REQUEST NO. BTL-72-133
REPORT FILE

Industrial BIO-TEST Laboratories, Inc.
1810 FRONTAGE ROAD
NORTHBROOK, ILLINOIS 60062

REPORT TO

MONSANTO COMPANY

# 90-DAY SUBACUTE ORAL TOXICITY STUDY WITH MCS 1016 IN BEAGLE DOGS

JANUARY 31, 1972

IBT NO. C9887

BTL-72-133 ✓
1-31-72

*Industrial* **BIO-TEST** *Laboratories, Inc.*
1810 FRONTAGE ROAD
NORTHBROOK, ILLINOIS 60062

January 31, 1972

Mr. Elmer P. Wheeler
Monsanto Company
800 N. Lindbergh Boulevard
St. Louis, Missouri 63166

Dear Mr. Wheeler:

Re: IBT No. C9887 - 90-Day Subacute Oral Toxicity Study with MCS 1016 in Beagle Dogs

We are submitting herewith our laboratory report dated January 31, 1972, prepared in connection with the above study.

Very truly yours,

J. C. Calandra
President

JCC/kjl

REPORT TO

MONSANTO COMPANY

90-DAY SUBACUTE ORAL TOXICITY STUDY WITH
MCS 1016
IN BEAGLE DOGS

JANUARY 31, 1972

IBT NO. C9887

## I. Introduction

A sample identified as MCS 1016, Drum J, was received from Monsanto Company for the purpose of conducting a 90-day subacute oral toxicity study using purebred beagle dogs. The following report presents the results of the investigation.

II. Summary

Ninety-day oral administration of MCS 1016 to purebred beagle dogs at dietary levels of 1 ppm (Days 1-28) to 30 ppm (Days 29-90), 10 ppm (Days 1-28) to 300 ppm (Days 29-90) and 100 ppm revealed no significant abnormalities in the following parameters:

| | |
|---|---|
| Body Weights | Hematologic Studies |
| Food Consumption | Blood Chemistry Studies |
| Behavioral Reactions | Urine Analyses |
| Mortality | Gross Pathologic Studies |
| | Histopathologic Studies |

Respectfully submitted,

INDUSTRIAL BIO-TEST LABORATORIES, INC.

Report prepared by:

Bruce R. Burtner, Ph. B.
Assistant Toxicologist
Dog Toxicity

Report approved by:

Dennis C. Lindberg, B. S.
Senior Group Leader
Dog Toxicity

Paul L. Wright, Ph. D.
Section Head, Toxicology

M. L. Keplinger, Ph. D.
Manager, Toxicology

January 31, 1972

trm:sjn:psh

III. Procedure

A. Organization

The 90-day toxicity study utilized an untreated control group and three test groups, each consisting of eight purebred beagle dogs (four males and four females). The beagles were all eligible for A.K.C. registration and had been previously immunized against rabies, distemper, infectious canine hepatitis and leptospirosis.

All dogs were acquired from our own (IBTL) colony and were under observation for two weeks prior to the start of the investigation, during which time they were reimmunized and rendered clinically free of any existing parasitic infestation.

During the investigation, the selected animals were housed in kennels equipped with outside runs, four dogs of the same sex and group being accommodated in a single kennel.

The material to be tested, MCS 1016, was incorporated into a stock diet and fed to the dogs seven days a week at three graded dietary levels. The original levels were 1, 10 and 100 parts per million of test material in the diet. After 28 days of testing, the two lower levels were raised, respectively, to 30 and 300 parts per million.

An outline of the test organization and diet composition is presented in Table I.

TABLE I

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Test Organization and Diet Composition

| Group | Number of Animals | | | Dietary Constituents | | |
|---|---|---|---|---|---|---|
| | Male | Female | | Dose Level (ppm) | (%) | Stock Ration* (%) |
| UC | 4 | 4 | | None | None | 100.0 |
| T-I | 4 | 4 | (Days 1-28) | 1 | 0.0001 | 99.9999 |
| | | | (Days 29-90) | 30 | 0.003 | 99.997 |
| T-II | 4 | 4 | (Days 1-28) | 10 | 0.001 | 99.999 |
| | | | (Days 29-90) | 300 | 0.03 | 99.97 |
| T-III | 4 | 4 | | 100 | 0.01 | 99.99 |

* Wayne Dog Meal, Allied Mills, Inc., Chicago, Illinois.



MONS 068745

B. Parameters Investigated

Initially, the body weight of each dog in every group was determined and recorded. Thereafter, weighings were conducted weekly for the duration of the test.

At the beginning of each week, the appropriate dietary constituents for each of the groups were thoroughly blended in a Hobart mixer. Preweighed amounts were distributed into self-feeding units and maintained in excess of the animals' consumption. One such unit was available to the dogs in each kennel for three hours each day. During these three-hour intervals, food was consumed on an ad libitum basis. At the end of each seven-day period, all unconsumed food was collected and weighed. Food consumption was then calculated and recorded. Water was available to the animals at all times.

The dogs were under observation during the investigation and were examined daily for clinical signs or symptoms indicative of systemic toxicity.

The following determinations were conducted upon each dog from the untreated control group and three test groups just prior to the inception of the study and after 45 and 90 days of testing:

Hematologic Studies

total leukocyte count
erythrocyte count
hemoglobin
hematocrit
differential leukocyte count

Blood Chemistry Studies

blood urea nitrogen
serum glucose
serum alkaline phosphatase
serum glutamic-oxalacetic transaminase
serum glutamic-pyruvic transaminase

Urine Analyses

albumin
glucose
pH
specific gravity
microscopic elements - leukocytes
erythrocytes
crystals

At the conclusion of the investigation, the dogs from each group were sacrificed by electric shock. All major tissues and organs were examined grossly. The weights of the following organs were obtained: liver, kidneys, heart, brain, spleen, gonads, adrenal glands, thyroid gland and pituitary gland. The following tissues and organs excised from these animals were examined histologically (Hematoxylin-Eosin Stain):

| | |
|---|---|
| Adrenal Glands | Pancreas |
| Aorta (thoracic) | Peripheral Nerve (sciatic) |
| Bone Marrow (sternum) | Pituitary Gland |
| Brain (cerebrum, cerebellum, pons) | Prostate Gland |
| Caecum | Salivary Gland (submaxillary) |
| Colon | Small Intestine (duodenum, |
| Esophagus | jejunum, ileum) |
| Gall Bladder | Spinal Cord |
| Gonads | Spleen |
| Heart | Stomach (cardia, fundus, pylor |
| Kidneys | Trachea |
| Liver | Thyroid Gland |
| Lungs | Uterus |
| Lymph Nodes (cervical, mesenteric) | Urinary Bladder |
| Muscle (skeletal) | |

In addition, individual samples of liver, fat and muscle were s d (frozen) for chemical residue analyses.

MONS 068748

## IV. Results

### A. Body Weight Data

The body weight data are presented in Tables II and III.

No significant deviations from normally expected body weight gains for dogs of this age were noted.

TABLE II

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Body Weight Data for Males, kilograms

| Group | Dietary Level (ppm) | Dog Number | Age at Inception of Test (months) | Body Weights at Week Indicated | | | | | | | | | | | | | | Overall Weight Gain |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | |
| UC | None | 1 | 5.8 | 7.4 | 7.5 | 7.5 | 7.0 | 7.2 | 8.0 | 8.4 | 7.0 | 7.9 | 7.5 | 7.3 | 8.2 | 7.9 | 8.0 | 0.6 |
| | | 2 | 6.5 | 7.4 | 7.6 | 7.5 | 7.3 | 8.1 | 8.4 | 8.3 | 8.1 | 9.0 | 8.1 | 8.4 | 8.7 | 8.7 | 9.1 | 1.7 |
| | | 3 | 6.2 | 6.7 | 6.7 | 7.1 | 7.2 | 7.8 | 7.8 | 8.0 | 7.9 | 8.2 | 8.1 | 8.4 | 8.2 | 8.7 | 8.6 | 1.9 |
| | | 4 | 5.5 | 8.3 | 8.4 | 8.5 | 8.3 | 9.0 | 9.3 | 9.3 | 9.6 | 10.2 | 9.7 | 10.1 | 10.3 | 10.6 | 10.6 | 2.3 |
| | | Mean | 6.0 | 7.4 | 7.6 | 7.6 | 7.4 | 8.0 | 8.4 | 8.5 | 8.2 | 8.8 | 8.4 | 8.7 | 8.8 | 9.0 | 9.1 | 1.7 |
| T-I | 1 | 9 | 6.0 | 7.9 | 8.5 | 8.8 | 9.5 | 9.6 | 9.7 | 9.7 | 9.9 | 10.4 | 10.7 | 11.0 | 10.9 | 10.9 | 10.7 | 2.8 |
| (Days | 1-28) | 10 | 6.5 | 5.9 | 6.1 | 6.2 | 7.0 | 7.0 | 7.3 | 8.0 | 7.3 | 7.5 | 7.1 | 6.8 | 6.3 | 7.0 | 6.7 | 0.8 |
| | 30 | 11 | 5.5 | 8.5 | 8.9 | 9.2 | 9.6 | 9.6 | 9.8 | 10.0 | 10.2 | 10.3 | 10.4 | 10.8 | 10.6 | 10.7 | 10.7 | 2.2 |
| (Days | 29-90) | 12 | 5.5 | 7.3 | 7.8 | 8.1 | 8.7 | 8.9 | 9.1 | 9.4 | 9.5 | 9.7 | 9.9 | 9.8 | 10.1 | 10.0 | 9.9 | 2.6 |
| | | Mean | 5.9 | 7.4 | 7.8 | 8.1 | 8.7 | 8.8 | 9.0 | 9.3 | 9.2 | 9.5 | 9.5 | 9.6 | 9.5 | 9.6 | 9.5 | 2.1 |
| T-II | 10 | 17 | 6.2 | 7.3 | 7.8 | 8.0 | 8.5 | 8.6 | 8.8 | 9.4 | 9.5 | 9.7 | 9.9 | 10.5 | 10.4 | 10.4 | 10.5 | 3.2 |
| (Days | 1-28) | 18 | 6.2 | 6.8 | 6.8 | 7.0 | 7.2 | 7.3 | 7.4 | 7.7 | 7.4 | 8.0 | 7.8 | 8.0 | 7.9 | 8.2 | 8.0 | 1.2 |
| | 300 | 19 | 6.2 | 6.0 | 6.7 | 6.9 | 6.7 | 6.7 | 6.9 | 7.4 | 7.2 | 7.3 | 7.4 | 7.6 | 7.4 | 7.5 | 7.5 | 1.5 |
| (Days | 29-90) | 20 | 6.2 | 7.3 | 7.7 | 8.0 | 8.4 | 8.5 | 8.4 | 8.5 | 8.4 | 8.5 | 8.9 | 9.4 | 9.5 | 9.8 | 10.0 | 2.7 |
| | | Mean | 6.2 | 6.8 | 7.3 | 7.4 | 7.7 | 7.8 | 7.9 | 8.2 | 8.1 | 8.4 | 8.5 | 8.9 | 8.8 | 9.0 | 9.0 | 2.2 |
| T-III | 100 | 25 | 5.8 | 8.1 | 8.6 | 9.1 | 9.6 | 9.7 | 10.0 | 10.2 | 10.1 | 10.5 | 10.4 | 10.8 | 11.1 | 11.2 | 11.3 | 3.2 |
| | | 26 | 5.5 | 7.1 | 7.3 | 7.3 | 7.2 | 7.6 | 8.0 | 8.6 | 8.4 | 8.7 | 8.4 | 8.6 | 9.2 | 9.2 | 9.2 | 2.1 |
| | | 27 | 5.8 | 7.1 | 7.5 | 7.5 | 7.2 | 7.9 | 8.2 | 8.9 | 9.1 | 7.9 | 8.1 | 8.4 | 8.6 | 9.2 | 9.2 | 2.1 |
| | | 28 | 5.8 | 7.2 | 7.5 | 7.7 | 7.7 | 8.1 | 8.9 | 9.0 | 8.8 | 8.7 | 9.2 | 9.3 | 9.3 | 9.5 | 9.7 | 2.5 |
| | | Mean | 5.7 | 7.4 | 7.8 | 7.9 | 7.9 | 8.3 | 8.8 | 9.2 | 9.1 | 9.0 | 9.0 | 9.3 | 9.6 | 9.8 | 9.8 | 2.4 |

MONS 068250

Industrial BIO-TEST Laboratories, Inc.

