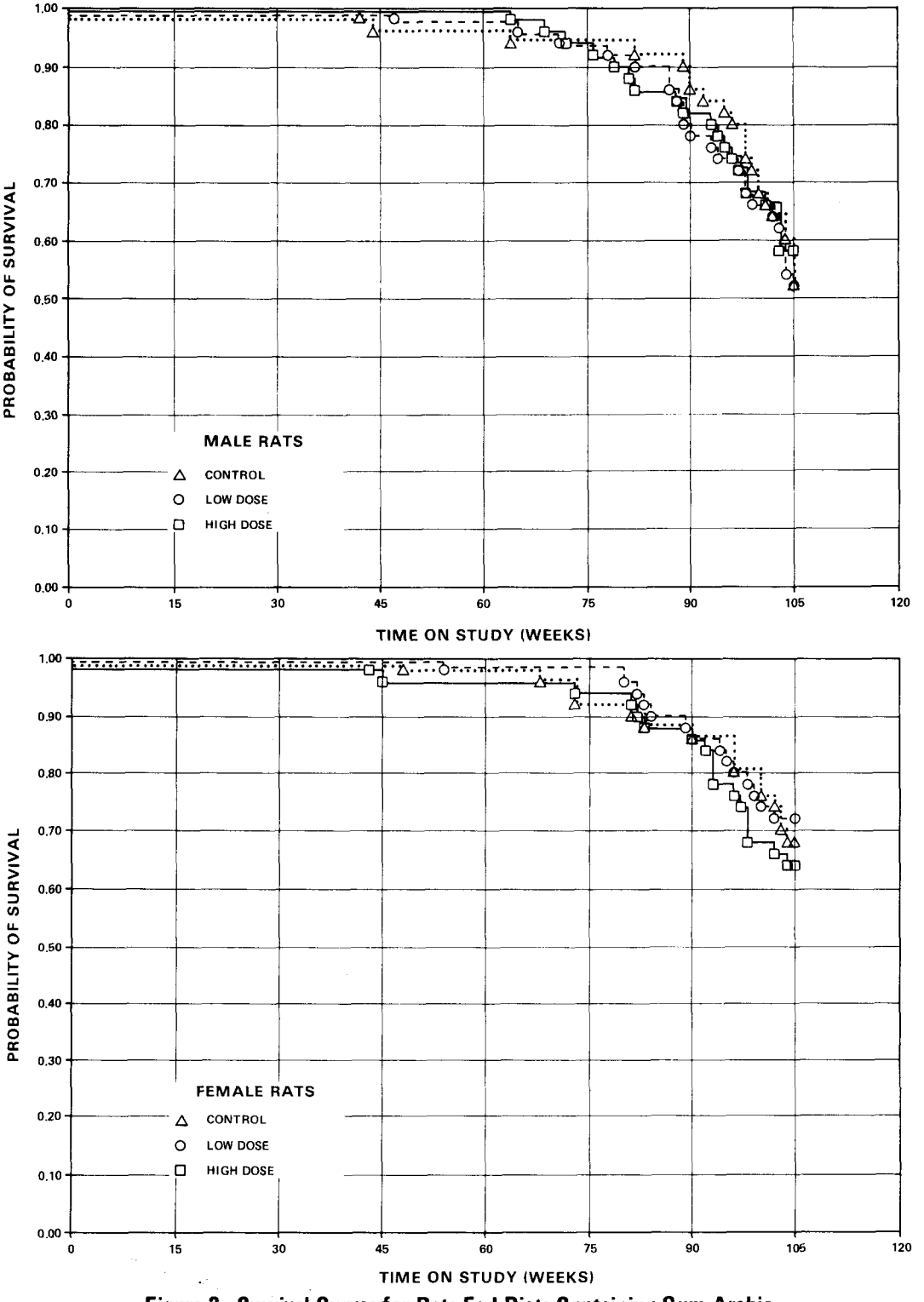

Figure 2. Survival Curves for Rats Fed Diets Containing Gum Arabic

The tumors encountered were those commonly found in aging rats of this strain. Rats in all groups exhibited a variety of nonneoplastic, inflammatory, and degenerative changes. None were considered to be associated with administration of the compound.

The results of the histopathologic examination indicated that gum arabic was not carcinogenic or toxic for F344 rats under the conditions of this bioassay.

D. Statistical Analyses of Results (Rats)

Tables 7 and 8 contain the statistical analyses of those primary tumors that met both of the following criteria: (1) at least two animals in one group had the tumor, and (2) the incidence in one or more groups was at least 5%.

Malignant lymphomas of the hematopoietic system were observed in male rats in a statistically significant negative relation (8/50, 16% in the controls; 4/50, 8% in the low-dose; and 1/50, 2% in the high-dose). The historical rate for malignant lymphomas in male control rats at EG&G Mason Laboratories is 28/834 (3.4%). The Cochran-Armitage test for linear trend was statistically significant in the negative direction (P=0.011), and the Fisher exact test between the high-dose group and the control group was significant (P=0.015). 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. In female rats, this tumor was not observed in statistically significant proportions, and no significant differences were observed in the incidence of animals with either leukemia or lymphoma.

Time adjusted analysis eliminating those animals dying before 52 weeks did not materially alter the results, since few early deaths occurred. Life table analyses, using the week of death with observed tumor, did not materially alter the results reported above.

Table 7. Analyses of the Incidence of Primary Tumors in Male Rats Fed Diets Containing Gum Arabic (a)

Topography: Morphology	Control	Low Dose	High Dose
Hematopoietic System:			
Leukemia (b)	10/50(20)	15/50(30)	14/50(28)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.500	1.400
Lower Limit		0.701	0.642
Upper Limit		3.359	3.177
Weeks to First Observed Tumor	90	88	69
Hematopoietic System:			
Malignant Lymphoma,			
Lymphocytic Leukemia (b)	2/50(4)	3/50(6)	1/50(2)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.500	0.500
Lower Limit		0.180	0.009
Upper Limit		17.329	9.290
Weeks to First Observed Tumor	98	104	98
Hematopoietic System:			
Malignant Lymphoma (b)	8/50(16)	4/50(8)	1/50(2)
P Values (c),(d)	P=0.011(N)	N.S.	P=0.015(N)
Relative Risk (Control) (e)		0.500	0.125
Lower Limit		0.117	0.003
Upper Limit		1.737	0.880
Weeks to First Observed Tumor	44	104	98

Table 7. Analyses of the Incidence of Primary Tumors in Male Rats Fed Diets Containing Gum Arabic (a)

(Continued)

Topography: Morphology	Control	Low Dose	High Dose
Hematopoietic System:			
Leukemia or Lymphoma (b)	18/50(36)	19/50(38)	16/50(32)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.056	0.889
Lower Limit		0.601	0.483
Upper Limit		1.860	1.624
Weeks to First Observed Tumor	44	88	69
Liver: Neoplastic Nodule (b)	3/49(6)	2/50(4)	4/50(8)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.653	1.307
Lower Limit		0.057	0.233
Upper Limit		5.457	8.508
Weeks to First Observed Tumor	100	105	101
Liver: Hepatocellular Carcinoma (b)	1/49(2)	3/50(6)	1/50(2)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		2.940	0.980
Lower Limit		0.246	0.013
Upper Limit		151.180	75.404
Weeks to First Observed Tumor	96	97	105

Table 7. Analyses of the Incidence of Primary Tumors in Male Rats Fed Diets Containing Gum Arabic (a)

(Continued)

Topography: Morphology	Control	Low Dose	High Dose
Liver: Neoplastic Nodule or Hepatocellular Carcinoma (b)	4/49(8)	5/50(10)	5/50(10)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.225	1.225
Lower Limit		0.280	0.280
Upper Limit		5.883	5.833
Weeks to First Observed Tumor	96	97	101
Pituitary: Adenoma, NOS (b)	9/45(20)	7/48(15)	10/44(23)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.729	1.136
Lower Limit		0.252	0.460
Upper Limit		2.013	2.850
Weeks to First Observed Tumor	101	71	82
Pituitary: Adenoma, NOS or Carcinoma, NOS (b)	10/45(22)	8/48(17)	11/44(25)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.750	1.125
Lower Limit		0.283	0.484
Upper Limit		1.919	2.646
Weeks to First Observed Tumor	101	71	82

Table 7. Analyses of the Incidence of Primary Tumors in Male Rats Fed Diets Containing Gum Arabic (a)

(Continued)

Topography: Morphology	Control	Low Dose	High Dose
Adrenal: Cortical Adenoma (b)	0/47(0)	1/50(2)	3/49(6)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		Infinite	Infinite
Lower Limit		0.050	0.578
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	99	105
Adrenal: Pheochromocytoma (b)	13/47(28)	11/50(22)	9/49(18)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.795	0.664
Lower Limit		0.360	0.278
Upper Limit		1.729	1.515
Weeks to First Observed Tumor	98	78	98
Adrenal: Pheochromocytoma or Pheochromocytoma, Malignant (b)	14/47(30)	11/50(22)	9/49(18)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.739	0.617
Lower Limit		0.339	0.262
Upper Limit		1.569	1.376
Weeks to First Observed Tumor	98	78	98

Table 7. Analyses of the Incidence of Primary Tumors in Male Rats Fed Diets Containing Gum Arabic (a)

(Continued)

Topography: Morphology	Control	Low Dose	High Dose
Thyroid: C-Cell Adenoma (b)	3/47(6)	3/45(7)	4/48(8)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.044	1.306
Lower Limit		0.147	0.234
Upper Limit		7.414	8.482
Weeks to First Observed Tumor	92	105	105
Thyroid: C-Cell Carcinoma (b)	0/47(0)	3/45(7)	1/48(2)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		Infinite	Infinite
Lower Limit		0.630	0.053
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	97	103
Thyroid: C-Cell Adenoma or Carcinoma (b)	3/47(6)	6/45(13)	5/48(10)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		2.089	1.632
Lower Limit		0.477	0.338
Upper Limit		12.215	9.987
Weeks to First Observed Tumor	92	97	103

Table 7. Analyses of the Incidence of Primary Tumors in Male Rats Fed Diets Containing Gum Arabic (a)

(Continued)

Topography: Morphology	Control	Low Dose	High Dose
Mammary Gland: Fibroadenoma (b)	1/50(2)	0/50(0)	3/50(6)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.000	3.000
Lower Limit		0.000	0.251
Upper Limit		18.658	154.270
Weeks to First Observed Tumor	105	--	103
Preputial Gland: Adenoma, NOS (b)	3/50(6)	1/50(2)	4/50(8)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.333	1.333
Lower Limit		0.006	0.238
Upper Limit		3.983	8.684
Weeks to First Observed Tumor	105	105	98
Preputial Gland: Adenoma, NOS or Carcinoma, NOS (b)	4/50(8)	2/50(4)	5/50(10)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.500	1.250
Lower Limit		0.047	0.286
Upper Limit		3.318	5.954
Weeks to First Observed Tumor	82	105	79

Table 7. Analyses of the Incidence of Primary Tumors in Male Rats Fed Diets Containing Gum Arabic (a)

(Continued)

Topography: Morphology	Control	Low Dose	High Dose
Testis: Interstitial-Cell Tumor (b)	36/44(82)	45/50(90)	42/49(86)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.100	1.048
Lower Limit		0.917	0.864
Upper Limit		1.285	1.263
Weeks to First Observed Tumor	82	65	79

(a) Dosed groups received doses of 25,000 or 50,000 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 untreated 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.

Table 8. Analyses of the Incidence of Primary Tumors in Female Rats Fed Diets Containing Gum Arabic (a)

Topography: Morphology	Control	Low Dose	High Dose
Hematopoietic System:			
Leukemia (b)	10/50(20)	7/50(14)	9/50(18)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.700	0.900
Lower Limit		0.246	0.354
Upper Limit		1.869	2.249
Weeks to First Observed Tumor	73	94	83
Hematopoietic System:			
Malignant Lymphoma or Leukemia (b)	11/50(22)	8/50(16)	9/50(18)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.727	0.818
Lower Limit		0.278	0.329
Upper Limit		1.811	1.976
Weeks to First Observed Tumor	73	80	83
Liver: Neoplastic Nodule (b)	3/49(6)	3/49(6)	2/50(4)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.000	0.653
Lower Limit		0.140	0.057
Upper Limit		7.126	5.457
Weeks to First Observed Tumor	105	100	97

Table 8. Analyses of the Incidence of Primary Tumors in Female Rats Fed Diets Containing Gum Arabic (a)

(Continued)

Topography: Morphology	Control	Low Dose	High Dose
Pituitary: Adenoma, (NOS) (b)	26/50(52)	25/44(57)	22/47(47)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.093	0.900
Lower Limit		0.725	0.576
Upper Limit		1.626	1.396
Weeks to First Observed Tumor	81	82	43
Pituitary: Adenoma, NOS or Carcinoma, NOS (b)	28/50(56)	26/44(59)	22/47(47)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.055	0.836
Lower Limit		0.718	0.544
Upper Limit		1.531	1.276
Weeks to First Observed Tumor	81	82	43
Adrenal: Pheochromocytoma (b)	2/48(4)	5/49(10)	1/50(2)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		2.449	0.480
Lower Limit		0.424	0.008
Upper Limit		24.745	8.916
Weeks to First Observed Tumor	105	94	105

Table 8. Analyses of the Incidence of Primary Tumors in Female Rats Fed Diets Containing Gum Arabic (a)

(Continued)

Topography: Morphology	Control	Low Dose	High Dose
Thyroid: C-Cell Adenoma (b)	3/49(6)	2/47(4)	2/49(4)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.695	0.667
Lower Limit		0.060	0.058
Upper Limit		5.793	5.565
Weeks to First Observed Tumor	81	105	105
Thyroid: C-Cell Adenoma or Carcinoma (b)	4/49(8)	3/47(6)	2/49(4)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.782	0.500
Lower Limit		0.120	0.047
Upper Limit		4.372	3.315
Weeks to First Observed Tumor	81	105	105
Mammary Gland: Fibroadenoma (b)	14/50(28)	12/50(24)	15/50(30)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.857	1.071
Lower Limit		0.404	0.542
Upper Limit		1.790	2.131
Weeks to First Observed Tumor	96	95	81

Table 8. Analyses of the Incidence of Primary Tumors in Female Rats Fed Diets Containing Gum Arabic (a)

(Continued)

Topography: Morphology	Control	Low Dose	High Dose
Clitoral Gland: Carcinoma, NOS (b)	1/50(2)	2/50(4)	3/50(6)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		2.000	3.000
Lower Limit		0.108	0.251
Upper Limit		115.621	154.270
Weeks to First Observed Tumor	105	98	105
Clitoral Gland: Adenoma, NOS or Carcinoma, NOS (b)	3/50(6)	3/50(6)	5/50(10)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.000	1.667
Lower Limit		0.140	0.344
Upper Limit		7.133	10.225
Weeks to First Observed Tumor	105	98	93
Uterus: Endometrial Stromal Polyp (b)	14/49(29)	10/49(20)	10/50(20)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.714	0.700
Lower Limit		0.315	0.309
Upper Limit		1.554	1.525
Weeks to First Observed Tumor	100	80	82

Table 8. Analyses of the Incidence of Primary Tumors in Female Rats Fed Diets Containing Gum Arabic (a)

(Continued)

(a) Dosed groups received doses of 25,000 or 50,000 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 untreated 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.