## TABLE III

### TEST MATERIAL: MCS 1016

### 90-Day Subacute Oral Toxicity Study - Beagle Dogs

### Body Weight Data for Females, kilograms

| Group | Dietary Level (ppm) | Dog Number | Age at Inception of Test (months) | Body Weights at Week Indicated 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | Overall Weight Gain |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| UC | None | 5 | 6.2 | 6.3 | 6.9 | 7.0 | 7.0 | 7.6 | 8.1 | 8.8 | 8.7 | 8.9 | 9.1 | 8.6 | 8.6 | 9.0 | 9.3 | 3.0 |
| | | 6 | 6.2 | 6.9 | 7.0 | 6.7 | 6.5 | 7.0 | 7.4 | 7.6 | 7.7 | 8.1 | 8.1 | 8.1 | 8.2 | 8.3 | 8.4 | 1.5 |
| | | 7 | 5.8 | 4.4 | 4.7 | 4.7 | 4.4 | 5.0 | 5.3 | 5.4 | 5.4 | 5.8 | 5.8 | 5.9 | 6.0 | 6.1 | 6.2 | 1.8 |
| | | 8 | 5.8 | 4.9 | 5.2 | 5.3 | 5.0 | 5.7 | 5.7 | 6.0 | 6.2 | 6.7 | 6.6 | 6.7 | 7.0 | 7.0 | 7.2 | 2.3 |
| | | Mean | 6.0 | 5.6 | 6.0 | 5.9 | 5.7 | 6.3 | 6.6 | 7.0 | 7.0 | 7.4 | 7.4 | 7.3 | 7.4 | 7.6 | 7.8 | 2.2 |
| T-I | 1 | 13 | 6.2 | 6.2 | 6.6 | 6.9 | 7.3 | 7.4 | 7.6 | 7.8 | 7.0 | 8.0 | 8.0 | 8.2 | 8.4 | 8.6 | 8.4 | 2.2 |
| (Days | 1-28) | 14 | 6.2 | 5.9 | 6.3 | 6.4 | 6.8 | 6.8 | 7.2 | 7.3 | 7.5 | 7.0 | 7.0 | 7.8 | 8.1 | 8.1 | 8.0 | 2.1 |
| | 30 | 15 | 6.2 | 5.6 | 6.0 | 6.0 | 6.5 | 6.7 | 6.7 | 6.9 | 7.3 | 7.5 | 7.7 | 7.4 | 7.6 | 7.9 | 8.2 | 2.6 |
| (Days | 29-90) | 16 | 6.2 | 7.1 | 7.6 | 7.9 | 8.5 | 8.8 | 8.8 | 9.0 | 8.9 | 9.4 | 9.5 | 9.6 | 9.7 | 10.1 | 9.7 | 2.6 |
| | | Mean | 6.2 | 6.2 | 6.6 | 6.8 | 7.2 | 7.5 | 7.6 | 7.8 | 7.9 | 8.1 | 8.0 | 8.2 | 8.4 | 8.7 | 8.6 | 2.4 |
| T-II | 10 | 21 | 6.2 | 5.4 | 5.8 | 6.1 | 6.4 | 6.4 | 6.6 | 7.1 | 6.9 | 7.1 | 7.3 | 7.5 | 7.6 | 7.7 | 7.6 | 2.2 |
| (Days | 1-28) | 22 | 5.8 | 5.2 | 5.4 | 5.7 | 6.0 | 6.0 | 6.3 | 6.9 | 6.4 | 6.8 | 6.7 | 6.8 | 6.8 | 7.1 | 7.0 | 1.8 |
| | 300 | 23 | 5.8 | 5.8 | 6.2 | 6.6 | 6.8 | 6.9 | 7.0 | 7.3 | 7.3 | 7.5 | 7.8 | 8.1 | 7.9 | 8.4 | 8.4 | 2.6 |
| (Days | 29-90) | 24 | 6.2 | 4.1 | 4.5 | 4.4 | 4.6 | 4.6 | 4.6 | 4.9 | 4.9 | 5.0 | 5.1 | 5.4 | 5.5 | 5.8 | 5.7 | 1.6 |
| | | Mean | 5.9 | 5.1 | 5.5 | 5.7 | 5.9 | 6.0 | 6.1 | 6.6 | 6.4 | 6.6 | 6.7 | 7.0 | 7.0 | 7.2 | 7.2 | 2.1 |
| T-III | 100 | 29 | 6.0 | 7.2 | 7.9 | 8.0 | 8.6 | 8.7 | 8.9 | 9.3 | 9.3 | 9.5 | 9.5 | 9.6 | 9.7 | 9.7 | 9.7 | 2.5 |
| | | 30 | 5.8 | 4.9 | 5.3 | 5.5 | 6.2 | 6.3 | 6.4 | 6.6 | 6.8 | 6.7 | 6.5 | 7.1 | 7.0 | 7.2 | 7.0 | 2.1 |
| | | 31 | 5.5 | 6.6 | 6.9 | 7.2 | 8.1 | 8.4 | 8.4 | 8.8 | 9.1 | 9.7 | 9.9 | 10.3 | 10.2 | 10.3 | 10.3 | 3.7 |
| | | 32 | 5.8 | 6.5 | 7.1 | 7.6 | 8.4 | 8.6 | 8.6 | 9.1 | 9.1 | 9.5 | 9.6 | 9.8 | 9.7 | 10.0 | 9.6 | 3.1 |
| | | Mean | 5.8 | 6.3 | 6.8 | 7.1 | 7.8 | 8.0 | 8.1 | 8.4 | 8.6 | 8.8 | 8.9 | 9.2 | 9.2 | 9.3 | 9.2 | 2.9 |



MONS 068751

B. Food Consumption Data

Food consumption data are presented in Table IV. The amount of food consumed by the test animals was essentially the same as untreated controls.

TABLE IV

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Food Consumption Data

| | | Mean Food Consumed During Week Indicated (g/kg of body weight) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Sex: | Males | | | | Females | | | |
| | Group: | UC | I | II | III | UC | I | II | III |
| Week | Dietary Level (ppm): | None | * | ** | 100 | None | * | ** | 100 |
| 1 | | 256 | 324 | 292 | 336 | 375 | 326 | 354 | 371 |
| 2 | | 250 | 290 | 267 | 266 | 318 | 312 | 333 | 338 |
| 3 | | 256 | 281 | 266 | 275 | 346 | 302 | 297 | 327 |
| 4 | | 281 | 293 | 240 | 340 | 321 | 337 | 325 | 334 |
| 5 | | 292 | 294 | 259 | 330 | 352 | 312 | 303 | 372 |
| 6 | | 274 | 285 | 259 | 283 | 318 | 340 | 310 | 289 |
| 7 | | 201 | 255 | 228 | 234 | 336 | 320 | 269 | 267 |
| 8 | | 290 | 258 | 238 | 322 | 318 | 302 | 318 | 302 |

* 1 ppm Days 1-28, 30 ppm Days 29-90.
** 10 ppm Days 1-28, 300 ppm Days 29-90.

TABLE IV continued

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Food Consumption Data

| | | Mean Food Consumed During Week Indicated (g/kg of body weight) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Sex: | Males | | | | Females | | | |
| | Group: | UC | I | II | III | UC | I | II | |
| Week | Dietary Level (ppm): | None | * | ** | 100 | None | * | ** | 1 |
| 9 | | 214 | 255 | 232 | 289 | 321 | 309 | 283 | |
| 10 | | 264 | 226 | 222 | 263 | 270 | 286 | 282 | |
| 11 | | 287 | 208 | 210 | 268 | 304 | 357 | 328 | |
| 12 | | 280 | 312 | 305 | 278 | 345 | 299 | 286 | |
| 13 | | 269 | 187 | 219 | 196 | 340 | 343 | 295 | |
| Mean | | 263 | 267 | 249 | 283 | 328 | 313 | 306 | |

* 1 ppm Days 1-28, 30 ppm Days 29-90.
** 10 ppm Days 1-28, 300 ppm Days 29-90.

C. Reactions

No untoward behavioral reactions were noted among any of the test animals.

D. Mortality

No fatalities occurred at any of the levels tested.

E. Hematologic Studies

The results of these determinations are presented in Tables V through IX. No significant abnormalities were noted at any of the levels tested.

TABLE V

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Hematologic Studies: Total Leukocyte Count, thousands/$mm^3$

| Group | Dietary Level (ppm) | Dog Number and Sex | Days: 0 | 45 | 90 |
|---|---|---|---|---|---|
| UC | None | 1-M | 14.0 | 14.5 | 10.9 |
| | | 2-M | 19.6 | 19.1 | 10.6 |
| | | 3-M | 18.2 | 12.8 | 15.1 |
| | | 4-M | 17.2 | 21.2 | 17.4 |
| | | 5-F | 23.7 | 19.2 | 16.4 |
| | | 6-F | 13.0 | 11.9 | 11.2 |
| | | 7-F | 25.9 | 27.1 | 19.2 |
| | | 8-F | 23.0 | 17.9 | 14.4 |
| T-I | 1 | 9-M | 16.5 | 13.7 | 10.6 |
| | (Days 1-28) | 10-M | 19.2 | 17.8 | 15.2 |
| | | 11-M | 25.2 | 17.1 | 18.3 |
| | 30 | 12-M | 19.3 | 21.5 | 16.2 |
| | (Days 29-90) | 13-F | 16.4 | 14.4 | 14.4 |
| | | 14-F | 15.5 | 18.8 | 16.4 |
| | | 15-F | 24.5 | 15.6 | 15.9 |
| | | 16-F | 14.5 | 15.4 | 15.4 |
| T-II | 10 | 17-M | 21.6 | 14.4 | 13.8 |
| | (Days 1-28) | 18-M | 18.5 | 18.5 | 15.8 |
| | 300 | 19-M | 28.8 | 19.4 | 16.0 |
| | (Days 29-90) | 20-M | 24.6 | 10.6 | 10.3 |
| | | 21-F | 17.1 | 24.6 | 18.8 |
| | | 22-F | 27.1 | 21.6 | 19.4 |
| | | 23-F | 31.4 | 17.2 | 18.0 |
| | | 24-F | 19.4 | 20.6 | 23.1 |
| T-III | 100 | 25-M | 17.8 | 13.8 | 12.4 |
| | | 26-M | 16.2 | 16.7 | 15.3 |
| | | 27-M | 16.7 | 19.6 | 15.6 |
| | | 28-M | 13.2 | 16.0 | 14.8 |
| | | 29-F | 28.7 | 13.5 | 14.3 |
| | | 30-F | 25.9 | 19.9 | 21.5 |
| | | 31-F | 21.1 | 17.7 | 14.6 |
| | | 32-F | 13.2 | 17.3 | 21.4 |

MONS 068756

TABLE VI

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Hematologic Studies: Erythrocyte Count, millions/$mm^3$

| Group | Dietary Level (ppm) | Dog Number and Sex | Days: 0 | 45 | 90 |
|---|---|---|---|---|---|
| UC | None | 1-M | 6.49 | 6.26 | 5.50 |
| | | 2-M | 5.66 | 5.13 | 5.50 |
| | | 3-M | 5.33 | 5.49 | 5.76 |
| | | 4-M | 5.60 | 5.69 | 5.77 |
| | | 5-F | 5.67 | 6.60 | 6.49 |
| | | 6-F | 6.21 | 6.68 | 6.77 |
| | | 7-F | 6.16 | 6.13 | 6.41 |
| | | 8-F | 5.95 | 6.32 | 6.76 |
| T-I | 1 | 9-M | 5.41 | 6.59 | 6.99 |
| | (Days 1-28) | 10-M | 5.99 | 6.11 | 6.16 |
| | | 11-M | 5.86 | 5.97 | 6.18 |
| | 30 | 12-M | 6.19 | 6.07 | 6.27 |
| | (Days 29-90) | 13-F | 6.03 | 6.28 | 6.38 |
| | | 14-F | 6.04 | 5.89 | 5.98 |
| | | 15-F | 6.16 | 6.07 | 6.29 |
| | | 16-F | 5.80 | 6.39 | 6.48 |
| T-II | 10 | 17-M | 6.01 | 6.71 | 6.91 |
| | (Days 1-28) | 18-M | 5.30 | 5.76 | 5.45 |
| | 300 | 19-M | 5.42 | 5.55 | 5.74 |
| | (Days 29-90) | 20-M | 5.63 | 5.59 | 5.34 |
| | | 21-F | 5.17 | 6.23 | 6.50 |
| | | 22-F | 5.60 | 6.13 | 5.96 |
| | | 23-F | 5.57 | 6.56 | 7.27 |
| | | 24-F | 6.30 | 5.44 | 5.30 |
| T-III | 100 | 25-M | 5.57 | 5.62 | 5.70 |
| | | 26-M | 6.03 | 6.15 | 5.80 |
| | | 27-M | 6.01 | 5.73 | 5.47 |
| | | 28-M | 5.95 | 5.75 | 6.18 |
| | | 29-F | 5.77 | 7.31 | 7.27 |
| | | 30-F | 5.84 | 6.35 | 6.39 |
| | | 31-F | 6.13 | 6.35 | 6.65 |
| | | 32-F | 6.06 | 6.23 | 5.89 |

TABLE VII

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Hematologic Studies: Hemoglobin, gm/100 ml

| Group | Dietary Level (ppm) | Dog Number and Sex | Days: 0 | 45 | 90 |
|---|---|---|---|---|---|
| UC | None | 1-M | 15.7 | 14.5 | 13.3 |
| | | 2-M | 14.2 | 12.3 | 12.9 |
| | | 3-M | 11.9 | 12.6 | 12.2 |
| | | 4-M | 13.4 | 13.5 | 12.9 |
| | | 5-F | 13.2 | 14.6 | 14.3 |
| | | 6-F | 14.2 | 15.4 | 14.8 |
| | | 7-F | 14.4 | 14.7 | 15.0 |
| | | 8-F | 12.8 | 14.2 | 15.2 |
| T-I | 1 | 9-M | 13.3 | 14.3 | 15.9 |
| | (Days 1-28) | 10-M | 14.5 | 14.0 | 14.2 |
| | | 11-M | 14.8 | 13.8 | 15.0 |
| | 30 | 12-M | 15.3 | 14.4 | 15.0 |
| | (Days 29-90) | 13-F | 14.3 | 14.4 | 15.3 |
| | | 14-F | 14.6 | 14.3 | 15.2 |
| | | 15-F | 15.0 | 13.9 | 15.0 |
| | | 16-F | 14.5 | 14.4 | 14.5 |
| T-II | 10 | 17-M | 14.9 | 14.0 | 15.3 |
| | (Days 1-28) | 18-M | 13.7 | 13.7 | 13.9 |
| | 300 | 19-M | 13.3 | 13.2 | 14.2 |
| | (Days 29-90) | 20-M | 13.6 | 12.6 | 12.9 |
| | | 21-F | 11.8 | 14.0 | 15.2 |
| | | 22-F | 13.7 | 14.3 | 14.7 |
| | | 23-F | 14.2 | 15.1 | 16.9 |
| | | 24-F | 13.0 | 13.7 | 13.8 |
| T-III | 100 | 25-M | 13.7 | 13.2 | 13.7 |
| | | 26-M | 13.6 | 14.1 | 14.0 |
| | | 27-M | 15.0 | 13.7 | 13.6 |
| | | 28-M | 14.6 | 13.3 | 14.9 |
| | | 29-F | 14.0 | 16.7 | 17.1 |
| | | 30-F | 13.9 | 15.0 | 15.7 |
| | | 31-F | 14.4 | 14.9 | 15.9 |
| | | 32-F | 14.3 | 14.1 | 14.0 |

TABLE VIII.

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Hematologic Studies: Hematocrit, percent

| Group | Dietary Level (ppm) | Dog Number and Sex | Days: 0 | 45 | 90 |
|---|---|---|---|---|---|
| UC | None | 1-M | 46 | 43 | 37 |
| | | 2-M | 38 | 35 | 36 |
| | | 3-M | 36 | 36 | 38 |
| | | 4-M | 39 | 39 | 39 |
| | | 5-F | 39 | 44 | 43 |
| | | 6-F | 43 | 46 | 46 |
| | | 7-F | 42 | 44 | 45 |
| | | 8-F | 38 | 42 | 46 |
| T-I | 1 (Days 1-28) 30 (Days 29-90) | 9-M | 36 | 42 | 43 |
| | | 10-M | 41 | 40 | 40 |
| | | 11-M | 41 | 40 | 42 |
| | | 12-M | 42 | 41 | 42 |
| | | 13-F | 40 | 41 | 42 |
| | | 14-F | 41 | 41 | 42 |
| | | 15-F | 40 | 40 | 42 |
| | | 16-F | 39 | 41 | 41 |
| T-II | 10 (Days 1-28) 300 (Days 29-90) | 17-M | 40 | 39 | 43 |
| | | 18-M | 39 | 40 | 38 |
| | | 19-M | 38 | 38 | 39 |
| | | 20-M | 37 | 35 | 35 |
| | | 21-F | 32 | 40 | 43 |
| | | 22-F | 38 | 42 | 42 |
| | | 23-F | 40 | 43 | 48 |
| | | 24-F | 35 | 39 | 39 |
| T-III | 100 | 25-M | 35 | 38 | 38 |
| | | 26-M | 39 | 40 | 38 |
| | | 27-M | 41 | 39 | 38 |
| | | 28-M | 40 | 38 | 42 |
| | | 29-F | 39 | 49 | 49 |
| | | 30-F | 39 | 44 | 43 |
| | | 31-F | 41 | 43 | 45 |
| | | 32-F | 40 | 41 | 39 |

MONS 068759

TABLE IX

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Hematologic Studies: Differential Leukocyte Count, percent - Neutrophils

| Group | Dietary Level (ppm) | Dog Number and Sex | Days: 0 | 45 | 90 |
|---|---|---|---|---|---|
| UC | None | 1-M | 68 | 55 | 58 |
| | | 2-M | 71 | 77 | 55 |
| | | 3-M | 71 | 54 | 59 |
| | | 4-M | 55 | 65 | 68 |
| | | 5-F | 49 | 55 | 54 |
| | | 6-F | 45 | 43 | 46 |
| | | 7-F | 62 | 74 | 55 |
| | | 8-F | 72 | 51 | 54 |
| T-I | 1 (Days 1-28) 30 (Days 29-90) | 9-M | 60 | 54 | 50 |
| | | 10-M | 65 | 61 | 74 |
| | | 11-M | 65 | 56 | 63 |
| | | 12-M | 57 | 65 | 67 |
| | | 13-F | 64 | 57 | 60 |
| | | 14-F | 57 | 62 | 63 |
| | | 15-F | 42 | 56 | 58 |
| | | 16-F | 69 | 56 | 53 |
| T-II | 10 (Days 1-28) 300 (Days 29-90) | 17-M | 56 | 58 | 51 |
| | | 18-M | 58 | 70 | 71 |
| | | 19-M | 70 | 60 | 62 |
| | | 20-M | 54 | 61 | 55 |
| | | 21-F | 74 | 63 | 60 |
| | | 22-F | 74 | 72 | 63 |
| | | 23-F | 71 | 56 | 54 |
| | | 24-F | 42 | 61 | 67 |
| T-III | 100 | 25-M | 67 | 69 | 58 |
| | | 26-M | 73 | 64 | 63 |
| | | 27-M | 43 | 68 | 54 |
| | | 28-M | 53 | 65 | 48 |
| | | 29-F | 67 | 51 | 58 |
| | | 30-F | 50 | 64 | 62 |
| | | 31-F | 68 | 65 | 54 |
| | | 32-F | 52 | 59 | 75 |

TABLE IX continued

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Hematologic Studies: Differential Leukocyte Count, percent - Lymphocytes

| Group | Dietary Level (ppm) | Dog Number and Sex | Days: 0 | 45 | 90 |
|---|---|---|---|---|---|
| UC | None | 1-M | 32 | 39 | 34 |
| | | 2-M | 23 | 17 | 35 |
| | | 3-M | 25 | 36 | 34 |
| | | 4-M | 41 | 31 | 23 |
| | | 5-F | 49 | 38 | 39 |
| | | 6-F | 54 | 49 | 49 |
| | | 7-F | 36 | 22 | 40 |
| | | 8-F | 20 | 40 | 39 |
| T-I | 1 (Days 1-28) 30 (Days 29-90) | 9-M | 35 | 40 | 45 |
| | | 10-M | 32 | 32 | 24 |
| | | 11-M | 28 | 34 | 29 |
| | | 12-M | 41 | 33 | 29 |
| | | 13-F | 32 | 39 | 30 |
| | | 14-F | 37 | 33 | 30 |
| | | 15-F | 54 | 37 | 35 |
| | | 16-F | 28 | 39 | 40 |
| T-II | 10 (Days 1-28) 300 (Days 29-90) | 17-M | 42 | 39 | 44 |
| | | 18-M | 30 | 30 | 27 |
| | | 19-M | 27 | 33 | 33 |
| | | 20-M | 34 | 27 | 39 |
| | | 21-F | 23 | 33 | 34 |
| | | 22-F | 21 | 24 | 31 |
| | | 23-F | 27 | 43 | 45 |
| | | 24-F | 54 | 36 | 27 |
| T-III | 100 | 25-M | 28 | 27 | 39 |
| | | 26-M | 24 | 32 | 29 |
| | | 27-M | 45 | 29 | 41 |
| | | 28-M | 39 | 26 | 41 |
| | | 29-F | 32 | 40 | 37 |
| | | 30-F | 41 | 31 | 32 |
| | | 31-F | 28 | 28 | 41 |
| | | 32-F | 41 | 32 | 20 |