IV. RESULTS - MICE

A. Body Weights and Clinical Signs (Mice)

Throughout most of the study, mean body weights of dosed and control mice were comparable (Figure 3 and Table 9). No compound-related clinical signs were observed. Mean daily feed consumption was 86% (6.3/7.3) for low-dose male mice, 85% (6.2/7.3) for high-dose male mice, and 88% (7.8/8.9) for low- and high-dose female mice, compared with controls (Appendix G).

B. Survival (Mice)

Estimates of the probabilities of survival of male and female mice fed diets containing gum arabic at the concentrations of this bioassay, together with those of the control group, are shown by the Kaplan and Meier curves in Figure 4. No significant differences in survival were observed between any of the groups of either sex of mice.

In male mice, 38/50 (76%) of the controls, 41/50 (82%) of the low-dose, and 40/50 (80%) of the high-dose group lived to the end of the study at 105 weeks. In female mice, 36/50 (72%) of the controls, 40/50 (80%) of the low-dose, and 39/50 (78%) 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; findings on nonneoplastic lesions are summarized in Appendix D, Tables D1 and D2.

The most frequent neoplasms found in all groups were those of the hematopoietic system in both sexes and tumors of the lung and liver in males.

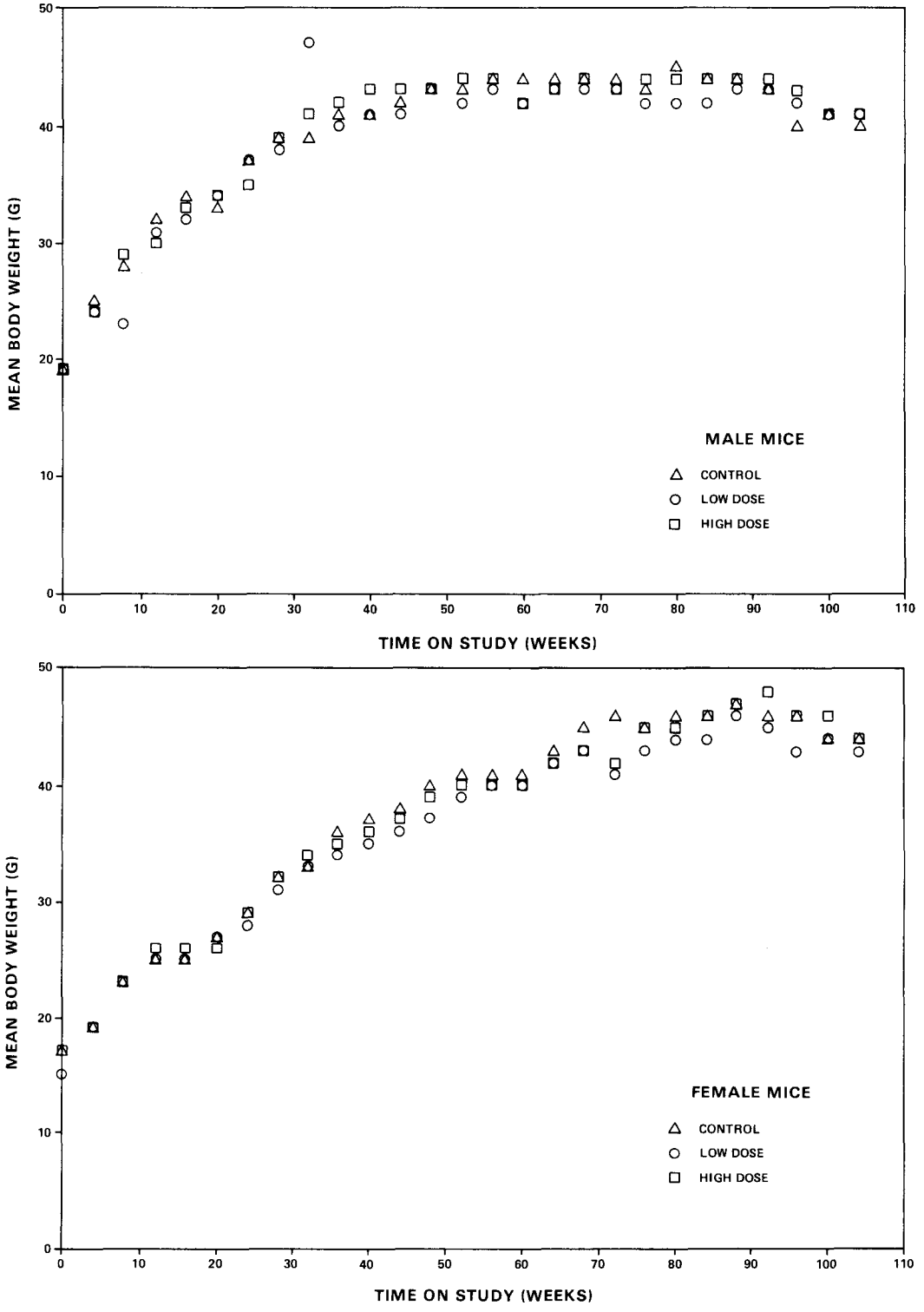

Figure 3. Growth Curves for Mice Fed Diets Containing Gum Arabic

Table 9. Mean Body Weight Change (Relative to Controls) of Mice Fed Diets Containing Gum Arabic

	Week No.	Mean Body Weight Change (grams) Control	Low Dose	High Dose	Weight Change Relative to Controls (a) (Percent) Low Dose	High Dose
	0	19(b)	19(b)	19(b)		
Male	4	6	5	5	-17	-17
Mice	24	18	18	16	0	-11
	44	23	22	24	-4	+4
	64	25	24	24	-4	-4
	84	25	23	25	-8	0
	104	21	22	22	+5	+5
	0	17(b)	15(b)	17(b)		
Female	4	2	4	2	+100	0
Mice	24	12	13	12	+8	0
	44	21	21	20	0	-5
	64	26	27	25	+4	-4
	84	29	29	29	0	0
	104	27	28	27	+4	0

(d) Weight Change Relative to Controls =

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

(b) Initial weight

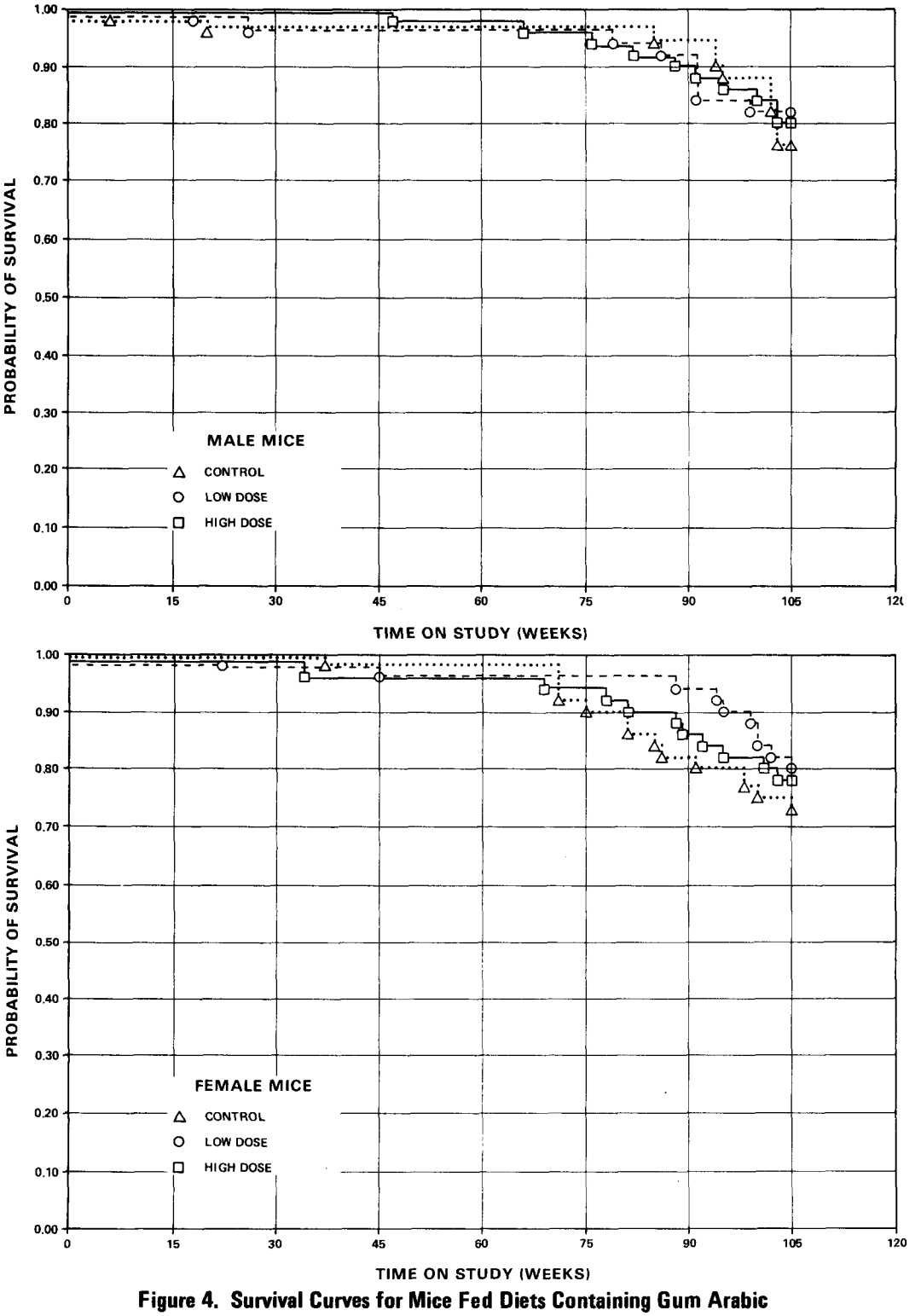

Figure 4. Survival Curves for Mice Fed Diets Containing Gum Arabic

Tumors of the liver were found in increased incidence in high-dose females (Table 10). Hepatocellular neoplasms were usually detected grossly as firm, nodular masses, often of a different color than normal liver. Microscopically, hepatocellular carcinomas were expansive masses of hepatocytes exhibiting loss of the normal architectural pattern. Both nuclei and cytoplasm varied from one region of the tumor to another. The tumor usually occupied more than half of the width of the liver. One tumor in a low-dose female had metastasized to the lung. Lesions classified as hepatocellular adenomas were smaller, better differentiated, and less pleomorphic.

A variety of nonneoplastic, inflammatory, and degenerative lesions occurred in all groups of mice. None could be related to administration of gum arabic.

The results of histopathologic examination showed, under the conditions of this bioassay, a marginal increase (although not statistically significant) in the number of hepatocellular adenomas, carcinomas, or neoplasms in high-dose female mice.

D. Statistical Analyses of Results (Mice)

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.

Hemangiomas of the circulatory system in male mice were observed in increased incidence in the high-dose group (0/49, 0% in the controls; 0/50, 0% in the low-dose; and 3/50, 6% in the high-dose group). The Cochran-Armitage test for linear trend was statistically significant in the positive direction (P=0.038). The Fisher exact tests were not significant. The historical records at this laboratory indicate an incidence of 15/852 (1.8%) male mice with hemangiomas. The incidence of mice with hemangiomas or hemangiosarcomas of the circulatory system was not significant in either sex. The incidence

Table 10. Incidences of Tumors of the Liver in Mice Fed Diets Containing Gum Arabic

	Males			Females		
	Control	Low Dose	High Dose	Control	Low Dose	High Dose
Liver						
(No. mice with tissues examined	49	49	50	49	50	50
Neoplasm, NOS	0	0	0	1	0	0
Hepatocellular adenoma	4	0	6	2	0	6
Hepatocellular carcinoma	13	11	10	1	2	6
No. of mice with either hepatocellular adenoma, carcinoma, or neoplasm, NOS	16(a)	11	15(a)	4	2	10(a)

(a) Some animals had both an hepatocellular adenoma and an hepatocellular carcinoma

of untreated male mice with hemangiomas or hemangiosarcomas of the circulatory system observed at this laboratory is 31/852 (3.6%). In female mice, this tumor was not observed in statistically significant proportions.

Hepatocellular adenomas, carcinomas, or neoplasms (unspecified) in female mice were observed in increased incidence in the high-dose group compared with the control group (4/49, 8% in the controls; 2/50, 4% in the low-dose; and 10/50, 20% in the high-dose group). The Cochran-Armitage test for linear trend was statistically significant in the positive direction (P=0.040), but the Fisher exact test between the high-dose group and the control group was not significant (P=0.080). By life table analysis, the dose-response trend was significant (P=0.044), but the high-dose effect was not. The historical records at this laboratory indicate the incidence of control female B6C3F1 mice with adenomas or carcinomas has been 77/859 (9.0%) with a range of 2% to 20.4%. Similarly, the trend in the incidence of hepatocellular carcinomas in female mice (1/49, 2/50, 6/50) was significant (P=0.031); comparing the control rate with the high-dose incidence was not significant (P=0.059). In male mice, this tumor was not observed in statistically significant proportions.

Neither time adjusted analysis, eliminating those animals dying before 52 weeks, nor life table analyses, using the week an animal died as the time point of examination for tumors, materially affected the previously reported results.

The conclusion based on statistical analysis is that there was no site at which an increase in tumor incidence could be clearly associated with the administration of the chemical.

Table 11. Analyses of the Incidence of Primary Tumors in Male Mice Fed Diets Containing Gum Arabic (a)

Topography: Morphology	Control	Low Dose	High Dose
Lung: Alveolar/Bronchiolar Adenoma (b)	9/49(18)	5/49(10)	4/50(8)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.556	0.436
Lower Limit		0.157	0.104
Upper Limit		1.705	1.448
Weeks to First Observed Tumor	105	105	105
Lung: Alveolar/Bronchiolar Carcinoma (b)	4/49(8)	6/49(12)	9/50(18)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.500	2.205
Lower Limit		0.380	0.664
Upper Limit		6.811	9.203
Weeks to First Observed Tumor	102	105	105
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma (b)	12/49(24)	10/49(20)	12/50(24)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.883	0.980
Lower Limit		0.357	0.448
Upper Limit		1.901	2.147
Weeks to First Observed Tumor	102	105	105

Table 11. Analyses of the Incidence of Primary Tumors in Male Mice Fed Diets Containing Gum Arabic (a)

(Continued)

Topography: Morphology	Control	Low Dose	High Dose
Hematopoietic System:			
Lymphoma, Malignant,			
Lymphocytic Type (b)	3/49(6)	4/50(8)	4/50(8)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.307	1.307
Lower Limit		0.233	0.233
Upper Limit		8.508	8.508
Weeks to First Observed Tumor	102	105	105
Hematopoietic System:			
Lymphoma, Malignant,			
Mixed Type (b)	4/49(8)	2/50(4)	1/50(2)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.490	0.245
Lower Limit		0.046	0.005
Upper Limit		3.251	2.362
Weeks to First Observed Tumor	105	105	105
Hematopoietic System:			
Malignant Lymphoma (b)	9/49(18)	6/50(12)	9/50(18)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.653	0.980
Lower Limit		0.207	0.377
Upper Limit		1.895	2.550
Weeks to First Observed Tumor	95	105	76

Table 11. Analyses of the Incidence of Primary Tumors in Male Mice Fed Diets Containing Gum Arabic (a)

(Continued)

Topography: Morphology	Control	Low Dose	High Dose
Hematopoietic System:			
Malignant Lymphoma or Leukemia (b)	9/49(18)	7/50(14)	9/50(18)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.762	0.980
Lower Limit		0.262	0.377
Upper Limit		2.115	2.550
Weeks to First Observed Tumor	95	105	76
Circulatory System:			
Hemangioma (b)	0/49(0)	0/50(0)	3/50(6)
P Values (c),(d)	P=0.038	N.S.	N.S.
Relative Risk (Control) (e)		--	Infinite
Lower Limit		--	0.590
Upper Limit		--	Infinite
Weeks to First Observed Tumor	--	--	105
Circulatory System:			
Hemangiosarcoma (b)	2/49(4)	3/50(6)	2/50(4)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.470	0.980
Lower Limit		0.176	0.074
Upper Limit		16.980	13.058
Weeks to First Observed Tumor	105	105	95

Table 11. Analyses of the Incidence of Primary Tumors in Male Mice Fed Diets Containing Gum Arabic (a)

(Continued)

Topography: Morphology	Control	Low Dose	High Dose
Circulatory System: Hemangioma or Hemangiosarcoma (b)	2/49(4)	3/50(6)	5/50(10)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.470	2.450
Lower Limit		0.176	0.424
Upper Limit		16.980	24.778
Weeks to First Observed Tumor	105	105	95
Liver: Hepatocellular Adenoma (b)	4/49(8)	0/49(0)	6/50(12)
P Values (c),(d)	N.S.	N.S.	N.S.
Departure from Linear Trend (f)	P=0.021		
Relative Risk (Control) (e)		0.000	1.470
Lower Limit		0.000	0.372
Upper Limit		1.078	6.681
Weeks to First Observed Tumor	94	--	82
Liver: Hepatocellular Carcinoma (b)	13/49(27)	11/49(22)	10/50(20)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.846	0.754
Lower Limit		0.375	0.328
Upper Limit		1.839	1.679
Weeks to First Observed Tumor	85	86	66

Table 11. Analyses of the Incidence of Primary Tumors in Male Mice Fed Diets Containing Gum Arabic (a)

(Continued)

Topography: Morphology	Control	Low Dose	High Dose
Liver: Hepatocellular Adenoma or Carcinoma (b)	16/49(33)	11/49(22)	15/50(30)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.688	0.919
Lower Limit		0.323	0.479
Upper Limit		1.408	1.755
Weeks to First Observed Tumor	85	86	66
Adrenal: Cortical Adenoma (b)	3/45(7)	1/48(2)	1/47(2)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.313	0.319
Lower Limit		0.006	0.006
Upper Limit		3.725	3.801
Weeks to First Observed Tumor	105	105	105
Pituitary: Adenoma, NOS (b)	1/40(3)	0/36(0)	2/38(5)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.000	2.105
Lower Limit		0.000	0.114
Upper Limit		20.582	120.862
Weeks to First Observed Tumor	105	--	105

Table 11. Analyses of the Incidence of Primary Tumors in Male Mice Fed Diets Containing Gum Arabic (a)

(Continued)

(a) Dosed groups received doses of 25,000 or 50,000 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 untreated 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 Mice Fed Diets Containing Gum Arabic (a)

Topography: Morphology	Control	Low Dose	High Dose
Lung: Alveolar/Bronchiolar Adenoma (b)	2/48(4)	5/49(10)	1/50(2)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		2.449	0.480
Lower Limit		0.424	0.008
Upper Limit		24.745	8.916
Weeks to First Observed Tumor	105	105	105
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma (b)	3/48(6)	7/49(14)	1/50(2)
P Values (c),(d)	N.S.	N.S.	N.S.
Departure from Linear Trend (f)	P=0.027		
Relative Risk (Control) (e)		2.286	0.320
Lower Limit		0.558	0.006
Upper Limit		13.001	3.822
Weeks to First Observed Tumor	98	95	105
Hematopoietic System: Lymphoma, Malignant, Lymphocytic Type (b)	8/49(16)	7/50(14)	5/50(10)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.858	0.613
Lower Limit		0.287	0.169
Upper Limit		2.497	1.969
Weeks to First Observed Tumor	105	105	105

Table 12. Analyses of the Incidence of Primary Tumors in Female Mice Fed Diets Containing Gum Arabic (a)

(Continued)

Topography: Morphology	Control	Low Dose	High Dose
Hematopoietic System:			
Lymphoma, Malignant,			
Histiocytic Type (b)	1/49(2)	1/50(2)	3/50(6)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.980	2.940
Lower Limit		0.013	0.246
Upper Limit		75.404	151.180
Weeks to First Observed Tumor	86	88	105
Hematopoietic System:			
Lymphoma, Malignant,			
Mixed Type (b)	8/49(16)	5/50(10)	11/50(22)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.613	1.348
Lower Limit		0.169	0.542
Upper Limit		1.969	3.529
Weeks to First Observed Tumor	105	100	105
Hematopoietic System			
Lymphoma, Malignant, NOS (b)	1/49(2)	3/50(6)	2/50(4)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		2.940	1.960
Lower Limit		0.246	0.106
Upper Limit		151.180	113.312
Weeks to First Observed Tumor	81	99	101

Table 12. Analyses of the Incidence of Primary Tumors in Female Mice Fed Diets Containing Gum Arabic (a)

(Continued)

Topography: Morphology	Control	Low Dose	High Dose
Hematopoietic System:			
Lymphoma (b)	18/49(37)	16/50(32)	21/50(42)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.871	1.143
Lower Limit		0.474	0.669
Upper Limit		1.590	1.972
Weeks to First Observed Tumor	81	88	101
Hematopoietic System:			
Lymphoma or Leukemia (b)	19/49(39)	16/50(32)	22/50(44)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.825	1.135
Lower Limit		0.454	0.679
Upper Limit		1.485	1.910
Weeks to First Observed Tumor	81	88	78
Liver: Hepatocellular Adenoma (b)	2/49(4)	0/50(0)	6/50(12)
P Values (c),(d)	N.S.	N.S.	N.S.
Departure from Linear Trend (f)	P=0.039		
Relative Risk (Control) (e)		0.000	2.940
Lower Limit		0.000	0.558
Upper Limit		3.313	28.662
Weeks to First Observed Tumor	98	--	105

Table 12. Analyses of the Incidence of Primary Tumors in Female Mice Fed Diets Containing Gum Arabic (a)

(Continued)

Topography: Morphology	Control	Low Dose	High Dose
Liver: Hepatocellular Carcinoma (b)	1/49(2)	2/50(4)	6/50(12)
P Values (c),(d)	P=0.031	N.S.	N.S.
Relative Risk (Control) (e)		1.960	5.880
Lower Limit		0.106	0.753
Upper Limit		113.312	264.516
Weeks to First Observed Tumor	105	105	105
Liver: Hepatocellular Adenoma, Carcinoma, or Neoplasm, NOS (b)	4/49(8)	2/50(4)	10/50(20)
P Values (c),(d)	P=0.040	N.S.	N.S.
Relative Risk (Control) (e)		0.490	2.450
Lower Limit		0.046	0.764
Upper Limit		3.251	10.037
Weeks to First Observed Tumor	75	105	105
Uterus: Endometrial Stromal Polyp (b)	1/48(2)	1/49(2)	4/49(8)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.980	3.918
Lower Limit		0.013	0.407
Upper Limit		75.342	188.792
Weeks to First Observed Tumor	105	105	105

Table 12. Analyses of the Incidence of Primary Tumors in Female Mice Fed Diets Containing Gum Arabic (a)

(Continued)

(a) Dosed groups received doses of 25,000 or 50,000 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 untreated 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

Fifty Fischer 344 rats and B6C3F1 mice of each sex were fed diets containing 25,000 ppm or 50,000 ppm of gum arabic for 103 weeks to determine the potential carcinogenicity in these laboratory animals. The doses chosen represent the suggested maximum levels (5%) of a chemical to be added to feed (NCI, 1976). When the prechronic studies do not give data that are useful for selecting more definitive dose levels, the NTP currently adheres (most often) to this recommendation.

Mean body weights of dosed mice of either sex and of dosed male rats were comparable with those of the controls throughout the study. The mean body weights of dosed female rats were slightly lower than those of the controls. No compound-related clinical signs or effects on survival were observed.

Feed consumption in rats was 87% to 94% that of controls (males: 94.1% for low-dose and 87.8% for high-dose; females: 87.7% for low-dose and 87.2% for high-dose); values for mice were 85% to 88% (males:86.3% for low-dose and 84.9% for high-dose; females: 87.6% for low- and high-dose).

A statistically significant (P=0.040) increasing trend was observed for the incidence of liver tumors in female mice (4/49, 8%, controls; 2/50, 4%, low-dose; 10/50, 20%, high-dose); the high-dose incidence, when compared with controls, was not statistically different. These results could be considered as a marginal effect; yet, when viewed from an historic vantage point and using life table analysis, a conclusion other than not carcinogenic would be misleading. The usual types of tumors seen in aging F344 rats and B6C3F1 mice were observed in this study, but the incidences of these tumors were not considered compound related.

Besides gum arabic, four other "gums" have been tested recently by the NCI/NTP bioassay program; each was added to the diet (2.5% and 5.0%) and fed for 104 weeks to F344 rats and B6C3F1 mice of each sex. Under these test conditions, all were considered not carcinogenic (agar, NTP 1982a; guar gum, NTP 1982b; locust bean gum, NTP 1982c; and tara gum, NTP 1982d).

VI. CONCLUSION

Under the conditions of this bioassay, gum arabic was not carcinogenic for F344 rats or B6C3F1 mice of either sex.

VII. BIBLIOGRAPHY

Anderson, D. and Dea, I., Recent advances in the chemistry of Acacia gums. J. Soc. Cosmet. Chem. 22:61-73, 1971.

Armitage, P., Statistical Methods in Medical Research, John Wiley & Sons, Inc., New York, 1971, pp. 362-365.

Bailey, D. and Morgareidge, K., Comparative acute oral toxicity of 12 food grade gums in the mouse, rat, hamster, and rabbit. Food and Drug Research Labs Papers No. 124, 1976.

Berenblum, I., ed., Carcinogenicity Testing: A Report of the Panel on Carcinogenicity of the Cancer Research Commission of UICC, Vol. 2, International Union Against Cancer, Geneva, 1969.

CFR, U.S. Code of Federal Regulations 21:121.101, 1974.

Cox, D. R., Analysis of Binary Data, Methuen & Co., Ltd., London, 1970, pp. 48-52.

Cox, D. R. Regression models and life tables. J. R. Stat. Soc. B34:187-220, 1972.

Furia, T., ed., CRC Handbook of Food Additives, CRC Press, Cleveland, Ohio, 1972, pp. 295-359.

Gart, J. J., The comparison of proportions: a review of significance tests, confidence limits and adjustments for stratification. Rev. Int. Stat. Inst. 39:148-169, 1971.

Green, S., Present and future uses of mutagenicity tests for assessment of the safety of food additives. J. Environ. Pathol. Toxicol. 1:49-54, 1977.

Kaplan, E. L. and Meier, P., Nonparametric estimation from incomplete observations. J. Amer. Stat. Assoc. 53:457-481, 1958.

Kirk, R. E. and Othmer, D. F., eds. Encyclopedia of Chemical Technology, 2nd ed. Vol. 10, Interscience Publishers, 1966, pp. 744-745.

Life Sciences Research Office, Evaluation of the health aspects of gum arabic as a food ingredient, Federation of American Societies for Experimental Biology, Bethesda, Maryland, March 1973.

Linhart, M. S., Cooper, J. A., Martin, R. L., Page, N. P., and Peters, J. A., Carcinogenesis bioassay data system. Comp. Biomed. Res. 7:230-248, 1974.

McNulty, J. A., J. Assoc. Off. Anal. Chem. 43(3):624-632, 1960.

Miller, R. G., Jr., Simultaneous Statistical Inference, McGraw-Hill Book Co., New York, 1966, pp. 6-10.

NCI, National Cancer Institute, Guidelines for Carcinogen Bioassay in Small Rodents. DHEW Publication No. (NIH) 76-801, Carcinogenesis Testing Program, National Cancer Institute, National Institutes of Health, Bethesda, Maryland, 1976.

NTP, National Toxicology Program, NCI/NTP Technical Report on the Carcinogenesis Bioassay of Agar, NTP TR 230, Department of Health and Human Services, Research Triangle Park, North Carolina, 1982a.

NTP, National Toxicology Program, NCI/NTP Technical Report on the Carcinogenesis Bioassay of Guar Gum, NTP TR 227, Department of Health and Human Services, Research Triangle Park, North Carolina, 1982b.

NTP, National Toxicology Program, NCI/NTP Technical Report on the Carcinogenesis Bioassay of Locust Bean Gum, NTP TR 221, Department of Health and Human Services, Research Triangle Park, North Carolina, 1982c.