MONS 068761

TABLE IX continued

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Hematologic Studies: Differential Leukocyte Count, percent - Monocytes

| Group | Dietary Level (ppm) | Dog Number and Sex | Days: 0 | 45 | 90 |
|---|---|---|---|---|---|
| UC | None | 1-M | 0 | 0 | 0 |
| | | 2-M | 0 | 0 | 0 |
| | | 3-M | 0 | 0 | 0 |
| | | 4-M | 0 | 0 | 0 |
| | | 5-F | 0 | 0 | 0 |
| | | 6-F | 0 | 1 | 0 |
| | | 7-F | 0 | 0 | 0 |
| | | 8-F | 0 | 0 | 0 |
| T-I | 1 (Days 1-28) 30 (Days 29-90) | 9-M | 0 | 0 | 0 |
| | | 10-M | 0 | 0 | 0 |
| | | 11-M | 0 | 0 | 0 |
| | | 12-M | 0 | 0 | 0 |
| | | 13-F | 0 | 0 | 0 |
| | | 14-F | 0 | 0 | 0 |
| | | 15-F | 0 | 0 | 0 |
| | | 16-F | 0 | 0 | 0 |
| T-II | 10 (Days 1-28) 300 (Days 29-90) | 17-M | 0 | 0 | 0 |
| | | 18-M | 0 | 0 | 0 |
| | | 19-M | 0 | 0 | 0 |
| | | 20-M | 0 | 0 | 0 |
| | | 21-F | 0 | 0 | 0 |
| | | 22-F | 0 | 0 | 0 |
| | | 23-F | 0 | 0 | 0 |
| | | 24-F | 0 | 0 | 0 |
| T-III | 100 | 25-M | 0 | 0 | 0 |
| | | 26-M | 0 | 0 | 0 |
| | | 27-M | 0 | 0 | 0 |
| | | 28-M | 0 | 0 | 0 |
| | | 29-F | 0 | 0 | 0 |
| | | 30-F | 0 | 0 | 0 |
| | | 31-F | 1 | 0 | 0 |
| | | 32-F | 0 | 0 | 0 |

MONS 068762

TABLE IX continued

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Hematologic Studies: Differential Leukocyte Count, percent - Eosinophils

| Group | Dietary Level (ppm) | Dog Number and Sex | Days: 0 | 45 | 90 |
|---|---|---|---|---|---|
| UC | None | 1-M | 0 | 6 | 8 |
| | | 2-M | 6 | 6 | 1 |
| | | 3-M | 4 | 10 | |
| | | 4-M | 4 | 4 | |
| | | 5-F | 2 | 7 | |
| | | 6-F | 0 | 7 | |
| | | 7-F | 2 | 3 | |
| | | 8-F | 8 | 9 | |
| T-I | 1 (Days 1-28) 30 (Days 29-90) | 9-M | 5 | 5 | |
| | | 10-M | 3 | 7 | |
| | | 11-M | 7 | 10 | |
| | | 12-M | 2 | 2 | |
| | | 13-F | 4 | 4 | 1 |
| | | 14-F | 5 | 5 | |
| | | 15-F | 4 | 7 | |
| | | 16-F | 3 | 5 | |
| T-II | 10 (Days 1-28) 300 (Days 29-90) | 17-M | 2 | 3 | |
| | | 18-M | 1 | 0 | |
| | | 19-M | 3 | 7 | |
| | | 20-M | 12 | 12 | |
| | | 21-F | 3 | 4 | |
| | | 22-F | 5 | 3 | |
| | | 23-F | 2 | 1 | |
| | | 24-F | 4 | 3 | |
| T-III | 100 | 25-M | 5 | 4 | |
| | | 26-M | 3 | 3 | |
| | | 27-M | 12 | 3 | |
| | | 28-M | 8 | 9 | 1 |
| | | 29-F | 1 | 8 | |
| | | 30-F | 9 | 5 | |
| | | 31-F | 3 | 7 | |
| | | 32-F | 6 | 9 | |

MONS 068763

TABLE IX continued

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Hematologic Studies: Differential Leukocyte Count, percent - Basophils

| Group | Dietary Level (ppm) | Dog Number and Sex | Days: 0 | 45 | 90 |
|---|---|---|---|---|---|
| UC | None | 1-M | 0 | 0 | 0 |
| | | 2-M | 0 | 0 | 0 |
| | | 3-M | 0 | 0 | 0 |
| | | 4-M | 0 | 0 | 0 |
| | | 5-F | 0 | 0 | 0 |
| | | 6-F | 1 | 0 | 0 |
| | | 7-F | 0 | 1 | 0 |
| | | 8-F | 0 | 0 | 0 |
| T-I | 1 (Days 1-28) | 9-M | 0 | 1 | 0 |
| | | 10-M | 0 | 0 | 0 |
| | | 11-M | 0 | 0 | 0 |
| | 30 (Days 29-90) | 12-M | 0 | 0 | 0 |
| | | 13-F | 0 | 0 | 0 |
| | | 14-F | 1 | 0 | 0 |
| | | 15-F | 0 | 0 | 0 |
| | | 16-F | 0 | 0 | 0 |
| T-II | 10 (Days 1-28) | 17-M | 0 | 0 | 0 |
| | | 18-M | 1 | 0 | 0 |
| | 300 (Days 29-90) | 19-M | 0 | 0 | 0 |
| | | 20-M | 0 | 0 | 0 |
| | | 21-F | 0 | 0 | 0 |
| | | 22-F | 0 | 1 | 0 |
| | | 23-F | 0 | 0 | 0 |
| | | 24-F | 0 | 0 | 0 |
| T-III | 100 | 25-M | 0 | 0 | 0 |
| | | 26-M | 0 | 1 | 0 |
| | | 27-M | 0 | 0 | 0 |
| | | 28-M | 0 | 0 | 0 |
| | | 29-F | 0 | 1 | 0 |
| | | 30-F | 0 | 0 | 0 |
| | | 31-F | 0 | 0 | 0 |
| | | 32-F | 1 | 0 | 0 |

F. Blood Chemistry Studies

The results of these determinations are presented in Tables X through XIV. No significant abnormalities were noted at any of the levels tested.

TABLE X

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Blood Chemistry Studies: Blood Urea Nitrogen, mg/100 ml

| Group | Dietary Level (ppm) | Dog Number and Sex | Days: 0 | 45 | 90 |
|---|---|---|---|---|---|
| UC | None | 1-M | 8 | 16 | 13 |
| | | 2-M | 7 | 13 | 10 |
| | | 3-M | 7 | 14 | 11 |
| | | 4-M | 8 | 15 | 12 |
| | | 5-F | 12 | 18 | 15 |
| | | 6-F | 10 | 16 | 13 |
| | | 7-F | 11 | 14 | 13 |
| | | 8-F | 16 | 18 | 14 |
| T-I | 1 | 9-M | 7 | 14 | 11 |
| | (Days 1-28) | 10-M | 8 | 13 | 12 |
| | | 11-M | 9 | 13 | 10 |
| | 30 | 12-M | 8 | 12 | 11 |
| | (Days 29-90) | 13-F | 11 | 13 | 14 |
| | | 14-F | 9 | 16 | 13 |
| | | 15-F | 9 | 15 | 11 |
| | | 16-F | 11 | 16 | 16 |
| T-II | 10 | 17-M | 7 | 13 | 10 |
| | (Days 1-28) | 18-M | 6 | 8 | 9 |
| | 300 | 19-M | 8 | 10 | 10 |
| | (Days 29-90) | 20-M | 9 | 13 | 14 |
| | | 21-F | 11 | 14 | 12 |
| | | 22-F | 8 | 10 | 11 |
| | | 23-F | 10 | 16 | 16 |
| | | 24-F | 10 | 25 | 13 |
| T-III | 100 | 25-M | 7 | 13 | 10 |
| | | 26-M | 7 | 11 | 12 |
| | | 27-M | 9 | 13 | 16 |
| | | 28-M | 6 | 8 | 8 |
| | | 29-F | 8 | 14 | 12 |
| | | 30-F | 11 | 13 | 11 |
| | | 31-F | 7 | 13 | 10 |
| | | 32-F | 9 | 14 | 10 |

note: colorimetric method by Roeckelt and Cochman.

MONS 068766

TABLE XI

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Blood Chemistry Studies: Serum Glucose, mg/100 ml

| Group | Dietary Level (ppm) | Dog Number and Sex | Days: 0 | 45 | 90 |
|---|---|---|---|---|---|
| UC | None | 1-M | 114 | 97 | 99 |
| | | 2-M | 108 | 91 | 97 |
| | | 3-M | 109 | 83 | 101 |
| | | 4-M | 121 | 103 | 104 |
| | | 5-F | 97 | 157 | 92 |
| | | 6-F | 96 | 85 | 92 |
| | | 7-F | 101 | 91 | 102 |
| | | 8-F | 107 | 104 | 112 |
| T-I | 1 (Days 1-28) | 9-M | 108 | 104 | 115 |
| | | 10-M | 106 | 97 | 99 |
| | | 11-M | 112 | 104 | 104 |
| | 30 (Days 29-90) | 12-M | 105 | 106 | 107 |
| | | 13-F | 103 | 99 | 104 |
| | | 14-F | 103 | 101 | 112 |
| | | 15-F | 101 | 89 | 99 |
| | | 16-F | 100 | 89 | 101 |
| T-II | 10 (Days 1-28) | 17-M | 110 | 99 | 112 |
| | | 18-M | 93 | 89 | 99 |
| | 300 (Days 29-90) | 19-M | 84 | 85 | 93 |
| | | 20-M | 110 | 93 | 101 |
| | | 21-F | 103 | 101 | 111 |
| | | 22-F | 108 | 95 | 104 |
| | | 23-F | 102 | 91 | 107 |
| | | 24-F | 110 | 97 | 115 |
| T-III | 100 | 25-M | 116 | 106 | 112 |
| | | 26-M | 99 | 85 | 101 |
| | | 27-M | 111 | 93 | 102 |
| | | 28-M | 106 | 97 | 106 |
| | | 29-F | 107 | 99 | 121 |
| | | 30-F | 104 | 99 | 104 |
| | | 31-F | 104 | 93 | 104 |
| | | 32-F | 109 | 101 | 111 |