NTP, National Toxicology Program, NCI/NTP Technical Report on the Carcinogenesis Bioassay of Tara Gum, NTP TR 224, Department of Health and Human Services, Research Triangle Park, North Carolina, 1982d.

Saffiotti, U., Montesano, R., Sellakumar, A. R., Cefis, F., and Kaufman, D. G., Respiratory tract carcinogenesis in hamsters induced by different numbers of administrations of benzo(a)pyrene and ferric oxide. Cancer Res. 32:1073-1081, 1972.

Tarone, R. E., Tests for trend in life table analysis. Biometrika 62:679-682, 1975.

USP, The Pharmacopeia of the United States of America, 18th ed., Mack Printing Company, Easton, Pennsylvania, 1970, pp. 378-379.

Varma, R., Varma, R. S., and Wardl, A. H., J. Chromatog. 77:22, 1973.

Ward, J. M., Goodman, D. G., Griesemer, R. A., Hardisty, J. F., Schueler, R. L., Squire, R. A., and Strandberg, J. D., Quality assurance for pathology in rodent carcinogenesis tests. J. Environ. Path. Toxicol. 2:371-378, 1978.

APPENDIX A

Summary of the Incidence of Neoplasms in Rats Fed Diets Containing Gum Arabic

TABLE A1.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS FED DIETS CONTAINING GUM ARABIC

	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)
PAPILLOMA, NOS			2 (4%)
SQUAMOUS CELL PAPILLOMA	1 (2%)	1 (2%)	
BASAL-CELL CARCINOMA		1 (2%)	
*SUBCUT TISSUE	(50)	(50)	(50)
SARCOMA, NOS		1 (2%)	
FIBROMA	2 (4%)	2 (4%)	1 (2%)
NEURILEMOMA	1 (2%)		
RESPIRATORY SYSTEM			
#LUNG	(50)	(50)	(50)
CARCINOMA, NOS, METASTATIC	1 (2%)		
ALVEOLAR/BRONCHIOLAR ADENOMA		1 (2%)	
PAPILLARY ADENOCARCINOMA, METAST			1 (2%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
MALIGNANT LYMPHOMA, NOS	6 (12%)	1 (2%)	
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	1 (2%)	3 (6%)	1 (2%)
LEUKEMIA,NOS	10.(20%)	15 (30%)	14 (28%)
LYMPHOCYTIC LEUKEMIA			1 (2%)
#LIVER	(49)	(50)	(50)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	1 (2%)		
CIRCULATORY SYSTEM			
NONE			

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

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(48)	(49)	(49)
SARCOMA, NOS		2 (4%)	1 (2%)
FIBROSARCOMA		1 (2%)	
#LIVER	(49)	(50)	(50)
NEOPLASTIC NODULE	3 (6%)	2 (4%)	4 (8%)
HEPATOCELLULAR CARCINOMA	1 (2%)	3 (6%)	1 (2%)
#STOMACH	(46)	(49)	(48)
SQUAMOUS CELL PAPILLOMA	1 (2%)		
LEIOMYOSARCOMA			1 (2%)
#CECUM	(42)	(48)	(46)
ADENOCARCINOMA, NOS			1 (2%)
URINARY SYSTEM			
#KIDNEY	(48)	(50)	(50)
SARCOMA, NOS		1 (2%)	
#KIDNEY/PELVIS	(48)	(50)	(50)
TRANSITIONAL-CELL PAPILLOMA	1 (2%)		
ENDOCRINE SYSTEM			
#PITUITARY	(45)	(48)	(44)
CARCINOMA,NOS	1 (2%)	1 (2%)	1 (2%)
ADENOMA, NOS	9 (20%)	7 (15%)	10 (23%)
CHROMOPHOBE ADENOMA	1 (2%)	2 (4%)	1 (2%)
#ADRENAL	(47)	(50)	(49)
CORTICAL ADENOMA		1 (2%)	3 (6%)
PHEOCHROMOCYTOMA	13 (28%)	11 (22%)	9 (18%)
PHEOCHROMOCYTOMA, MALIGNANT	1 (2%)		
#THYROID	(47)	(45)	(48)
C-CELL ADENOMA	3 (6%)	3 (7%)	4 (8%)
C-CELL CARCINOMA		3 (7%)	1 (2%)
#THYROID FOLLICLE	(47)	(45)	(48)
PAPILLARY ADENOCARCINOMA	1 (2%)		

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

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#PANCREATIC ISLETS	(41)	(48)	(48)
ISLET-CELL ADENOMA		1 (2%)	1 (2%)
ISLET-CELL CARCINOMA		1 (2%)	1 (2%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
ADENOCARCINOMA, NOS	1 (2%)		
PAPILLARY ADENOCARCINOMA			1 (2%)
FIBROADENOMA	1 (2%)		3 (6%)
*PREPUTIAL GLAND	(50)	(50)	(50)
CARCINOMA,NOS	1 (2%)	1 (2%)	1 (2%)
SQUAMOUS CELL CARCINOMA			1 (2%)
ADENOMA, NOS	3 (6%)	1 (2%)	4 (8%)
#PROSTATE	(40)	(45)	(44)
ADENOMA, NOS	1 (3%)	1 (2%)	1 (2%)
#TESTIS	(44)	(50)	(49)
INTERSTITIAL-CELL TUMOR	36 (82%)	45 (90%)	42 (86%)
NERVOUS SYSTEM			
#BRAIN	(49)	(49)	(50)
ASTROCYTOMA		1 (2%)	
SPECIAL SENSE ORGANS			
*HARDERIAN GLAND	(50)	(50)	(50)
ADENOMA, NOS	1 (2%)		
*ZYMBAL'S GLAND	(50)	(50)	(50)
CERUMINOUS CARCINOMA		1 (2%)	
MUSCULOSKELETAL SYSTEM			
*SKULL	(50)	(50)	(50)
OSTEOSARCOMA		1 (2%)	
*FEMUR	(50)	(50)	(50)
OSTEOSARCOMA		1 (2%)	

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

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
BODY CAVITIES			
*PERITONEUM	(50)	(50)	(50)
MESOTHELIOMA, NOS		1 (2%)	
*MESENTERY	(50)	(50)	(50)
LIPOMA	1 (2%)		
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
NEOPLASM, NOS			1 (2%)
SARCOMA, NOS, METASTATIC		1 (2%)	
OSTEOSARCOMA, METASTATIC		1 (2%)	
NECK			
SARCOMA, NOS, INVASIVE			1
SITE UNKNOWN			
CARCINOMA,NOS	1		
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	18	15	13
MORIBUND SACRIFICE	6	9	8
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	26	26	29
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*	48	49	48
TOTAL PRIMARY TUMORS	103	117	112
TOTAL ANIMALS WITH BENIGN TUMORS	42	47	45
TOTAL BENIGN TUMORS	75	76	81
TOTAL ANIMALS WITH MALIGNANT TUMORS	25	29	25
TOTAL MALIGNANT TUMORS	25	38	26
TOTAL ANIMALS WITH SECONDARY TUMORS#	1	2	2
TOTAL SECONDARY TUMORS	1	2	2
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	3	3	5
TOTAL UNCERTAIN TUMORS	3	3	5
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 GUM ARABIC

	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 PAPILLOMA		2 (4%)	
SQUAMOUS CELL CARCINOMA			1 (2%)
KERATOACANTHOMA			1 (2%)
*SUBCUT TISSUE	(50)	(50)	(50)
SARCOMA, NOS			1 (2%)
FIBROSARCOMA			1 (2%)
LIPOMA			1 (2%)
CARCINOSARCOMA			1 (2%)
NEURILEMOMA		1 (2%)	
RESPIRATORY SYSTEM			
#LUNG	(50)	(49)	(50)
ALVEOLAR/BRONCHIOLAR CARCINOMA		1 (2%)	1 (2%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
MALIGNANT LYMPHOMA, NOS	1 (2%)	1 (2%)	
LEUKEMIA,NOS	10 (20%)	7 (14%)	9 (18%)
CIRCULATORY SYSTEM			
#UTERUS	(49)	(49)	(50)
HEMANGIOMA		1 (2%)	
DIGESTIVE SYSTEM			
#LIVER	(49)	(49)	(50)
NEOPLASTIC NODULE	3 (6%)	3 (6%)	2 (4%)

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

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
URINARY SYSTEM			
NONE			
ENDOCRINE SYSTEM			
#PITUITARY	(50)	(44)	(47)
CARCINOMA,NOS	2 (4%)	1 (2%)	
ADENOMA, NOS	26 (52%)	25 (57%)	22 (47%)
CHROMOPHOBE ADENOMA	1 (2%)	1 (2%)	2 (4%)
#ADRENAL	(48)	(49)	(50)
CORTICAL ADENOMA		2 (4%)	1 (2%)
PHEOCHROMOCYTOMA	2 (4%)	5 (10%)	1 (2%)
#THYROID	(49)	(47)	(49)
FOLLICULAR-CELL CARCINOMA	1 (2%)		
C-CELL ADENOMA	3 (6%)	2 (4%)	2 (4%)
C-CELL CARCINOMA	1 (2%)	1 (2%)	
#THYROID FOLLICLE	(49)	(47)	(49)
PAPILLARY CYSTADENOMA, NOS	1 (2%)	1 (2%)	
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
FIBROADENOMA	14 (28%)	12 (24%)	15 (30%)
*CLITORAL GLAND	(50)	(50)	(50)
CARCINOMA,NOS	1 (2%)	2 (4%)	3 (6%)
ADENOMA, NOS	2 (4%)	1 (2%)	2 (4%)
#UTERUS	(49)	(49)	(50)
SARCOMA, NOS	1 (2%)		1 (2%)
ENDOMETRIAL STROMAL POLYP	14 (29%)	10 (20%)	10 (20%)
ENDOMETRIAL STROMAL SARCOMA	1 (2%)	1 (2%)	
#CERVIX UTERI	(49)	(49)	(50)
LEIOMYOSARCOMA	1 (2%)		
#OVARY	(48)	(48)	(50)
GRANULOSA-CELL TUMOR			2 (4%)

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

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
NERVOUS SYSTEM			
#BRAIN	(50)	(50)	(49)
GRANULAR-CELL TUMOR, NOS		1 (2%)	
GLIOMA, NOS			1 (2%)
ASTROCYTOMA			1 (2%)
SPECIAL SENSE ORGANS			
*HARDERIAN GLAND	(50)	(50)	(50)
ADENOMA, NOS		1 (2%)	
*ZYMBAL'S GLAND	(50)	(50)	(50)
CERUMINOUS CARCINOMA		1 (2%)	1 (2%)
MUSCULOSKELETAL SYSTEM			
*SKULL	(50)	(50)	(50)
OSTEOSARCOMA			1 (2%)
*VERTEBRA	(50)	(50)	(50)
CHORDOMA		1 (2%)	
BODY CAVITIES			
*ABDOMINAL WALL	(50)	(50)	(50)
LIPOMA		1 (2%)	
*MESENTERY	(50)	(50)	(50)
LIPOMA	1 (2%)		
ALL OTHER SYSTEMS			
NONE			

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

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	10	6	9
MORIBUND SACRIFICE	6	8	9
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	34	36	32
ANIMAL MISSING			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	45	46	47
TOTAL PRIMARY TUMORS	86	85	83
TOTAL ANIMALS WITH BENIGN TUMORS	37	42	38
TOTAL BENIGN TUMORS	64	65	57
TOTAL ANIMALS WITH MALIGNANT TUMORS	18	16	20
TOTAL MALIGNANT TUMORS	19	16	22
TOTAL ANIMALS WITH SECONDARY TUMORS#			
TOTAL SECONDARY TUMORS			
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	3	4	4
TOTAL UNCERTAIN TUMORS	3	4	4
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

@ INCLUDES AUTOLYZED ANIMALS

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

APPENDIX B

Summary of the Incidence of Neoplasms in Mice Fed Diets Containing Gum Arabic

TABLE B1.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE FED DIETS CONTAINING GUM ARABIC

	CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	49	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	49	50	50
INTEGUMENTARY SYSTEM			
*SUBCUT TISSUE	(49)	(50)	(50)
SARCOMA, NOS	1 (2%)		2 (4%)
FIBROMA		1 (2%)	
FIBROSARCOMA	2 (4%)	2 (4%)	
FIBROUS HISTIOCYTOMA			1 (2%)
RESPIRATORY SYSTEM			
#LUNG	(49)	(49)	(50)
HEPATOCELLULAR CARCINOMA, METAST	2 (4%)	1 (2%)	2 (4%)
ALVEOLAR/BRONCHIOLAR ADENOMA	9 (18%)	5 (10%)	4 (8%)
ALVEOLAR/BRONCHIOLAR CARCINOMA	4 (8%)	6 (12%)	9 (18%)
SARCOMA, NOS, METASTATIC			2 (4%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(49)	(50)	(50)
MALIGNANT LYMPHOMA, NOS	1 (2%)		2 (4%)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	2 (4%)	1 (2%)	2 (4%)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	1 (2%)		1 (2%)
MALIGNANT LYMPHOMA, MIXED TYPE	4 (8%)	1 (2%)	
LEUKEMIA,NOS		1 (2%)	
*HEMATOPOIETIC SYSTEM	(49)	(50)	(50)
NEOPLASM, NOS		1 (2%)	
#SPLEEN	(47)	(48)	(49)
NEOPLASM, NOS			1 (2%)
MALIGNANT LYMPHOMA, MIXED TYPE			1 (2%)
#MEDIASTINAL L.NODE	(42)	(45)	(48)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE		1 (2%)	

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

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#MESENTERIC L. NODE	(42)	(45)	(48)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE			1 (2%)
MALIGNANT LYMPHOMA, MIXED TYPE		1 (2%)	
#DUODENUM	(44)	(45)	(47)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	1 (2%)	1 (2%)	
#JEJUNUM	(44)	(45)	(47)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE		1 (2%)	1 (2%)
#KIDNEY	(48)	(50)	(50)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE			1 (2%)
CIRCULATORY SYSTEM			
*MULTIPLE ORGANS	(49)	(50)	(50)
HEMANGIOSARCOMA	1 (2%)		
#SPLEEN	(47)	(48)	(49)
HEMANGIOMA			1 (2%)
HEMANGIOSARCOMA		2 (4%)	2 (4%)
#MYOCARDIUM	(49)	(48)	(50)
SARCOMA, NOS			1 (2%)
#LIVER	(49)	(49)	(50)
HEMANGIOMA			2 (4%)
HEMANGIOSARCOMA	1 (2%)	1 (2%)	2 (4%)
DIGESTIVE SYSTEM			
#LIVER	(49)	(49)	(50)
HEPATOCELLULAR ADENOMA	4 (8%)		6 (12%)
HEPATOCELLULAR CARCINOMA	13 (27%)	11 (22%)	10 (20%)
LIPOMA			1 (2%)
#STOMACH	(46)	(47)	(48)
ADENOCARCINOMA, NOS			1 (2%)
#JEJUNUM	(44)	(45)	(47)
ADENOCARCINOMA, NOS		1 (2%)	
*RECTUM	(49)	(50)	(50)
ADENOCARCINOMA, NOS			1 (2%)

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

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
URINARY SYSTEM			
NONE			
ENDOCRINE SYSTEM			
#PITUITARY	(40)	(36)	(38)
ADENOMA, NOS	1 (3%)		2 (5%)
#ADRENAL	(45)	(48)	(47)
CORTICAL ADENOMA	3 (7%)	1 (2%)	1 (2%)
PHEOCHROMOCYTOMA	2 (4%)		
#THYROID	(45)	(46)	(49)
FOLLICULAR-CELL ADENOMA	1 (2%)	1 (2%)	
C-CELL TUMOR	1 (2%)		
C-CELL CARCINOMA			1 (2%)
#THYROID FOLLICLE	(45)	(46)	(49)
CYSTADENOMA, NOS	1 (2%)		
#PANCREATIC ISLETS	(45)	(46)	(49)
ISLET-CELL ADENOMA			1 (2%)
REPRODUCTIVE SYSTEM			
*PREPUTIAL GLAND	(49)	(50)	(50)
ADENOMA, NOS	1 (2%)		
#TESTIS	(47)	(49)	(49)
INTERSTITIAL-CELL TUMOR		1 (2%)	1 (2%)
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
*HARDERIAN GLAND	(49)	(50)	(50)
ADENOMA, NOS	2 (4%)		1 (2%)

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

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
MUSCULOSKELETAL SYSTEM			
*VERTEBRAL COLUMN	(49)	(50)	(50)
OSTEOSARCOMA			1 (2%)
BODY CAVITIES			
NONE			
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(49)	(50)	(50)
HEPATOCELLULAR CARCINOMA, METAST	1 (2%)		
TAIL			
SARCOMA, NOS			1
FIBROSARCOMA		1	
OSTEOSARCOMA	1		
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	12	8	9
MORIBUND SACRIFICE		1	1
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	38	41	40
ANIMAL MISSING			

@ INCLUDES AUTOLYZED ANIMALS

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

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	36	28	40
TOTAL PRIMARY TUMORS	57	41	62
TOTAL ANIMALS WITH BENIGN TUMORS	19	8	16
TOTAL BENIGN TUMORS	24	9	21
TOTAL ANIMALS WITH MALIGNANT TUMORS	27	23	34
TOTAL MALIGNANT TUMORS	32	31	40
TOTAL ANIMALS WITH SECONDARY TUMORS#	3	1	4
TOTAL SECONDARY TUMORS	3	1	4
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	1	1	1
TOTAL UNCERTAIN TUMORS	1	1	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 GUM ARABIC

	CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS MISSING	1		
ANIMALS NECROPSIED	49	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	49	50	50
INTEGUMENTARY SYSTEM			
*SUBCUT TISSUE	(49)	(50)	(50)
FIBROSARCOMA			1 (2%)
RESPIRATORY SYSTEM			
#LUNG	(48)	(49)	(50)
CARCINOMA, NOS, METASTATIC		1 (2%)	
HEPATOCELLULAR CARCINOMA, METAST		1 (2%)	
ALVEOLAR/BRONCHIOLAR ADENOMA	2 (4%)	5 (10%)	1 (2%)
ALVEOLAR/BRONCHIOLAR CARCINOMA	1 (2%)	2 (4%)	
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(49)	(50)	(50)
MALIGNANT LYMPHOMA, NOS	1 (2%)	2 (4%)	2 (4%)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	6 (12%)	5 (10%)	2 (4%)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	1 (2%)	1 (2%)	2 (4%)
MALIGNANT LYMPHOMA, MIXED TYPE	6 (12%)	3 (6%)	9 (18%)
LEUKEMIA,NOS	1 (2%)		1 (2%)
#SPLEEN	(47)	(48)	(49)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE			2 (4%)
MALIGNANT LYMPHOMA, MIXED TYPE		1 (2%)	
#LYMPH NODE	(45)	(46)	(41)
ALVEOLAR/BRONCHIOLAR CA, METASTA	1 (2%)		
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	1 (2%)		
#MANDIBULAR L. NODE	(45)	(46)	(41)
SARCOMA, NOS, METASTATIC		1 (2%)	
MALIG.LYMPHOMA, LYMPHOCYTIC 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
#MESENTERIC L. NODE	(45)	(46)	(41)
MALIGNANT LYMPHOMA, NOS		1 (2%)	
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	1 (2%)		1 (2%)
#LIVER	(49)	(50)	(50)
MALIGNANT LYMPHOMA, MIXED TYPE	1 (2%)		
#DUODENUM	(45)	(48)	(48)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE			1 (2%)
#JEJUNUM	(45)	(48)	(48)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE		1 (2%)	
MALIGNANT LYMPHOMA, MIXED TYPE			1 (2%)
#ILEUM	(45)	(48)	(48)
MALIGNANT LYMPHOMA, MIXED TYPE			1 (2%)
#KIDNEY	(49)	(48)	(48)
MALIGNANT LYMPHOMA, MIXED TYPE	1 (2%)	1 (2%)	
CIRCULATORY SYSTEM			
#SPLEEN	(47)	(48)	(49)
HEMANGIOMA	1 (2%)	1 (2%)	
#HEART	(49)	(47)	(50)
ALVEOLAR/BRONCHIOLAR CA, METASTA	1 (2%)		
*VULVA	(49)	(50)	(50)
HEMANGIOMA			1 (2%)
#OVARY	(40)	(40)	(43)
HEMANGIOMA			1 (2%)
DIGESTIVE SYSTEM			
#LIVER	(49)	(50)	(50)
NEOPLASM, NOS	1 (2%)		
HEPATOCELLULAR ADENOMA	2 (4%)		6 (12%)
HEPATOCELLULAR CARCINOMA	1 (2%)	2 (4%)	6 (12%)
#STOMACH	(45)	(46)	(49)
SQUAMOUS CELL PAPILLOMA	1 (2%)		

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

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
URINARY SYSTEM			
NONE			
ENDOCRINE SYSTEM			
#PITUITARY	(39)	(41)	(40)
CARCINOMA,NOS		1 (2%)	1 (3%)
ADENOMA, NOS	1 (3%)	1 (2%)	1 (3%)
ACIDOPHIL ADENOMA			1 (3%)
#ADRENAL	(48)	(44)	(43)
PHEOCHROMOCYTOMA		1 (2%)	1 (2%)
#THYROID	(45)	(45)	(43)
FOLLICULAR-CELL ADENOMA		1 (2%)	
FOLLICULAR-CELL CARCINOMA		1 (2%)	
C-CELL ADENOMA	1 (2%)		
#THYROID FOLLICLE	(45)	(45)	(43)
CYSTADENOMA, NOS			1 (2%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(49)	(50)	(50)
ACINAR-CELL CARCINOMA	1 (2%)	1 (2%)	
MIXED TUMOR, MALIGNANT	1 (2%)		
#UTERUS	(48)	(49)	(49)
SARCOMA, NOS	1 (2%)	1 (2%)	
ENDOMETRIAL STROMAL POLYP	1 (2%)	1 (2%)	4 (8%)
ENDOMETRIAL STROMAL SARCOMA		1 (2%)	
#OVARY	(40)	(40)	(43)
SERTOLI-CELL TUMOR			1 (2%)
TERATOMA, NOS	1 (3%)	1 (3%)	
NERVOUS SYSTEM			
#BRAIN	(49)	(49)	(50)
CARCINOMA, NOS, INVASIVE		1 (2%)	1 (2%)

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

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
SPECIAL SENSE ORGANS			
*HARDERIAN GLAND	(49)	(50)	(50)
CARCINOMA,NOS		1 (2%)	
ADENOMA, NOS	2 (4%)	1 (2%)	
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*PERITONEUM	(49)	(50)	(50)
MESOTHELIOMA, NOS		1 (2%)	
ALL OTHER SYSTEMS			
NONE			
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	13	10	10
MORIBUND SACRIFICE			1
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	36	40	39
ANIMAL MISSING	1		

@ 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*	30	33	31
TOTAL PRIMARY TUMORS	37	39	48
TOTAL ANIMALS WITH BENIGN TUMORS	10	11	16
TOTAL BENIGN TUMORS	11	11	18
TOTAL ANIMALS WITH MALIGNANT TUMORS	24	23	27
TOTAL MALIGNANT TUMORS	24	26	30
TOTAL ANIMALS WITH SECONDARY TUMORS#	1	4	1
TOTAL SECONDARY TUMORS	2	4	1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	2	2	
TOTAL UNCERTAIN TUMORS	2	2	
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

APPENDIX C

Summary of the Incidence of Nonneoplastic Lesions in Rats Fed Diets Containing Gum Arabic

TABLE C1.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS FED DIETS CONTAINING GUM ARABIC

	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)
EPIDERMAL INCLUSION CYST	1 (2%)		
EDEMA, NOS		1 (2%)	
HEMORRHAGIC CYST	1 (2%)		
ABSCESS, NOS			1 (2%)
RESPIRATORY SYSTEM			
*NOSE	(50)	(50)	(50)
SKIN TAG			1 (2%)
#LUNG	(50)	(50)	(50)
HEMORRHAGE	1 (2%)		1 (2%)
PNEUMONIA, CHRONIC MURINE		1 (2%)	
CALCIFICATION, FOCAL		1 (2%)	
HEMATOPOIETIC SYSTEM			
#BONE MARROW	(48)	(50)	(49)
FIBROSIS	1 (2%)		
FIBROSIS, FOCAL	1 (2%)	1 (2%)	
HYPOPLASIA, NOS		1 (2%)	
HYPERPLASIA, NOS	2 (4%)	7 (14%)	2 (4%)
#SPLEEN	(46)	(50)	(50)
HEMATOMA, NOS			1 (2%)
ABSCESS, NOS			1 (2%)
FIBROSIS, FOCAL	1 (2%)		
HEMOSIDEROSIS			1 (2%)
HEMATOPOIESIS	6 (13%)	1 (2%)	2 (4%)
#MEDIASTINAL L.NODE	(47)	(47)	(48)
CONGESTION, 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
#PANCREATIC L.NODE	(47)	(47)	(48)
CONGESTION, NOS			1 (2%)
#MESENTERIC L. NODE	(47)	(47)	(48)
CONGESTION, NOS			1 (2%)
CIRCULATORY SYSTEM			
#MESENTERIC L. NODE	(47)	(47)	(48)
LYMPHANGIECTASIS	3 (6%)	1 (2%)	1 (2%)
#HEART	(50)	(50)	(50)
THROMBOSIS, NOS		1 (2%)	1 (2%)
THROMBUS, MURAL	1 (2%)	2 (4%)	
#MYOCARDIUM	(50)	(50)	(50)
DEGENERATION, NOS	23 (46%)	27 (54%)	18 (36%)
#PANCREAS	(41)	(48)	(48)
PERIARTERITIS		1 (2%)	
#STOMACH	(46)	(49)	(48)
PERIARTERITIS		1 (2%)	
#TESTIS	(44)	(50)	(49)
PERIVASCULITIS		1 (2%)	
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(48)	(49)	(49)
INFLAMMATION, CHRONIC	2 (4%)		
#LIVER	(49)	(50)	(50)
CONGESTION, CHRONIC PASSIVE			1 (2%)
FIBROSIS		2 (4%)	
NECROSIS, FOCAL			1 (2%)
METAMORPHOSIS FATTY	7 (14%)	4 (8%)	4 (8%)
CYTOPLASMIC CHANGE, NOS	1 (2%)		
BASOPHILIC CYTO CHANGE	3 (6%)		1 (2%)
CLEAR-CELL CHANGE	2 (4%)	1 (2%)	
ANGIECTASIS		1 (2%)	
#LIVER/CENTRILOBULAR	(49)	(50)	(50)
NECROSIS, 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
#BILE DUCT	(49)	(50)	(50)
CYST, NOS			1 (2%)
HYPERPLASIA, NOS	33 (67%)	24 (48%)	26 (52%)
#STOMACH	(46)	(49)	(48)
MINERALIZATION			1 (2%)
INFLAMMATION, NOS		1 (2%)	
ULCER, NOS	5 (11%)	4 (8%)	2 (4%)
HYPERPLASIA, BASAL CELL	1 (2%)	3 (6%)	1 (2%)
ACANTHOSIS	1 (2%)	1 (2%)	
#GASTRIC MUCOSA	(46)	(49)	(48)
CALCIFICATION, NOS	4 (9%)		
#GASTRIC SUBMUCOSA	(46)	(49)	(48)
INFLAMMATION, NOS	1 (2%)		1 (2%)
INFLAMMATION, FOCAL		1 (2%)	
FIBROSIS			1 (2%)
#FORESTOMACH	(46)	(49)	(48)
HYPERPLASIA, BASAL CELL		1 (2%)	
#COLON	(42)	(48)	(46)
PARASITISM	5 (12%)	7 (15%)	7 (15%)
URINARY SYSTEM			
#KIDNEY	(48)	(50)	(50)
MINERALIZATION	2 (4%)		
HYDRONEPHROSIS			1 (2%)
CYST, NOS			1 (2%)
PARASITISM			1 (2%)
NEPHROPATHY	1 (2%)	1 (2%)	
NEPHROSIS, NOS	41 (85%)	43 (86%)	34 (68%)
NEPHROSIS, CHOLEMIC		3 (6%)	3 (6%)
CALCIFICATION, FOCAL	2 (4%)	1 (2%)	
#KIDNEY/PELVIS	(48)	(50)	(50)
HYPERPLASIA, EPITHELIAL	1 (2%)		
#URINARY BLADDER	(43)	(50)	(46)
CALCULUS, NOS	1 (2%)	1 (2%)	1 (2%)
HYPERPLASIA, EPITHELIAL		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
ENDOCRINE SYSTEM			
#PITUITARY	(45)	(48)	(44)
CYST, NOS		1 (2%)	
HEMORRHAGE			1 (2%)
HEMORRHAGIC CYST	2 (4%)		
HYPERPLASIA, FOCAL	2 (4%)	1 (2%)	3 (7%)
VASCULARIZATION		2 (4%)	
#ADRENAL	(47)	(50)	(49)
HEMORRHAGE			1 (2%)
#ADRENAL CORTEX	(47)	(50)	(49)
HYPERPLASIA, NODULAR	3 (6%)	3 (6%)	
#ADRENAL MEDULLA	(47)	(50)	(49)
HYPERPLASIA, FOCAL	1 (2%)	6 (12%)	1 (2%)
#THYROID	(47)	(45)	(48)
HYPERPLASIA, C-CELL	1 (2%)	2 (4%)	1 (2%)
#PANCREATIC ISLETS	(41)	(48)	(48)
HYPERPLASIA, NOS	1 (2%)		
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
GALACTOCELE		1 (2%)	1 (2%)
LACTATION		1 (2%)	
*PREPUTIAL GLAND	(50)	(50)	(50)
NECROSIS, NOS			1 (2%)
#PROSTATE	(40)	(45)	(44)
INFLAMMATION, ACUTE		1 (2%)	
INFLAMMATION ACUTE AND CHRONIC	4 (10%)	1 (2%)	
INFLAMMATION, CHRONIC	2 (5%)	1 (2%)	
ATROPHY, NOS			3 (7%)
HYPERPLASIA, NOS	2 (5%)		
HYPERPLASIA, EPITHELIAL		2 (4%)	2 (5%)
*SEMINAL VESICLE	(50)	(50)	(50)
INFLAMMATION ACUTE AND CHRONIC			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
ATROPHY, NOS			3 (6%)
HYPERPLASIA, NOS	1 (2%)		
#TESTIS	(44)	(50)	(49)
HEMORRHAGE		1 (2%)	
INFARCT, NOS		1 (2%)	
CALCIFICATION, NOS		1 (2%)	
ATROPHY, NOS	2 (5%)	1 (2%)	3 (6%)
SPERMATOGENIC ARREST			1 (2%)
#TESTIS/TUBULE	(44)	(50)	(49)
ATROPHY, FOCAL		1 (2%)	
NERVOUS SYSTEM			
#BRAIN	(49)	(49)	(50)
HYDROCEPHALUS, NOS			1 (2%)
HEMORRHAGE		2 (4%)	
SPECIAL SENSE ORGANS			
NONE			
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*PERITONEUM	(50)	(50)	(50)
ABSCESS, NOS			1 (2%)
*MESENTERY	(50)	(50)	(50)
NECROSIS, FAT	4 (8%)	2 (4%)	1 (2%)
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
CONGESTION, NOS		2 (4%)	
OMENTUM			
NECROSIS, FAT		1	