TABLE XII

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Blood Chemistry Studies: Serum Alkaline Phosphatase, King-Armstrong Units/100 ml

| Group | Dietary Level (ppm) | Dog Number and Sex | Days: 0 | 45 | 90 |
|---|---|---|---|---|---|
| UC | None | 1-M | 8.2 | 5.3 | 5.4 |
| | | 2-M | 7.3 | 7.2 | 5.4 |
| | | 3-M | 5.5 | 5.1 | 5.0 |
| | | 4-M | 6.9 | 6.5 | 6.5 |
| | | 5-F | 7.4 | 6.2 | 4.6 |
| | | 6-F | 6.7 | 6.2 | 6.0 |
| | | 7-F | 9.4 | 8.5 | 6.0 |
| | | 8-F | 8.5 | 7.0 | 6.2 |
| T-I | 1 (Days 1-28) 30 (Days 29-90) | 9-M | 7.1 | 6.7 | 4.8 |
| | | 10-M | 7.0 | 6.2 | 4.6 |
| | | 11-M | 6.7 | 5.5 | 4.0 |
| | | 12-M | 7.5 | 6.2 | 4.6 |
| | | 13-F | 6.5 | 5.3 | 4.8 |
| | | 14-F | 9.1 | 6.5 | 5.6 |
| | | 15-F | 7.7 | 6.5 | 6.7 |
| | | 16-F | 10.3 | 8.0 | 7.1 |
| T-II | 10 (Days 1-28) 300 (Days 29-90) | 17-M | 7.4 | 7.7 | 6.7 |
| | | 18-M | 12.4 | 9.7 | 8.4 |
| | | 19-M | 12.5 | 11.6 | 9.8 |
| | | 20-M | 7.5 | 6.0 | 7.6 |
| | | 21-F | 8.3 | 11.1 | 7.8 |
| | | 22-F | 7.3 | 6.7 | 6.2 |
| | | 23-F | 7.3 | 6.0 | 5.8 |
| | | 24-F | 11.5 | 10.0 | 11.5 |
| T-III | 100 | 25-M | 7.4 | 6.5 | 5.4 |
| | | 26-M | 8.2 | 5.3 | 4.8 |
| | | 27-M | 7.1 | 5.1 | 4.4 |
| | | 28-M | 6.6 | 4.6 | 4.2 |
| | | 29-F | 8.8 | 8.0 | 7.6 |
| | | 30-F | 9.3 | 7.2 | 6.7 |
| | | 31-F | 8.3 | 8.2 | 6.5 |
| | | 32-F | 8.2 | 8.0 | 8.0 |

note: colorimetric method by Babson.

MONS 068768

TABLE XIII

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Blood Chemistry Studies: Serum Glutamic-Oxalacetic Transaminase, Dade Units/ml

| Group | Dietary Level (ppm) | Dog Number and Sex | Days: 0 | 45 | 90 |
|---|---|---|---|---|---|
| UC | None | 1-M | 16 | 14 | 24 |
| | | 2-M | 15 | 14 | 28 |
| | | 3-M | 18 | 19 | 30 |
| | | 4-M | 15 | 22 | 27 |
| | | 5-F | 18 | 28 | 30 |
| | | 6-F | 21 | 26 | 29 |
| | | 7-F | 21 | 31 | 28 |
| | | 8-F | 21 | 27 | 32 |
| T-I | 1 (Days 1-28) 30 (Days 29-90) | 9-M | 25 | 26 | 25 |
| | | 10-M | 17 | 25 | 21 |
| | | 11-M | 22 | 23 | 22 |
| | | 12-M | 16 | 22 | 23 |
| | | 13-F | 20 | 29 | 32 |
| | | 14-F | 22 | 30 | 25 |
| | | 15-F | 20 | 26 | 31 |
| | | 16-F | 28 | 31 | 31 |
| T-II | 10 (Days 1-28) 300 (Days 29-90) | 17-M | 21 | 29 | 27 |
| | | 18-M | 71 | 28 | 22 |
| | | 19-M | 56 | 27 | 29 |
| | | 20-M | 22 | 22 | 29 |
| | | 21-F | 21 | 23 | 25 |
| | | 22-F | 20 | 25 | 21 |
| | | 23-F | 16 | 18 | 20 |
| | | 24-F | 21 | 21 | 26 |
| T-III | 100 | 25-M | 23 | 27 | 28 |
| | | 26-M | 20 | 23 | 28 |
| | | 27-M | 21 | 16 | 28 |
| | | 28-M | 18 | 21 | 23 |
| | | 29-F | 23 | 38 | 24 |
| | | 30-F | 20 | 27 | 25 |
| | | 31-F | 14 | 27 | 28 |
| | | 32-F | 14 | 26 | 25 |

note: fluorometric method by Levine and Hill.

TABLE XIV

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Blood Chemistry Studies: Serum Glutamic-Pyruvic Transaminase, Dade Units/ml

| Group | Dietary Level (ppm) | Dog Number and Sex | Days: 0 | 45 | 90 |
|---|---|---|---|---|---|
| UC | None | 1-M | 30 | 29 | 25 |
| | | 2-M | 16 | 14 | 26 |
| | | 3-M | 26 | 24 | 21 |
| | | 4-M | 34 | 41 | 41 |
| | | 5-F | 30 | 53 | 31 |
| | | 6-F | 23 | 37 | 29 |
| | | 7-F | 18 | 23 | 20 |
| | | 8-F | 40 | 29 | 56 |
| T-I | 1 (Days 1-28) | 9-M | 35 | 41 | 66 |
| | | 10-M | 20 | 9 | 20 |
| | | 11-M | 33 | 33 | 42 |
| | 30 (Days 29-90) | 12-M | 37 | 45 | 50 |
| | | 13-F | 35 | 33 | 43 |
| | | 14-F | 34 | 52 | 43 |
| | | 15-F | 34 | 38 | 47 |
| | | 16-F | 30 | 34 | 37 |
| T-II | 10 (Days 1-28) | 17-M | 29 | 27 | 38 |
| | | 18-M | 30 | 26 | 27 |
| | 300 (Days 29-90) | 19-M | 28 | 29 | 41 |
| | | 20-M | 26 | 29 | 41 |
| | | 21-F | 29 | 31 | 50 |
| | | 22-F | 24 | 29 | 37 |
| | | 23-F | 24 | 23 | 31 |
| | | 24-F | 41 | 34 | 51 |
| T-III | 100 | 25-M | 31 | 26 | 31 |
| | | 26-M | 35 | 31 | 33 |
| | | 27-M | 40 | 29 | 42 |
| | | 28-M | 37 | 32 | 34 |
| | | 29-F | 26 | 37 | 47 |
| | | 30-F | 26 | 20 | 27 |
| | | 31-F | 29 | 31 | 40 |
| | | 32-F | 29 | 31 | 35 |

note: fluorometric method by Levine and Hill.

G. Urine Analyses

The results of the urine analyses are presented in Tables XV through XIX.

No significant abnormalities were noted at any of the levels tested.

MONS 068771

TABLE XV

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Urine Analyses: Albumin, mg/100 ml

| Group | Dietary Level (ppm) | Dog Number and Sex | Days: 0 | 45 | 90 |
|---|---|---|---|---|---|
| UC | None | 1-M | 0 | 11-50 | 51-200 |
| | | 2-M | 0 | 11-50 | 11-50 |
| | | 3-M | 0 | 11-50 | 11-50 |
| | | 4-M | 0 | 11-50 | 11-50 |
| | | 5-F | 0 | 1-10 | 11-50 |
| | | 6-F | 0 | 1-10 | 11-50 |
| | | 7-F | 0 | 1-10 | 11-50 |
| | | 8-F | 0 | 1-10 | 1-10 |
| T-I | 1 (Days 1-28) | 9-M | 0 | 1-10 | 11-50 |
| | | 10-M | 1-10 | 1-10 | 1-10 |
| | | 11-M | 1-10 | 1-10 | 1-10 |
| | 30 (Days 29-90) | 12-M | 1-10 | 1-10 | 1-10 |
| | | 13-F | 11-50 | 1-10 | 0 |
| | | 14-F | 1-10 | 1-10 | 0 |
| | | 15-F | 1-10 | 1-10 | 11-50 |
| | | 16-F | 11-50 | 1-10 | 1-10 |
| T-II | 10 (Days 1-28) | 17-M | 11-50 | 1-10 | 1-10 |
| | | 18-M | 51-200 | 0 | 1-10 |
| | 300 (Days 29-90) | 19-M | 1-10 | 1-10 | 0 |
| | | 20-M | 1-10 | 1-10 | 11-50 |
| | | 21-F | 11-50 | 1-10 | 1-10 |
| | | 22-F | 1-10 | 1-10 | 0 |
| | | 23-F | 11-50 | 1-10 | 1-10 |
| | | 24-F | 1-10 | 1-10 | 1-10 |
| T-III | 100 | 25-M | 1-10 | 1-10 | 1-10 |
| | | 26-M | 1-10 | 0 | 1-10 |
| | | 27-M | 1-10 | 0 | 0 |
| | | 28-M | 1-10 | 1-10 | 0 |
| | | 29-F | 51-100 | 0 | 11-50 |
| | | 30-F | 11-50 | 0 | 0 |
| | | 31-F | 1-10 | 0 | 11-50 |
| | | 32-F | 1-10 | 0 | 1-10 |

TABLE XVI

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Urine Analyses: Glucose, mg/100 ml

| Group | Dietary Level (ppm) | Dog Number and Sex | Days: 0 | 45 | 90 |
|---|---|---|---|---|---|
| UC | None | 1-M | 0 | 0 | 0 |
| | | 2-M | 0 | 0 | 0 |
| | | 3-M | 0 | 0 | 0 |
| | | 4-M | 0 | 0 | 0 |
| | | 5-F | 0 | 0 | 0 |
| | | 6-F | 0 | 0 | 0 |
| | | 7-F | 0 | 0 | 0 |
| | | 8-F | 0 | 0 | 0 |
| T-I | 1 (Days 1-28) | 9-M | 0 | 0 | 0 |
| | | 10-M | 0 | 0 | 0 |
| | | 11-M | 0 | 0 | 0 |
| | 30 (Days 29-90) | 12-M | 0 | 0 | 0 |
| | | 13-F | 0 | 0 | 0 |
| | | 14-F | 0 | 0 | 0 |
| | | 15-F | 0 | 0 | 0 |
| | | 16-F | 0 | 0 | 0 |
| T-II | 10 (Days 1-28) | 17-M | 0 | 0 | 0 |
| | | 18-M | 0 | 0 | 0 |
| | 300 (Days 29-90) | 19-M | 0 | 0 | 0 |
| | | 20-M | 0 | 0 | 0 |
| | | 21-F | 0 | 0 | 0 |
| | | 22-F | 0 | 0 | 0 |
| | | 23-F | 0 | 0 | 0 |
| | | 24-F | 0 | 0 | 0 |
| T-III | 100 | 25-M | 0 | 0 | 0 |
| | | 26-M | 0 | 0 | 0 |
| | | 27-M | 0 | 0 | 0 |
| | | 28-M | 0 | 0 | 0 |
| | | 29-F | 0 | 0 | 0 |
| | | 30-F | 0 | 0 | 0 |
| | | 31-F | 0 | 0 | 0 |
| | | 32-F | 0 | 0 | 0 |

note: COMBISTIX, Ames Company, Inc., Elkhart, Indiana.

MONS 068773

TABLE XVII

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Urine Analyses: pH

| Group | Dietary Level (ppm) | Dog Number and Sex | Days: 0 | 45 | 90 |
|---|---|---|---|---|---|
| UC | None | 1-M | 7 | 8 | 9 |
| | | 2-M | 7 | 7 | 9 |
| | | 3-M | 7 | 7 | 9 |
| | | 4-M | 6 | 7 | 9 |
| | | 5-F | 6 | 8 | 8 |
| | | 6-F | 7 | 8 | 9 |
| | | 7-F | 7 | 7 | 9 |
| | | 8-F | 7 | 7 | 8 |
| T-I | 1 | 9-M | 8 | 8 | 7 |
| | (Days 1-28) | 10-M | 7 | 8 | 8 |
| | | 11-M | 7 | 8 | 8 |
| | 30 | 12-M | 7 | 8 | 8 |
| | (Days 29-90) | 13-F | 8 | 6 | 7 |
| | | 14-F | 7 | 8 | 6 |
| | | 15-F | 8 | 8 | 7 |
| | | 16-F | 8 | 8 | 8 |
| T-II | 10 | 17-M | 8 | 7 | 8 |
| | (Days 1-28) | 18-M | 8 | 6 | 8 |
| | 300 | 19-M | 8 | 8 | 7 |
| | (Days 29-90) | 20-M | 8 | 9 | 8 |
| | | 21-F | 8 | 8 | 8 |
| | | 22-F | 8 | 8 | 6 |
| | | 23-F | 8 | 7 | 8 |
| | | 24-F | 8 | 6 | 7 |
| T-III | 100 | 25-M | 8 | 8 | 8 |
| | | 26-M | 8 | 7 | 6 |
| | | 27-M | 7 | 6 | 7 |
| | | 28-M | 8 | 7 | 8 |
| | | 29-F | 8 | 8 | 8 |
| | | 30-F | 8 | 8 | 6 |
| | | 31-F | 8 | 8 | 8 |
| | | 32-F | 8 | 7 | 8 |

note: COMBISTIX, Ames Company, Inc., Elkhart, Indiana.

MONS 068774

TABLE XVIII

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Urine Analyses: Specific Gravity

| Group | Dietary Level (ppm) | Dog Number and Sex | Days: 0 | 45 | 90 |
|---|---|---|---|---|---|
| UC | None | 1-M | 1.005 | 1.038 | 1.0 |
| | | 2-M | 1.005 | 1.041 | 1.0 |
| | | 3-M | 1.032 | 1.045 | 1.0 |
| | | 4-M | 1.019 | 1.010 | 1.0 |
| | | 5-F | 1.012 | 1.022 | 1.0 |
| | | 6-F | 1.015 | 1.026 | 1.0 |
| | | 7-F | 1.019 | 1.012 | 1.0 |
| | | 8-F | 1.022 | 1.032 | 1.0 |
| T-I | 1 (Days 1-28) 30 (Days 29-90) | 9-M | 1.010 | 1.017 | 1.0 |
| | | 10-M | 1.015 | 1.024 | 1.0 |
| | | 11-M | 1.032 | 1.024 | 1.0 |
| | | 12-M | 1.048 | 1.019 | 1.0 |
| | | 13-F | 1.026 | 1.007 | 1.0 |
| | | 14-F | 1.038 | 1.026 | 1.0 |
| | | 15-F | 1.038 | 1.026 | 1.0 |
| | | 16-F | 1.038 | 1.024 | 1.0 |
| T-II | 10 (Days 1-28) 300 (Days 29-90) | 17-M | 1.029 | 1.015 | 1.0 |
| | | 18-M | 1.034 | 1.029 | 1.0 |
| | | 19-M | 1.029 | 1.019 | 1.0 |
| | | 20-M | 1.034 | 1.022 | 1.0 |
| | | 21-F | 1.032 | 1.026 | 1.0 |
| | | 22-F | 1.036 | 1.015 | 1.0 |
| | | 23-F | 1.036 | 1.026 | 1.0 |
| | | 24-F | 1.036 | 1.019 | 1.0 |
| T-III | 100 | 25-M | 1.034 | 1.015 | 1.0 |
| | | 26-M | 1.019 | 1.017 | 1.0 |
| | | 27-M | 1.029 | 1.022 | 1.0 |
| | | 28-M | 1.029 | 1.029 | 1.0 |
| | | 29-F | 1.029 | 1.012 | 1.0 |
| | | 30-F | 1.038 | 1.010 | 1.0 |
| | | 31-F | 1.045 | 1.010 | 1.0 |
| | | 32-F | 1.034 | 1.024 | 1.0 |

TABLE XIX

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Urine Analyses: Microscopic Elements, average per high power field - Leukocytes

| Group | Dietary Level (ppm) | Dog Number and Sex | Days: 0 | Days: 45 | Days: 90 |
|---|---|---|---|---|---|
| UC | None | 1-M | 0 | 0 | 0 |
| | | 2-M | 0 | 0 | 2 |
| | | 3-M | 0 | 0 | 0 |
| | | 4-M | 0 | 0 | 0 |
| | | 5-F | 0 | 6-8 | 20 |
| | | 6-F | 0 | 0 | 6 |
| | | 7-F | 0 | 0 | 20 |
| | | 8-F | 0 | 3-5 | 3 |
| T-I | 1 | 9-M | 0 | 0 | 0 |
| | (Days 1-28) | 10-M | 0 | 0 | 3 |
| | | 11-M | 0 | 0 | 6 |
| | 30 | 12-M | 0 | 0 | 2 |
| | (Days 29-90) | 13-F | >500 | 0 | 10 |
| | | 14-F | 0 | 12-15 | 3 |
| | | 15-F | 4-6 | 0 | 20 |
| | | 16-F | 6-8 | 0 | 12 |
| T-II | 10 | 17-M | 0 | 3-5 | 0 |
| | (Days 1-28) | 18-M | 0 | 0 | 3 |
| | 300 | 19-M | 0 | 0 | 0 |
| | (Days 29-90) | 20-M | 0 | 3-5 | 0 |
| | | 21-F | 4-6 | 90-100 | 50 |
| | | 22-F | 0 | 0 | 3 |
| | | 23-F | 0 | 10-12 | 20 |
| | | 24-F | 2-4 | 90-100 | 20 |
| T-III | 100 | 25-M | 0 | 0 | 0 |
| | | 26-M | 0 | 0 | 0 |
| | | 27-M | 0 | 0 | 0 |
| | | 28-M | 0 | 0 | 0 |
| | | 29-F | 8-12 | 0 | 20 |
| | | 30-F | 12-15 | 0 | 3 |
| | | 31-F | 0 | 0 | 3 |
| | | 32-F | 0 | 0 | 15 |

TABLE XIX continued

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

**Urine Analyses:** Microscopic Elements, average per high power field - Erythrocytes

| Group | Dietary Level (ppm) | Dog Number and Sex | Days: 0 | 45 | 90 |
|---|---|---|---|---|---|
| UC | None | 1-M | 0 | 0 | 4 |
| | | 2-M | 0 | 0 | 1 |
| | | 3-M | 0 | 6-8 | 0 |
| | | 4-M | 0 | 0 | 0 |
| | | 5-F | 0 | 0 | 2 |
| | | 6-F | 0 | 0 | 0 |
| | | 7-F | 0 | 0 | 2 |
| | | 8-F | 0 | 0 | 0 |
| T-I | 1 (Days 1-28) | 9-M | 0 | 0 | 0 |
| | | 10-M | 0 | 0 | 1 |
| | | 11-M | 0 | 0 | 0 |
| | 30 (Days 29-90) | 12-M | 0 | 0 | 0 |
| | | 13-F | 6-8 | 0 | 3 |
| | | 14-F | 0 | 0 | 0 |
| | | 15-F | 0 | 0 | 0 |
| | | 16-F | 0 | 0 | 3 |
| T-II | 10 (Days 1-28) | 17-M | 0 | 0 | 0 |
| | | 18-M | 0 | 0 | 0 |
| | 300 (Days 29-90) | 19-M | 0 | 0 | 0 |
| | | 20-M | 0 | 4-6 | 0 |
| | | 21-F | 0 | 0 | 0 |
| | | 22-F | 0 | 0 | 0 |
| | | 23-F | 0 | 0 | 0 |
| | | 24-F | 0 | 0 | 0 |
| T-III | 100 | 25-M | 0 | 0 | 0 |
| | | 26-M | 0 | 0 | 0 |
| | | 27-M | 0 | 0 | 0 |
| | | 28-M | 0 | 0 | 0 |
| | | 29-F | 0 | 0 | 0 |
| | | 30-F | 0 | 0 | 0 |
| | | 31-F | 0 | 0 | 0 |
| | | 32-F | 0 | 0 | 0 |

TABLE XIX continued

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Urine Analyses: Microscopic Elements, average per high power field - Crystals

| Group | Dietary Level (ppm) | Dog Number and Sex | Days: 0 | 45 | 90 |
|---|---|---|---|---|---|
| UC | None | 1-M | 1-3 | 1-3 | 1-3 |
| | | 2-M | 1-3 | 1-3 | 1-3 |
| | | 3-M | 1-3 | 1-3 | 1-3 |
| | | 4-M | 1-3 | 1-3 | 1-3 |
| | | 5-F | 1-3 | 4 | 1-3 |
| | | 6-F | 1-3 | 1-3 | 1-3 |
| | | 7-F | 1-3 | 1-3 | 1-3 |
| | | 8-F | 1-3 | 1-3 | 1-3 |
| T-I | 1 (Days 1-28) | 9-M | 1-3 | 1-3 | 1-3 |
| | | 10-M | 1-3 | 1-3 | 1-3 |
| | | 11-M | 1-3 | 1-3 | 1-3 |
| | 30 (Days 29-90) | 12-M | 1-3 | 1-3 | 1-3 |
| | | 13-F | 1-3 | 1-3 | 1-3 |
| | | 14-F | 1-3 | 1-3 | 1-3 |
| | | 15-F | 1-3 | 1-3 | 1-3 |
| | | 16-F | 1-3 | 1-3 | 1-3 |
| T-II | 10 (Days 1-28) | 17-M | 1-3 | 1-3 | 1-3 |
| | | 18-M | 1-3 | 1-3 | 1-3 |
| | 300 (Days 29-90) | 19-M | 1-3 | 1-3 | 1-3 |
| | | 20-M | 1-3 | 1-3 | 1-3 |
| | | 21-F | 1-3 | 1-3 | 1-3 |
| | | 22-F | 1-3 | 1-3 | 1-3 |
| | | 23-F | 1-3 | 1-3 | 1-3 |
| | | 24-F | 1-3 | 1-3 | 1-3 |
| T-III | 100 | 25-M | 1-3 | 1-3 | 1-3 |
| | | 26-M | 1-3 | 1-3 | 1-3 |
| | | 27-M | 1-3 | 1-3 | 1-3 |
| | | 28-M | 1-3 | 1-3 | 1-3 |
| | | 29-F | 1-3 | 1-3 | 1-3 |
| | | 30-F | 1-3 | 1-3 | 1-3 |
| | | 31-F | 1-3 | 1-3 | 1-3 |
| | | 32-F | 1-3 | 1-3 | 1-3 |

H. Pathologic Findings

1. Organ Weight Data

The organ weight data are presented in Tables XX through XXVIII.

All organ weights and ratios fall within limits accepted as normal for the beagle, with the exception of elevated liver to body weight ratios for two animals at the highest dietary level of MCS 1016 (10 ppm Days 1-28, 300 ppm Days 29-90), 21-F and 22-F. There were no clinical or histological indications of liver pathology in these two animals.