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
SPECIAL MORPHOLOGY SUMMARY			
AUTO/NECROPSY/HISTO PERF	2		

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 GUM ARABIC

	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)
ABSCESS, NOS	1 (2%)		
SKIN TAG	1 (2%)		
RESPIRATORY SYSTEM			
*NASAL TURBINATE	(50)	(50)	(50)
CONGESTION, NOS		1 (2%)	
#LUNG/BRONCHIOLE	(50)	(49)	(50)
METAPLASIA, NOS			1 (2%)
#LUNG	(50)	(49)	(50)
BRONCHOPNEUMONIA, NOS			1 (2%)
BRONCHOPNEUMONIA NECROTIZING			1 (2%)
PNEUMONIA, CHRONIC MURINE			1 (2%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
HEMATOPOIESIS			1 (2%)
#BONE MARROW	(49)	(49)	(47)
FIBROSIS, FOCAL			1 (2%)
HYPERPLASIA, NOS			2 (4%)
#SPLEEN	(48)	(49)	(50)
HEMOSIDEROSIS		2 (4%)	
HEMATOPOIESIS	3 (6%)	7 (14%)	2 (4%)
#LYMPH NODE	(50)	(46)	(48)
CONGESTION, 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
INFLAMMATION, NOS	1 (2%)		
#ABDOMINAL LYMPH NODE	(50)	(46)	(48)
CONGESTION, NOS			1 (2%)
#MESENTERIC L. NODE	(50)	(46)	(48)
CONGESTION, NOS			1 (2%)
#THYMUS	(37)	(43)	(40)
ATROPHY, NOS	1 (3%)		1 (3%)
CIRCULATORY SYSTEM			
#MESENTERIC L. NODE	(50)	(46)	(48)
LYMPHANGIECTASIS	1 (2%)	2 (4%)	1 (2%)
#HEART	(49)	(49)	(50)
THROMBUS, MURAL		1 (2%)	1 (2%)
#HEART/ATRIUM	(49)	(49)	(50)
THROMBUS, MURAL		1 (2%)	
#MYOCARDIUM	(49)	(49)	(50)
DEGENERATION, NOS	26 (53%)	16 (33%)	20 (40%)
#PANCREAS	(48)	(48)	(47)
PERIARTERITIS			1 (2%)
#UTERUS	(49)	(49)	(50)
THROMBOSIS, NOS	4 (8%)	1 (2%)	
DIGESTIVE SYSTEM			
#LIVER	(49)	(49)	(50)
CYST, NOS		1 (2%)	
CONGESTION, CHRONIC PASSIVE			1 (2%)
FIBROSIS			1 (2%)
NECROSIS, FOCAL		2 (4%)	
METAMORPHOSIS FATTY	7 (14%)	9 (18%)	6 (12%)
CYTOPLASMIC VACUOLIZATION	1 (2%)		
BASOPHILIC CYTO CHANGE	5 (10%)	1 (2%)	7 (14%)
CLEAR-CELL CHANGE		1 (2%)	
ANGIECTASIS			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
#LIVER/CENTRILOBULAR	(49)	(49)	(50)
NECROSIS, NOS		1 (2%)	
#BILE DUCT	(49)	(49)	(50)
HYPERPLASIA, NOS	15 (31%)	14 (29%)	15 (30%)
#PANCREAS	(48)	(48)	(47)
FIBROSIS, FOCAL	1 (2%)		
NECROSIS, FOCAL			1 (2%)
#ESOPHAGUS	(45)	(46)	(43)
HYPERKERATOSIS			1 (2%)
#STOMACH	(49)	(49)	(50)
ULCER, NOS	2 (4%)	2 (4%)	3 (6%)
INFLAMMATION, CHRONIC		1 (2%)	
INFLAMMATION, CHRONIC FOCAL			2 (4%)
HYPERPLASIA, BASAL CELL	1 (2%)	3 (6%)	1 (2%)
ACANTHOSIS	1 (2%)	1 (2%)	
#GASTRIC MUCOSA	(49)	(49)	(50)
ULCER, NOS		1 (2%)	
#GASTRIC SUBMUCOSA	(49)	(49)	(50)
INFLAMMATION, FOCAL			1 (2%)
#FORESTOMACH	(49)	(49)	(50)
HYPERPLASIA, BASAL CELL		1 (2%)	
#COLON	(46)	(47)	(50)
EPIDERMAL INCLUSION CYST	1 (2%)		
EDEMA, NOS		1 (2%)	
PARASITISM	4 (9%)	2 (4%)	1 (2%)
HYPERTROPHY, NOS		1 (2%)	
URINARY SYSTEM			
#KIDNEY	(49)	(49)	(50)
MINERALIZATION	1 (2%)		
CYST, NOS	1 (2%)		
INFLAMMATION, CHRONIC FOCAL			1 (2%)
NEPHROSIS, NOS	16 (33%)	13 (27%)	9 (18%)
NEPHROSIS, CHOLEMIC	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
NECROSIS, MEDULLARY		1 (2%)	
CALCIFICATION, FOCAL	15 (31%)	8 (16%)	12 (24%)
#KIDNEY/CAPSULE	(49)	(49)	(50)
ABSCESS, NOS		1 (2%)	
#RENAL PAPILLA	(49)	(49)	(50)
CALCIFICATION, NOS		1 (2%)	
#URINARY BLADDER	(50)	(49)	(48)
HEMATOMA, NOS		1 (2%)	
INFLAMMATION, CHRONIC		1 (2%)	
ENDOCRINE SYSTEM			
#PITUITARY	(50)	(44)	(47)
CYST, NOS	2 (4%)	2 (5%)	12 (26%)
MULTIPLE CYSTS	1 (2%)		1 (2%)
HEMORRHAGIC CYST		1 (2%)	1 (2%)
HYPERPLASIA, NOS	2 (4%)		1 (2%)
HYPERPLASIA, FOCAL	1 (2%)		
HYPERPLASIA, CHROMOPHOBE-CELL		1 (2%)	1 (2%)
VASCULARIZATION	3 (6%)	1 (2%)	1 (2%)
#ADRENAL	(48)	(49)	(50)
HEMORRHAGE			1 (2%)
CALCIFICATION, FOCAL	1 (2%)		
#ADRENAL CORTEX	(48)	(49)	(50)
HEMORRHAGE	1 (2%)		
HYPERPLASIA, NODULAR	2 (4%)	2 (4%)	6 (12%)
DYSPLASIA, NOS		1 (2%)	
#ADRENAL MEDULLA	(48)	(49)	(50)
HYPERPLASIA, NOS	1 (2%)		
HYPERPLASIA, FOCAL			1 (2%)
#THYROID	(49)	(47)	(49)
HYPERPLASIA, C-CELL	7 (14%)	4 (9%)	2 (4%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
GALACTOCELE	12 (24%)	7 (14%)	9 (18%)

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#UTERUS	(49)	(49)	(50)
HYDROMETRA	1 (2%)	1 (2%)	1 (2%)
HEMORRHAGIC CYST			1 (2%)
INFLAMMATION, NOS			1 (2%)
#UTERUS/ENDOMETRIUM	(49)	(49)	(50)
CYST, NOS			1 (2%)
DECIDUAL ALTERATION, NOS			1 (2%)
#OVARY	(48)	(48)	(50)
CYST, NOS	1 (2%)		
NERVOUS SYSTEM			
#BRAIN	(50)	(50)	(49)
HYDROCEPHALUS, NOS		3 (6%)	2 (4%)
HEMORRHAGE			2 (4%)
SPECIAL SENSE ORGANS			
*EXTERNAL EAR	(50)	(50)	(50)
HEMATOMA, NOS			1 (2%)
MUSCULOSKELETAL SYSTEM			
*SKULL	(50)	(50)	(50)
DEFORMITY, NOS	1 (2%)		
BODY CAVITIES			
*ABDOMINAL VISCERA	(50)	(50)	(50)
CONGESTION, ACUTE			1 (2%)
*PLEURA	(50)	(50)	(50)
EMPYEMA	1 (2%)		
*PERICARDIUM	(50)	(50)	(50)
INFLAMMATION, ACUTE	1 (2%)		
INFLAMMATION ACUTE AND CHRONIC			1 (2%)
*MESENTERY	(50)	(50)	(50)
NECROSIS, FAT	4 (8%)	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
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
HEMORRHAGE		1 (2%)	
GRANULOMA, FOREIGN BODY	1 (2%)		
CALCIFICATION, FOCAL			1 (2%)
OMENTUM			
NECROSIS, FAT			3
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED	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 Gum Arabic

TABLE D1.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE FED DIETS CONTAINING GUM ARABIC

	CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	49	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	49	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(49)	(50)	(50)
ULCER, NOS	1 (2%)		
INFLAMMATION, FOCAL		1 (2%)	
ABSCESS, NOS	1 (2%)		
INFLAMMATION, CHRONIC FOCAL	1 (2%)		
*SUBCUT TISSUE	(49)	(50)	(50)
HEMORRHAGE		1 (2%)	
INFLAMMATION, NOS		1 (2%)	
ABSCESS, NOS			1 (2%)
GRANULOMA, NOS			1 (2%)
INFECTION, FUNGAL			1 (2%)
RESPIRATORY SYSTEM			
NONE			
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(49)	(50)	(50)
HYPERPLASIA, LYMPHOID		1 (2%)	
HEMATOPOIESIS			1 (2%)
#SPLEEN	(47)	(48)	(49)
CONGESTION, NOS	1 (2%)	1 (2%)	2 (4%)
HEMORRHAGE			1 (2%)
NECROSIS, NOS			1 (2%)
INFARCT, NOS		1 (2%)	
HYPERPLASIA, LYMPHOID		1 (2%)	
HEMATOPOIESIS	2 (4%)	2 (4%)	2 (4%)
#MEDIASTINAL L.NODE	(42)	(45)	(48)
HYPERPLASIA, NOS			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
#MESENTERIC L. NODE	(42)	(45)	(48)
CONGESTION, NOS	18 (43%)	20 (44%)	24 (50%)
HEMORRHAGE		1 (2%)	
HEMORRHAGIC CYST	2 (5%)		
HYPERPLASIA, LYMPHOID			1 (2%)
#THYMUS	(15)	(21)	(23)
CYST, NOS			1 (4%)
CIRCULATORY SYSTEM			
*MULTIPLE ORGANS	(49)	(50)	(50)
PERIVASCULITIS	1 (2%)		
#LUNG	(49)	(49)	(50)
PERIVASCULITIS			1 (2%)
#AURICULAR APPENDAGE	(49)	(48)	(50)
THROMBOSIS, NOS			1 (2%)
#MYOCARDIUM	(49)	(48)	(50)
DEGENERATION, NOS	2 (4%)	1 (2%)	2 (4%)
*MESENTERY	(49)	(50)	(50)
PERIARTERITIS	1 (2%)		
DIGESTIVE SYSTEM			
#LIVER	(49)	(49)	(50)
NECROSIS, FOCAL			2 (4%)
METAMORPHOSIS FATTY			1 (2%)
BASOPHILIC CYTO CHANGE	1 (2%)		
ANGIECTASIS			1 (2%)
#PANCREAS	(45)	(46)	(49)
DILATATION/DUCTS		1 (2%)	
#STOMACH	(46)	(47)	(48)
INFLAMMATION ACUTE AND CHRONIC		1 (2%)	
INFLAMMATION, CHRONIC FOCAL	1 (2%)		
ATYPIA, NOS		1 (2%)	1 (2%)
HYPERPLASIA, BASAL CELL	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
HYPERKERATOSIS	4 (9%)	1 (2%)	
ACANTHOSIS	1 (2%)	1 (2%)	1 (2%)
#GASTRIC MUCOSA	(46)	(47)	(48)
ATYPIA, NOS			1 (2%)
METAPLASIA, SQUAMOUS	1 (2%)	1 (2%)	2 (4%)
#GASTRIC SUBMUCOSA	(46)	(47)	(48)
INFLAMMATION, ACUTE	1 (2%)		
#COLON	(41)	(44)	(43)
PARASITISM	1 (2%)		
URINARY SYSTEM			
#KIDNEY	(48)	(50)	(50)
HYDRONEPHROSIS		2 (4%)	
PYELONEPHRITIS, NOS		1 (2%)	
PYELONEPHRITIS, FOCAL			1 (2%)
ABSCESS, NOS			1 (2%)
NEPHROPATHY	1 (2%)	2 (4%)	2 (4%)
AMYLOID, NOS			2 (4%)
CALCIFICATION, FOCAL	1 (2%)		
ATROPHY, FOCAL	2 (4%)		
#URINARY BLADDER	(46)	(47)	(50)
CALCULUS, NOS	1 (2%)	3 (6%)	
INFLAMMATION ACUTE AND CHRONIC		1 (2%)	
HYPERPLASIA, EPITHELIAL		1 (2%)	
*URETHRA	(49)	(50)	(50)
CALCULUS, NOS	1 (2%)		
*PROSTATIC URETHRA	(49)	(50)	(50)
CALCULUS, NOS			1 (2%)
ENDOCRINE SYSTEM			
#PITUITARY	(40)	(36)	(38)
HYPERPLASIA, FOCAL		2 (6%)	
#ADRENAL CORTEX	(45)	(48)	(47)
HYPERPLASIA, NODULAR	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, FOCAL		1 (2%)	
#THYROID	(45)	(46)	(49)
HYPERPLASIA, FOLLICULAR-CELL		1 (2%)	
#PANCREATIC ISLETS	(45)	(46)	(49)
HYPERPLASIA, NOS	1 (2%)		
REPRODUCTIVE SYSTEM			
*PREPUTIAL GLAND	(49)	(50)	(50)
CYSTIC DUCTS	1 (2%)		
INFLAMMATION, NOS		1 (2%)	
ABSCESS, NOS		2 (4%)	1 (2%)
#PROSTATE	(44)	(43)	(44)
INFLAMMATION ACUTE AND CHRONIC		1 (2%)	
*SEMINAL VESICLE	(49)	(50)	(50)
INFLAMMATION ACUTE AND CHRONIC		1 (2%)	
#TESTIS	(47)	(49)	(49)
MINERALIZATION	1 (2%)		
ATROPHY, FOCAL	2 (4%)		1 (2%)
NERVOUS SYSTEM			
#SUBARACHNOID SPACE	(46)	(49)	(49)
HEMORRHAGE	1 (2%)		
#BRAIN	(46)	(49)	(49)
CALCIFICATION, FOCAL	17 (37%)	15 (31%)	15 (31%)
SPECIAL SENSE ORGANS			
NONE			
MUSCULOSKELETAL SYSTEM			
NONE			