TABLE XX

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Organ Weight Data: Liver

| Group | Dietary Level (ppm) | Dog Number and Sex | Organ Weight (g) | Organ/Body Weight Ratio (g/1,000 g) |
|---|---|---|---|---|
| UC | None | 1-M | 318.4 | 39.8 |
| | | 2-M | 335.4 | 36.8 |
| | | 3-M | 299.4 | 34.8 |
| | | 4-M | 315.0 | 29.7 |
| | | 5-F | 278.2 | 29.9 |
| | | 6-F | 277.8 | 33.1 |
| | | 7-F | 211.7 | 34.1 |
| | | 8-F | 234.1 | 32.5 |
| T-I | 1 (Days 1-28) | 9-M | 254.7 | 23.8 |
| | | 10-M | 199.7 | 29.8 |
| | | 11-M | 275.0 | 25.7 |
| | 30 (Days 29-90) | 12-M | 258.5 | 26.1 |
| | | 13-F | 245.4 | 29.2 |
| | | 14-F | 219.1 | 27.4 |
| | | 15-F | 180.1 | 22.0 |
| | | 16-F | 220.0 | 22.7 |
| T-II | 10 (Days 1-28) | 17-M | 281.2 | 26.7 |
| | | 18-M | 236.1 | 29.5 |
| | 300 (Days 29-90) | 19-M | 224.7 | 30.0 |
| | | 20-M | 289.9 | 29.0 |
| | | 21-F | 382.8 | 50.4 |
| | | 22-F | 375.1 | 53.6 |
| | | 23-F | 358.6 | 42.7 |
| | | 24-F | 251.2 | 44.1 |
| T-III | 100 | 25-M | 423.1 | 37.4 |
| | | 26-M | 242.1 | 26.3 |
| | | 27-M | 289.6 | 31.5 |
| | | 28-M | 410.1 | 42.3 |
| | | 29-F | 315.8 | 32.6 |
| | | 30-F | 300.2 | 42.9 |
| | | 31-F | 358.0 | 34.8 |
| | | 32-F | 374.0 | 39.0 |

TABLE XXI

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Organ Weight Data: Kidneys

| Group | Dietary Level (ppm) | Dog Number and Sex | Organ Weight (g) | Organ/Body Weight Ratio (g/1,000 g) |
|---|---|---|---|---|
| UC | None | 1-M | 47.3 | 5.91 |
| | | 2-M | 46.6 | 5.12 |
| | | 3-M | 53.0 | 6.16 |
| | | 4-M | 56.3 | 5.31 |
| | | 5-F | 41.2 | 4.43 |
| | | 6-F | 47.1 | 5.61 |
| | | 7-F | 33.7 | 5.44 |
| | | 8-F | 38.2 | 5.30 |
| T-I | 1 | 9-M | 47.2 | 4.41 |
| | (Days 1-28) | 10-M | 29.7 | 4.43 |
| | | 11-M | 56.2 | 5.25 |
| | 30 | 12-M | 60.1 | 6.07 |
| | (Days 29-90) | 13-F | 39.6 | 4.71 |
| | | 14-F | 43.3 | 5.34 |
| | | 15-F | 44.4 | 5.41 |
| | | 16-F | 47.9 | 4.94 |
| T-II | 10 | 17-M | 46.0 | 4.38 |
| | (Days 1-28) | 18-M | 49.8 | 6.22 |
| | 300 | 19-M | 39.0 | 5.20 |
| | (Days 29-90) | 20-M | 42.3 | 4.23 |
| | | 21-F | 34.8 | 4.58 |
| | | 22-F | 36.1 | 5.16 |
| | | 23-F | 47.9 | 5.70 |
| | | 24-F | 38.3 | 6.72 |
| T-III | 100 | 25-M | 56.7 | 5.02 |
| | | 26-M | 40.2 | 4.37 |
| | | 27-M | 43.5 | 4.73 |
| | | 28-M | 57.8 | 5.96 |
| | | 29-F | 47.8 | 4.93 |
| | | 30-F | 40.0 | 5.71 |
| | | 31-F | 48.4 | 4.70 |
| | | 32-F | 48.0 | 5.00 |

TABLE XXII

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Organ Weight Data: Heart

| Group | Dietary Level (ppm) | Dog Number and Sex | Organ Weight (g) | Organ/Body Weight Ratio (g/1,000 g) |
|---|---|---|---|---|
| UC | None | 1-M | 68.3 | 8.54 |
| | | 2-M | 61.5 | 6.76 |
| | | 3-M | 56.6 | 6.58 |
| | | 4-M | 79.6 | 7.51 |
| | | 5-F | 72.8 | 7.83 |
| | | 6-F | 69.4 | 8.26 |
| | | 7-F | 47.7 | 7.69 |
| | | 8-F | 54.5 | 7.57 |
| T-I | 1 | 9-M | 88.1 | 8.23 |
| | (Days 1-28) | 10-M | 47.1 | 7.03 |
| | | 11-M | 66.6 | 6.22 |
| | 30 | 12-M | 67.8 | 6.85 |
| | (Days 29-90) | 13-F | 61.7 | 7.35 |
| | | 14-F | 63.5 | 7.94 |
| | | 15-F | 74.1 | 9.04 |
| | | 16-F | 78.7 | 8.11 |
| T-II | 10 | 17-M | 75.1 | 7.15 |
| | (Days 1-28) | 18-M | 64.3 | 8.04 |
| | 300 | 19-M | 52.3 | 6.97 |
| | (Days 29-90) | 20-M | 70.1 | 7.01 |
| | | 21-F | 55.9 | 7.36 |
| | | 22-F | 56.2 | 8.03 |
| | | 23-F | 61.9 | 7.37 |
| | | 24-F | 39.6 | 6.95 |
| T-III | 100 | 25-M | 87.7 | 7.76 |
| | | 26-M | 57.2 | 6.22 |
| | | 27-M | 65.0 | 7.06 |
| | | 28-M | 78.2 | 8.06 |
| | | 29-F | 69.4 | 7.15 |
| | | 30-F | 50.1 | 7.16 |
| | | 31-F | 60.3 | 5.85 |
| | | 32-F | 72.2 | 7.52 |

MONS 068782

TABLE XXIII

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Organ Weight Data: Brain

| Group | Dietary Level (ppm) | Dog Number and Sex | Organ Weight (g) | Organ/Body Weight Ratio (g/1,000 g) |
|---|---|---|---|---|
| UC | None | 1-M | 69.3 | 8.66 |
| | | 2-M | 80.5 | 8.85 |
| | | 3-M | 74.6 | 8.67 |
| | | 4-M | 75.9 | 7.16 |
| | | 5-F | 82.6 | 8.88 |
| | | 6-F | 73.3 | 8.73 |
| | | 7-F | 64.5 | 10.4 |
| | | 8-F | 72.1 | 10.0 |
| T-I | 1 | 9-M | 80.6 | 7.53 |
| | (Days 1-28) | 10-M | 68.1 | 10.2 |
| | | 11-M | 80.2 | 7.50 |
| | 30 | 12-M | 79.0 | 7.98 |
| | (Days 29-90) | 13-F | 73.3 | 8.73 |
| | | 14-F | 68.5 | 8.56 |
| | | 15-F | 71.2 | 8.68 |
| | | 16-F | 78.9 | 8.13 |
| T-II | 10 | 17-M | 80.8 | 7.70 |
| | (Days 1-28) | 18-M | 73.7 | 9.21 |
| | 300 | 19-M | 76.0 | 10.1 |
| | (Days 29-90) | 20-M | 78.3 | 7.83 |
| | | 21-F | 83.9 | 11.0 |
| | | 22-F | 65.4 | 9.34 |
| | | 23-F | 65.7 | 7.82 |
| | | 24-F | 68.6 | 12.0 |
| T-III | 100 | 25-M | 81.5 | 7.21 |
| | | 26-M | 79.9 | 8.68 |
| | | 27-M | 73.8 | 8.02 |
| | | 28-M | 74.1 | 7.64 |
| | | 29-F | 68.2 | 7.03 |
| | | 30-F | 62.3 | 8.90 |
| | | 31-F | 73.8 | 7.16 |
| | | 32-F | 43.6 | 4.54 |

TABLE XXIV

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Organ Weight Data: Spleen

| Group | Dietary Level (ppm) | Dog Number and Sex | Organ Weight (g) | Organ/Body Weight Ratio (g/1,000 g) |
|---|---|---|---|---|
| UC | None | 1-M | 19.2 | 2.40 |
| | | 2-M | 27.4 | 3.01 |
| | | 3-M | 17.2 | 2.00 |
| | | 4-M | 23.6 | 2.23 |
| | | 5-F | 23.1 | 2.48 |
| | | 6-F | 20.0 | 2.38 |
| | | 7-F | 15.8 | 2.55 |
| | | 8-F | 15.3 | 2.12 |
| T-I | 1 (Days 1-28) | 9-M | 19.8 | 1.85 |
| | | 10-M | 14.2 | 2.12 |
| | | 11-M | 20.7 | 1.93 |
| | 30 (Days 29-90) | 12-M | 21.7 | 2.19 |
| | | 13-F | 19.3 | 2.30 |
| | | 14-F | 14.8 | 1.85 |
| | | 15-F | 14.9 | 1.82 |
| | | 16-F | 16.9 | 1.74 |
| T-II | 10 (Days 1-28) | 17-M | 16.9 | 1.61 |
| | | 18-M | 18.0 | 2.25 |
| | 300 (Days 29-90) | 19-M | 16.5 | 2.20 |
| | | 20-M | 15.1 | 1.51 |
| | | 21-F | 24.1 | 3.17 |
| | | 22-F | 21.6 | 3.08 |
| | | 23-F | 24.2 | 2.88 |
| | | 24-F | 10.4 | 1.82 |
| T-III | 100 | 25-M | 20.3 | 1.80 |
| | | 26-M | 17.2 | 1.87 |
| | | 27-M | 17.4 | 1.89 |
| | | 28-M | 20.8 | 2.14 |
| | | 29-F | 23.0 | 2.37 |
| | | 30-F | 21.4 | 3.06 |
| | | 31-F | 21.2 | 2.06 |
| | | 32-F | 21.2 | 2.21 |

MONS 068784

TABLE XXV

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Organ Weight Data: Gonads

| Group | Dietary Level (ppm) | Dog Number and Sex | Organ Weight (g) | Organ/Body Weight Ratio (g/1,000 g) |
|---|---|---|---|---|
| UC | None | 1-M | 4.9 | 0.612 |
| | | 2-M | 18.2 | 2.00 |
| | | 3-M | 4.5 | 0.523 |
| | | 4-M | 5.8 | 0.547 |
| | | 5-F | 0.627 | 0.0670 |
| | | 6-F | 0.486 | 0.0570 |
| | | 7-F | 0.573 | 0.0920 |
| | | 8-F | 0.460 | 0.0630 |
| T-I | 1 | 9-M | 17.5 | 1.84 |
| | (Days 1-28) | 10-M | 7.3 | 1.09 |
| | | 11-M | 6.7 | 0.626 |
| | 30 | 12-M | 11.4 | 1.15 |
| | (Days 29-90) | 13-F | 0.776 | 0.0924 |
| | | 14-F | 0.590 | 0.0738 |
| | | 15-F | 0.680 | 0.0829 |
| | | 16-F | 0.816 | 0.0841 |
| T-II | 10 | 17-M | 14.2 | 1.35 |
| | (Days 1-28) | 18-M | 5.9 | 0.738 |
| | 300 | 19-M | 3.5 | 0.467 |
| | (Days 29-90) | 20-M | 5.3 | 0.530 |
| | | 21-F | 0.556 | 0.0732 |
| | | 22-F | 0.541 | 0.0773 |
| | | 23-F | 0.548 | 0.0652 |
| | | 24-F | 0.351 | 0.0616 |
| T-III | 100 | 25-M | 19.7 | 1.74 |
| | | 26-M | 11.8 | 1.28 |
| | | 27-M | 15.2 | 1.65 |
| | | 28-M | 10.4 | 1.07 |
| | | 29-F | 0.656 | 0.0676 |
| | | 30-F | 0.502 | 0.0717 |
| | | 31-F | 0.624 | 0.0606 |
| | | 32-F | 0.856 | 0.0892 |