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
BODY CAVITIES			
*ABDOMINAL CAVITY	(49)	(50)	(50)
NECROSIS, FAT	2 (4%)		
ALL OTHER SYSTEMS			
TAIL			
NECROSIS, HEMORRHAGIC			1
LEG			
ULCER, NOS		1	
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED	1	6	1
AUTO/NECROPSY/HISTO PERF	2		
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 GUM ARABIC

	CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS MISSING	1		
ANIMALS NECROPSIED	49	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	49	50	50
INTEGUMENTARY SYSTEM			
NONE			
RESPIRATORY SYSTEM			
#LUNG	(48)	(49)	(50)
EDEMA, NOS			1 (2%)
HEMORRHAGE			1 (2%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(49)	(50)	(50)
HYPERPLASIA, LYMPHOID			1 (2%)
HEMATOPOIESIS			1 (2%)
#BONE MARROW	(47)	(48)	(47)
FIBROSIS, FOCAL	33 (70%)	39 (81%)	30 (64%)
HYPERPLASIA, HEMATOPOIETIC	3 (6%)		
#SPLEEN	(47)	(48)	(49)
CONGESTION, NOS	1 (2%)		3 (6%)
HYPERPLASIA, LYMPHOID		1 (2%)	2 (4%)
HEMATOPOIESIS	2 (4%)	2 (4%)	2 (4%)
#LYMPH NODE	(45)	(46)	(41)
HEMATOPOIESIS	1 (2%)		
#MANDIBULAR L. NODE	(45)	(46)	(41)
CONGESTION, NOS	1 (2%)		
#MEDIASTINAL L.NODE	(45)	(46)	(41)
INFLAMMATION, CHRONIC	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
#ABDOMINAL LYMPH NODE	(45)	(46)	(41)
INFLAMMATION ACUTE AND CHRONIC		1 (2%)	
#MESENTERIC L. NODE	(45)	(46)	(41)
CONGESTION, NOS	3 (7%)	2 (4%)	1 (2%)
#LIVER	(49)	(50)	(50)
HEMATOPOIESIS			1 (2%)
CIRCULATORY SYSTEM			
*MULTIPLE ORGANS	(49)	(50)	(50)
PERIVASCULITIS			1 (2%)
*ABDOMINAL CAVITY	(49)	(50)	(50)
PERIVASCULITIS	1 (2%)		
#LUNG	(48)	(49)	(50)
EMBOLISM, NOS		1 (2%)	
PERIVASCULITIS			1 (2%)
#PANCREAS	(47)	(47)	(45)
LYMPHANGIECTASIS	1 (2%)		
#COLON	(42)	(45)	(44)
PERIARTERITIS		1 (2%)	
DIGESTIVE SYSTEM			
#LIVER	(49)	(50)	(50)
INFLAMMATION, ACUTE/CHRONIC		1 (2%)	
NECROSIS, FOCAL	1 (2%)	2 (4%)	1 (2%)
METAMORPHOSIS FATTY	1 (2%)	2 (4%)	3 (6%)
CYTOPLASMIC VACUOLIZATION	1 (2%)		
*GALLBLADDER	(49)	(50)	(50)
INFLAMMATION ACUTE AND CHRONIC	1 (2%)		
#PANCREAS	(47)	(47)	(45)
DILATATION/DUCTS	1 (2%)	3 (6%)	
INFLAMMATION, NOS	1 (2%)		
#PANCREATIC ACINUS	(47)	(47)	(45)
ATROPHY, NOS		3 (6%)	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
#STOMACH	(45)	(46)	(49)
ULCER, NOS	2 (4%)		
HYPERPLASIA, BASAL CELL		1 (2%)	3 (6%)
HYPERKERATOSIS	4 (9%)	5 (11%)	
ACANTHOSIS	2 (4%)	1 (2%)	5 (10%)
#GASTRIC MUCOSA	(45)	(46)	(49)
ABSCESS, NOS		1 (2%)	
ATYPIA, NOS		1 (2%)	3 (6%)
#GASTRIC SUBMUCOSA	(45)	(46)	(49)
INFLAMMATION, ACUTE FOCAL	1 (2%)		
INFLAMMATION, CHRONIC FOCAL	1 (2%)		
#FORESTOMACH	(45)	(46)	(49)
INFLAMMATION, CHRONIC		1 (2%)	
URINARY SYSTEM			
#KIDNEY	(49)	(48)	(48)
INFLAMMATION, CHRONIC FOCAL		1 (2%)	
NEPHROPATHY		1 (2%)	1 (2%)
GLOMERULOSCLEROSIS, NOS		1 (2%)	
CALCIFICATION, FOCAL	1 (2%)		
ATROPHY, FOCAL		1 (2%)	
ENDOCRINE SYSTEM			
#PITUITARY	(39)	(41)	(40)
HYPERPLASIA, NODULAR	1 (3%)		
HYPERPLASIA, NOS	1 (3%)		
HYPERPLASIA, FOCAL		1 (2%)	2 (5%)
HYPERPLASIA, CHROMOPHOBE-CELL	1 (3%)	1 (2%)	
ANGIECTASIS	1 (3%)		
#ADRENAL CORTEX	(48)	(44)	(43)
METAMORPHOSIS FATTY		1 (2%)	
#ADRENAL MEDULLA	(48)	(44)	(43)
HYPERPLASIA, FOCAL	2 (4%)		2 (5%)
#THYROID	(45)	(45)	(43)
HYPERPLASIA, C-CELL			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
REPRODUCTIVE SYSTEM			
#UTERUS	(48)	(49)	(49)
HYDROMETRA	6 (13%)	4 (8%)	5 (10%)
INFLAMMATION, NOS	1 (2%)		1 (2%)
PYOMETRA			2 (4%)
ABSCESS, NOS		1 (2%)	
ATROPHY, NOS	1 (2%)		
#UTERUS/ENDOMETRIUM	(48)	(49)	(49)
HYPERPLASIA, CYSTIC	24 (50%)	25 (51%)	25 (51%)
METAPLASIA, SQUAMOUS		1 (2%)	1 (2%)
#UTERUS/MYOMETRIUM	(48)	(49)	(49)
INFLAMMATION, ACUTE			1 (2%)
#TUBO OVARIAN COMBINE	(48)	(49)	(49)
ABSCESS, NOS		1 (2%)	1 (2%)
#OVARY	(40)	(40)	(43)
CYST, NOS	2 (5%)	3 (8%)	4 (9%)
MULTIPLE CYSTS		1 (3%)	
HEMORRHAGE	1 (3%)		
HEMORRHAGIC CYST		1 (3%)	
INFLAMMATION, NOS	1 (3%)		
ABSCESS, NOS			1 (2%)
NERVOUS SYSTEM			
#BRAIN/MENINGES	(49)	(49)	(50)
INFLAMMATION, NOS	1 (2%)		
#BRAIN	(49)	(49)	(50)
CALCIFICATION, FOCAL	13 (27%)	11 (22%)	16 (32%)
SPECIAL SENSE ORGANS			
NONE			
MUSCULOSKELETAL SYSTEM			
NONE			

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
BODY CAVITIES			
*ABDOMINAL CAVITY	(49)	(50)	(50)
HEMORRHAGE			1 (2%)
ABSCESS, NOS	1 (2%)		
NECROSIS, FAT	2 (4%)		
*PERITONEUM	(49)	(50)	(50)
HEMOPERITONEUM	1 (2%)		
INFLAMMATION, ACUTE	1 (2%)		
*PLEURA	(49)	(50)	(50)
INFLAMMATION, NOS			1 (2%)
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(49)	(50)	(50)
INFLAMMATION, ACUTE FOCAL	1 (2%)		
OMENTUM			
NECROSIS, FAT			1
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED	2		2
ANIMAL MISSING/NO NECROPSY	1		
AUTO/NECROPSY/HISTO PERF	1		1

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

APPENDIX E

Analysis of Gum Arabic (Lot No. 54-36431)
Midwest Research Institute

APPENDIX E

Analysis of Gum Arabic (Lot No. 54-36431)
Midwest Research Institute

A. MELTING POINT

Determined	Literature Values
m.p.: 210° to 300°C (visual, capilliary) Exotherm beginning at 274°C, decomp (Dupont 900 DTA)	No literature value found

B. THIN-LAYER CHROMATOGRAPHY OF ACID HYDROLYSIS PRODUCTS (Varma et al., 1973)

Plates Silica Gel 60 F-254

Ref. Standard: D-galactose
L-arabinose
L-rhamnose

Amount spotted: 42 μg

Visualization: 0.5% potassium permanganate in 1 N sodium hydroxide

System 1: n-Butanol:water: Acetic acid (50:20:10)	System 2: n-Butanol:pyridine: water (30:20:15)
R_f: 0.43 (rhamnose) 0.24 (arabinose) 0.18 (galactose) 0.04 (possibly glucuronic acid)	R_f: 0.63, 0.45, 0.36, 0.19
R_{st}: 2.5, 1.4, 1.1, 0.24 relative to D-galactose 1.7, 0.96, 0.72, 0.16 relative to L-arabinose 0.98, 0.55, 0.41, 0.09 relative to L-rhamnose	R_{st}: 1.7, 1.2, 0.97, 0.51 relative to D-galactose 1.4, 0.98, 0.78, 0.41 relative to L-arabinose 0.97, 0.69, 0.55, 0.29 relative to L-rhamnose

C. WATER ANALYSIS (Karl Fisher)

12.3 ± 0.8 (δ)%

D. CATION ANALYSIS

Na - $\leq 0.08\%$
K - $0.70 \pm 0.02\%$
Mg - $0.20 \pm 0.01\%$
Ca - $0.66 \pm 0.01\%$

E. TITRATION BY PERIODATE OXIDATION

Modification of USP Assay for Mannitol (USP, 1970): Samples were dissolved in 25 ml of water in 250 ml volumetric flasks and left at room temperature for 65 hours. The solutions were then boiled for 55 minutes on a hot plate. The flasks were cooled and diluted to volume with water. Aliquots (5 ml) were transferred to 125-ml Erlenmeyer flasks and 50.0 ml potassium periodate/sulfuric acid solution was added. The sample and the blank were heated on a steam bath for 25 hours. Potassium iodide was added and the samples were titrated with sodium thiosulfate.

Results: $80.8\% \pm 2.4$ (δ)% as compared with a glucose standard. (The assumption was made that 5 moles of periodate were needed for each monomer unit of the polysaccharide).