TABLE XXVI

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Organ Weight Data: Adrenal Glands

| Group | Dietary Level (ppm) | Dog Number and Sex | Organ Weight (g) | Organ/Body Weight Ratio (g/1,000 g) |
|---|---|---|---|---|
| UC | None | 1-M | 1.042 | 0.130 |
| | | 2-M | 1.110 | 0.121 |
| | | 3-M | 0.754 | 0.0870 |
| | | 4-M | 1.073 | 0.101 |
| | | 5-F | 1.188 | 0.127 |
| | | 6-F | 1.122 | 0.133 |
| | | 7-F | 0.831 | 0.134 |
| | | 8-F | 0.808 | 0.112 |
| T-I | 1 | 9-M | 1.092 | 0.102 |
| | (Days 1-28) | 10-M | 0.752 | 0.109 |
| | | 11-M | 1.395 | 0.130 |
| | 30 | 12-M | 1.135 | 0.115 |
| | (Days 29-90) | 13-F | 1.057 | 0.126 |
| | | 14-F | 0.994 | 0.124 |
| | | 15-F | 0.983 | 0.120 |
| | | 16-F | 0.674 | 0.0695 |
| T-II | 10 | 17-M | 1.007 | 0.0959 |
| | (Days 1-28) | 18-M | 0.996 | 0.124 |
| | 300 | 19-M | 0.842 | 0.112 |
| | (Days 29-90) | 20-M | 1.262 | 0.126 |
| | | 21-F | 0.894 | 0.118 |
| | | 22-F | 0.740 | 0.106 |
| | | 23-F | 0.889 | 0.106 |
| | | 24-F | 0.700 | 0.123 |
| T-III | 100 | 25-M | 1.357 | 0.120 |
| | | 26-M | 0.949 | 0.103 |
| | | 27-M | 0.927 | 0.101 |
| | | 28-M | 1.150 | 0.118 |
| | | 29-F | 1.194 | 0.123 |
| | | 30-F | 0.823 | 0.118 |
| | | 31-F | 0.972 | 0.0944 |
| | | 32-F | 1.180 | 0.123 |

TABLE XXVII

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Organ Weight Data: Thyroid Gland

| Group | Dietary Level (ppm) | Dog Number and Sex | Organ Weight (g) | Organ/Body Weight Ratio (g/1,000 g) |
|---|---|---|---|---|
| UC | None | 1-M | 1.017 | 0.127 |
| | | 2-M | 0.894 | 0.0980 |
| | | 3-M | 0.768 | 0.0890 |
| | | 4-M | 1.438 | 0.135 |
| | | 5-F | 0.782 | 0.0840 |
| | | 6-F | 1.082 | 0.128 |
| | | 7-F | 0.870 | 0.140 |
| | | 8-F | 0.663 | 0.0920 |
| T-I | 1 | 9-M | 0.903 | 0.0844 |
| | (Days 1-28) | 10-M | 0.547 | 0.0816 |
| | | 11-M | 1.150 | 0.106 |
| | 30 | 12-M | 1.110 | 0.112 |
| | (Days 29-90) | 13-F | 1.382 | 0.164 |
| | | 14-F | 0.774 | 0.0968 |
| | | 15-F | 0.992 | 0.121 |
| | | 16-F | 1.002 | 0.103 |
| T-II | 10 | 17-M | 0.830 | 0.0790 |
| | (Days 1-28) | 18-M | 0.952 | 0.119 |
| | 300 | 19-M | 0.660 | 0.0880 |
| | (Days 29-90) | 20-M | 0.877 | 0.0877 |
| | | 21-F | 0.793 | 0.104 |
| | | 22-F | 0.772 | 0.110 |
| | | 23-F | 0.834 | 0.0993 |
| | | 24-F | 0.470 | 0.0824 |
| T-III | 100 | 25-M | 1.053 | 0.0932 |
| | | 26-M | 0.896 | 0.0974 |
| | | 27-M | 0.808 | 0.0878 |
| | | 28-M | 1.101 | 0.114 |
| | | 29-F | 0.607 | 0.0626 |
| | | 30-F | 0.669 | 0.0956 |
| | | 31-F | 0.750 | 0.0728 |
| | | 32-F | 1.141 | 0.119 |

TABLE XXVIII

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Organ Weight Data: Pituitary Gland

| Group | Dietary Level (ppm) | Dog Number and Sex | Organ Weight (g) | Organ/Body Weight Ratio (g/1,000 g) |
|---|---|---|---|---|
| UC | None | 1-M | 0.087 | 0.0100 |
| | | 2-M | 0.106 | 0.0116 |
| | | 3-M | 0.093 | 0.0108 |
| | | 4-M | 0.063 | 0.00594 |
| | | 5-F | 0.080 | 0.00860 |
| | | 6-F | 0.095 | 0.0113 |
| | | 7-F | 0.062 | 0.0100 |
| | | 8-F | 0.073 | 0.0101 |
| T-I | 1 | 9-M | 0.089 | 0.00852 |
| | (Days 1-28) | 10-M | 0.082 | 0.0122 |
| | | 11-M | 0.083 | 0.00748 |
| | 30 | 12-M | 0.085 | 0.00858 |
| | (Days 29-90) | 13-F | 0.099 | 0.0116 |
| | | 14-F | 0.106 | 0.0132 |
| | | 15-F | 0.091 | 0.0111 |
| | | 16-F | 0.106 | 0.0109 |
| T-II | 10 | 17-M | 0.081 | 0.00771 |
| | (Days 1-28) | 18-M | 0.094 | 0.0118 |
| | 300 | 19-M | 0.076 | 0.0101 |
| | (Days 29-90) | 20-M | 0.114 | 0.0114 |
| | | 21-F | 0.072 | 0.00947 |
| | | 22-F | 0.092 | 0.0131 |
| | | 23-F | 0.084 | 0.0100 |
| | | 24-F | 0.075 | 0.0132 |
| T-III | 100 | 25-M | 0.112 | 0.00991 |
| | | 26-M | 0.090 | 0.00978 |
| | | 27-M | 0.073 | 0.00793 |
| | | 28-M | 0.118 | 0.0122 |
| | | 29-F | 0.085 | 0.00876 |
| | | 30-F | 0.092 | 0.0131 |
| | | 31-F | 0.074 | 0.00718 |
| | | 32-F | 0.105 | 0.0109 |

2. Gross and Histologic Findings

The gross and histologic findings are presented in Tables XXIX through XXXII. All tissues and organs not mentioned were normal.

The grading system used is as follows:

\+ = minimal/trace
++ = mild
+++ = moderate
++++ = severe

IBT No. C9887
Monsanto

January 4, 1972

I have completed a histopathologic evaluation of tissues from dogs of the above study. No lesions were observed that could be attributed to the test material. The lesions described are those of naturally occurring disease and they are not unusual in beagle dogs.

Donovan E. Gordon, D. V. M., Ph. D.
Diplomate, American College of
Veterinary Pathologists

## TABLE XXIX

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Gross and Histologic Findings

Untreated Control Group

| Dog Number and Sex | Organ | Gross | Grade | Histologic | Grade |
|---|---|---|---|---|---|
| 1-M | Kidney | - | - | Proteinaceous tubular casts | + |
| 2-M | Liver | - | - | Focal congestion | + |
| 3-M | Spleen | - | - | Siderofibrotic nodules | + |
| 4-M | Lungs | Petechiae | +++ | Focal hemorrhages | + |
| 5-F | Kidney | - | - | Focal interstitial lymphocytic infiltration | + |
| 6-F | - | - | - | - | - |
| 7-F | Liver | - | - | Focal sinusoidal infiltrations of lymphoidal cells | + |
| 8-F | - | - | - | - | - |



MONS 068791

TABLE XXX

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Gross and Histologic Findings

Test Group I: 1 ppm (Days 1-28), 30 ppm (Days 29-90)

| Dog Number and Sex | Organ | Gross | Grade | Histologic | Grade |
|---|---|---|---|---|---|
| 9-M | Lymph node (mesenteric) | - | - | Focal lymphoid hyperplasia | + |
| | Prostate gland | - | - | Chronic focal prostatitis | + |
| 10-M | Lymph node (mesenteric) | - | - | Subcapsular granuloma (parasitic) | + |
| | Prostate gland | - | - | Chronic focal prostatitis | + |
| 11-M | Lungs | - | - | Focal hemorrhage (agonal) | + |
| 12-M | Small intestine (ileum) | - | - | Submucosal granuloma (parasitic) | + |
| 13-F | - | - | - | - | - |
| 14-F | Lungs | - | - | Focal hemorrhage (agonal) | + |
| 15-F | Lymph node (mesenteric) | - | - | Parasitic granuloma | + |
| 16-F | Lungs | - | - | Focal hemorrhage (agonal) | + |

TABLE XXXI

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Gross and Histologic Findings

Test Group II: 10 ppm (Days 1-28), 300 ppm (Days 29-90)

| Dog Number and Sex | Organ | Gross | Grade | Histologic | Grade |
|---|---|---|---|---|---|
| 17-M | - | - | - | - | - |
| 18-M | - | - | - | - | - |
| 19-M | - | - | - | - | - |
| 20-M | - | - | - | - | - |
| 21-F | Lymph node (mesenteric) | - | - | Parasitic granuloma | + |
| | Thyroid gland | - | - | Parasitic granuloma | + |
| 22-F | - | - | - | - | - |
| 23-F | Lymph node (mesenteric) | - | - | Subcapsular granulomas (parasitic) | + |
| 24-F | Lungs | - | - | Focal hemorrhage and emphysema (agonal) | + |

Industrial BIO-TEST Laboratories, Inc.

MONS 068793

## TABLE XXXII

### TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Gross and Histologic Findings

Test Group III: 100 ppm

| Dog Number and Sex | Organ | Gross | Grade | Histologic | Grade |
|---|---|---|---|---|---|
| 25-M | Lymph node (mesenteric) | - | - | Parasitic granulomas | ++ |
| 26-M | Lymph node (mesenteric) | - | - | Parasitic granulomas | + |
| 27-M | - | - | - | - | - |
| 28-M | Liver | - | - | Portal infiltrations of cosinophils (parasitic) | + |
| | Lymph node (mesenteric) | - | - | Focal subcapsular infiltrations of eosinophils (parasitic) | + |
| 29-F | Lymph node (mesenteric) | - | - | Parasitic granuloma | + |
| 30-F | - | - | - | - | - |
| 31-F | Lymph node (mesenteric) | - | - | Parasitic granulomas | + |
| | Small intestine (jejunum) | - | - | Focal enteritis (parasitic) | + |
| 32-F | Lymph node (mesenteric) | - | - | Subcapsular infiltrations of eosinophils (parasitic) | + |



MONS 068794