F. SPECTRAL DATA

(1) Infrared:

Instrument: Beckman IR-12 Cell: 1% in potassium bromide Results: See Figure 5.	Consistent with literature spectrum (McNulty, 1960)

(2) Ultraviolet/Visible:

Instrument: No absorbance between 200 and 350 nm (ultraviolet range) or between 350 and 800 nm (visible range) Concentration: 0.1 mg/ml Solvent: Water	No literature reference found

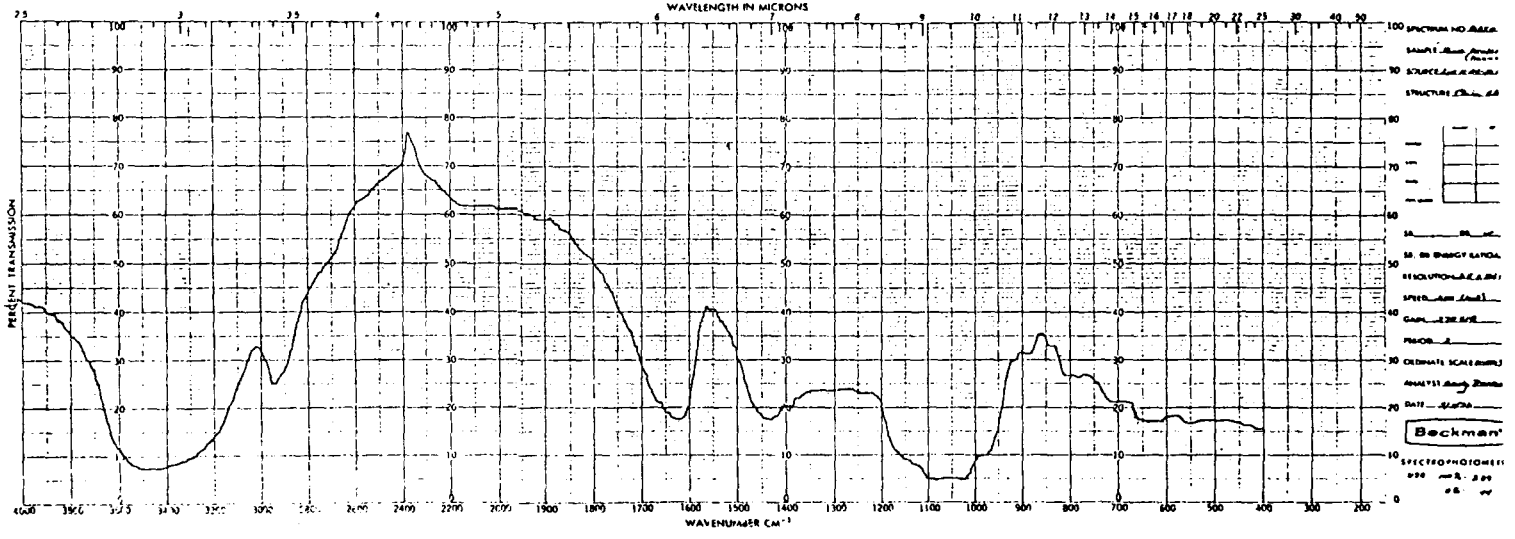

Figure 5. Infrared Absorption Spectrum of Gum Arabic (Lot No. 54-36431)

APPENDIX F

Analysis of Gum Arabic (Lot No. 54-77890)
Midwest Research Institute

APPENDIX F

Analysis of Gum Arabic (Lot No. 54-77890)
Midwest Research Institute

A. THIN-LAYER CHROMATOGRAPHY OF ACID HYDROLYSIS PRODUCTS (Varma et al., 1973)

Plates: Silica Gel 60 F-254

Ref. Standards: D-galactose
L-arabinose
L-rhamnose

Amount Spotted: 40μg, 2μg/μl in H_2O:methanol (25:75)

Visualization: 0.5% potassium permanganate in 1 N sodium hydroxide

System 1: n-Butanol:acetic acid:water (63:12:25)

System 2: n-Butanol:pyridine: water (46:31:23)

R_f: 0.04 (trace), 0.20, 0.26, 0.45 (trace)

R_f: 0.19, 0.49, 0.57, 0.71

R_{st}: 0.21, 1.02, 1.34
2.31 relative to D-galactose
0.16, 0.78, 1.02, 1.76
relative to L-arabinose
0.09, 0.45, 0.59, 1.02
relative to L-rhamnose

R_{st}: 0.39, 1.02, 1.18, 1.47
relative to D-galactose
0.34, 0.88, 1.02, 1.27
relative to L-arabinose
0.27, 0.71, 0.84, 1.03
relative to L-rhamnose

B. WATER ANALYSIS
(Karl Fisher)

9.0 $\pm$ 0.9 (δ)%

C. TITRATION BY PERIODATE OXIDATION (USP, 1970)

Modification of U.S.P. Assay for Mannitol

Samples were dissolved in 25 ml concentrated sulfuric acid and 150 ml water in 250-ml volumetric flasks and left at room temperature for 18 hours.

The solutions were then boiled on a hot plate until they started to discolor. All samples began to discolor before 15 minutes. The flasks were cooled and diluted to volume with water. Aliquots (5 ml) were transferred to 125-ml Erlenmeyer flasks and 50.0 ml potassium periodate/sulfuric acid solutions was added. Each sample and a blank were heated on a steam bath for 2.5 hours. Potassium iodide was added and the samples titrated with sodium thiosulfate. The assumption was made that each monomer unit reacted with 5 moles of periodate.

Results: 85.5 $\pm$ 2.1 (δ)%

D. SPECTRAL DATA

Infrared Spectrum

Instrument: Beckman IR-12

Consistent with literature spectrum (McNulty, 1960)

Cell: Thin film

Results: See Figure 6

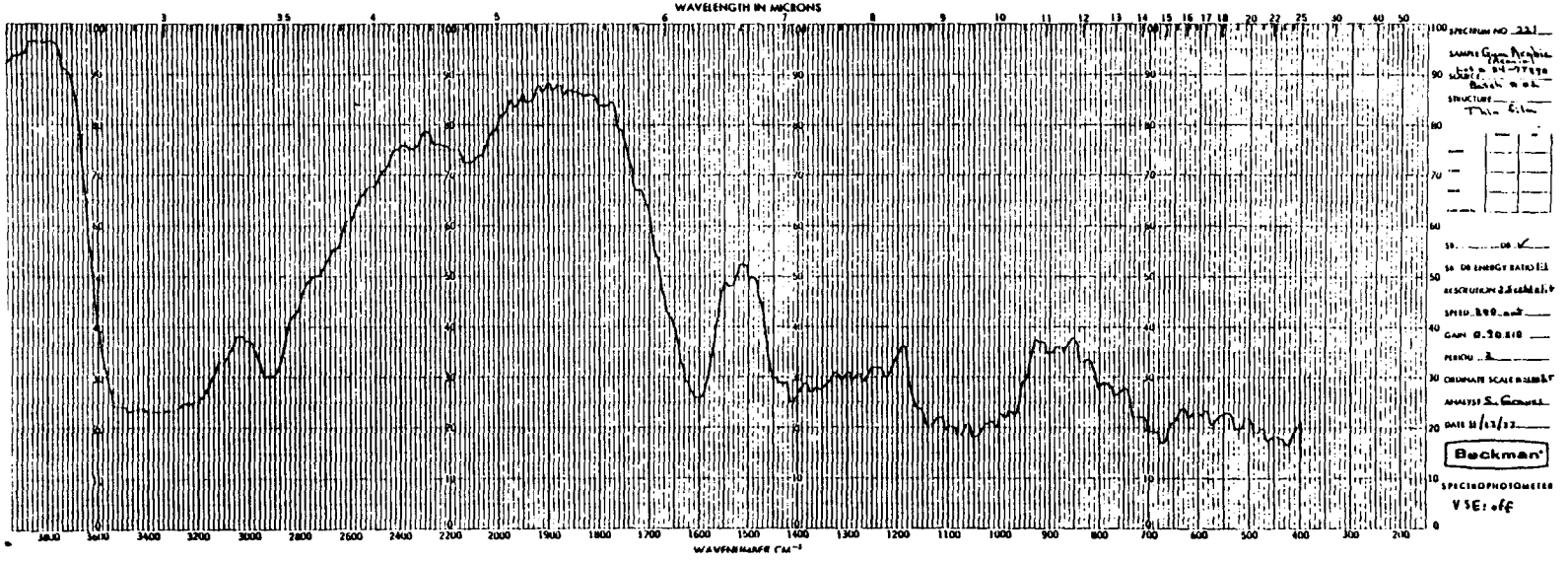

Figure 6. Infrared Absorption Spectrum of Gum Arabic (Lot No. 54-77890)

APPENDIX G

Feed Consumption by Rats and Mice Receiving Gum Arabic

Table G1. Feed Consumption by Male Rats Receiving Gum Arabic

Week	Control Grams Feed/ Day(a)	Low Grams Feed/ Day(a)	Low Low/ Control (b)	High Grams Feed/ Day(a)	High High/ Control (b)
4	24.3	24.6	1.0	9.4	0.4
8	24.0	22.3	0.9	22.4	0.9
12	20.4	19.1	0.9	16.4	0.8
16	18.7	17.3	0.9	17.1	0.9
20	20.6	19.0	0.9	18.3	0.9
24	21.7	20.0	0.9	20.6	0.9
28	16.0	19.3	1.2	19.3	1.2
32	21.7	16.4	0.8	19.1	0.9
36	23.0	22.4	1.0	20.9	0.9
40	22.0	20.0	0.9	20.7	0.9
44	23.7	21.1	0.9	21.4	0.9
48	23.1	21.1	0.9	21.6	0.9
52	22.1	21.4	1.0	20.9	0.9
56	25.4	22.6	0.9	21.7	0.9
60	24.9	22.9	0.9	22.6	0.9
64	27.1	23.9	0.9	22.7	0.8
68	23.9	23.1	1.0	22.1	0.9
72	17.9	19.6	1.1	20.3	1.1
76	23.0	20.7	0.9	21.9	1.0
80	21.0	20.6	1.0	19.0	0.9
84	21.1	18.1	0.9	17.9	0.8
88	20.0	18.3	0.9	13.0	0.7
92	21.7	20.9	1.0	18.6	0.9
96	27.0	24.0	0.9	20.0	0.7
100	18.9	20.9	1.1	17.6	0.9
Mean	22.1	20.8	1.0	19.4	0.9
SD (c)	2.7	2.1	0.1	3.1	0.1
CV (d)	12.2	10.1	10.0	16.0	11.1

(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 G2. Feed Consumption by Female Rats Receiving Gum Arabic

Week	Control Grams Feed/ Day(a)	Low Grams Feed/ Day(a)	Low Low/ Control (b)	High Grams Feed/ Day(a)	High High/ Control (b)
4	15.9	16.7	1.1	15.9	1.0
8	14.3	14.1	1.0	13.3	0.9
12	16.9	14.4	0.9	15.0	0.9
16	17.9	14.9	0.8	16.1	0.9
20	19.4	16.0	0.8	15.3	0.8
24	18.0	15.7	0.9	16.6	0.9
28	18.1	15.9	0.9	16.0	0.9
29	17.0	17.8	1.0	15.4	0.9
32	15.9	19.7	1.2	16.3	1.0
36	19.0	16.7	0.9	17.6	0.9
40	20.9	17.1	0.8	17.6	0.8
44	17.7	15.7	0.9	16.6	0.9
48	18.0	15.3	0.8	15.4	0.9
52	19.6	15.3	0.8	16.1	0.8
56	20.7	16.1	0.8	15.0	0.7
60	19.9	16.6	0.8	15.9	0.8
64	21.9	17.6	0.8	17.4	0.8
68	20.9	16.9	0.8	17.7	0.8
72	18.6	17.9	1.0	15.6	0.8
76	22.1	17.7	0.8	17.4	0.8
80	20.0	16.3	0.8	16.3	0.8
84	20.0	16.4	0.8	17.7	0.9
88	18.1	15.3	0.8	15.6	0.9
92	18.1	16.6	0.9	16.6	0.9
96	19.0	17.3	0.9	18.6	1.0
100	18.3	17.1	0.9	16.3	0.9
Mean	18.7	16.4	0.9	16.3	0.9
SD (c)	1.9	1.2	0.1	1.1	0.1
CV (d)	10.2	7.3	11.1	6.7	11.1

(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 G3. Feed Consumption by Male Mice Receiving Gum Arabic

Week	Control Grams Feed/ Day(a)	Low Grams Feed/ Day(a)	Low Low/ Control (b)	High Grams Feed/ Day(a)	High High/ Control (b)
4	8.4	7.3	0.9	7.4	0.9
8	8.0	6.9	0.9	7.6	1.0
12	7.1	6.6	0.9	7.3	1.0
16	7.7	7.0	0.9	6.7	0.9
20	5.1	4.4	0.9	4.1	0.8
24	7.1	6.6	0.9	6.6	0.9
28	7.6	6.1	0.8	6.6	0.9
32	7.3	6.0	0.8	6.0	0.8
36	7.6	9.0	1.2	5.9	0.8
40	6.9	6.6	1.0	6.0	0.9
44	6.0	5.9	1.0	6.0	1.0
48	5.9	5.6	0.9	5.9	1.0
52	5.4	8.1	1.5	5.9	1.1
56	6.1	5.6	0.9	5.1	0.8
60	7.1	5.9	0.8	5.7	0.8
64	7.6	6.9	0.9	7.3	1.0
68	6.9	5.9	0.9	5.7	0.8
72	9.1	6.0	0.7	6.6	0.7
76	8.9	6.3	0.7	6.0	0.7
80	9.3	6.3	0.7	6.4	0.7
84	6.1	6.1	1.0	6.3	1.0
88	6.4	5.6	0.9	5.6	0.9
92	6.9	5.6	0.8	6.6	1.0
96	7.4	5.9	0.8	6.4	0.9
100	9.6	6.9	0.7	6.6	0.7
Mean	7.3	6.3	0.9	6.2	0.9
SD (c)	1.2	0.9	0.2	0.7	0.1
CV (d)	16.4	14.3	22.2	11.3	11.1

(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 G4. Feed Consumption by Female Mice Receiving Gum Arabic

Week	Control Grams Feed/ Day(a)	Low Grams Feed/ Day(a)	Low Low/ Control (b)	High Grams Feed/ Day(a)	High High/ Control (b)
4	9.0	7.6	0.8	7.4	0.8
8	10.0	7.9	0.8	8.1	0.8
12	10.6	10.1	1.0	8.6	0.8
16	9.4	8.7	0.9	8.7	0.9
20	6.1	5.3	0.9	5.1	0.8
24	9.7	9.3	1.0	8.7	0.9
28	10.1	8.7	0.9	8.1	0.8
32	9.6	8.3	0.9	7.3	0.8
36	8.7	8.0	0.9	8.4	1.0
40	9.6	8.4	0.9	8.3	0.9
44	7.1	4.4	0.6	7.3	1.0
48	8.1	6.7	0.8	8.1	1.0
52	7.9	7.1	0.9	6.9	0.9
56	7.4	7.4	1.0	7.6	1.0
60	7.0	6.9	1.0	7.1	1.0
64	9.0	8.7	1.0	8.9	1.0
68	8.9	7.9	0.9	8.1	0.9
72	10.3	7.6	0.7	7.3	0.7
76	10.9	8.9	0.8	8.1	0.7
80	10.1	8.9	0.9	9.0	0.9
84	9.1	8.6	0.9	8.1	0.9
88	7.6	6.7	0.9	6.0	0.8
92	7.1	7.3	1.0	6.9	1.0
96	9.1	7.9	0.9	8.1	0.9
100	10.0	8.0	0.8	8.7	0.9
Mean	8.9	7.8	0.9	7.8	0.9
SD (c)	1.3	1.2	0.1	0.9	0.1
CV (d)	14.6	15.4	11.1	11.5	11.1

(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.

☆U.S. GOVERNMENT PRINTING OFFICE: 1982-361-132:566

NIH Publication No. 82-1783
MAY 1982