OJECT 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

TOXSTUDIES1962

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

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TOXSTUDIES1963

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.

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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.
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Paul L. Wright, Ph. D.
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Manager, Toxicology

January 31, 1972

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TOXSTUDIES1965

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.

TOXSTUDIES1966

TABLE I

TEST MATERIAL: MCS 1016

90-Day Subacute Oral Toxicity Study - Beagle Dogs

Test Organization and Diet Composition

Group	Number of Animals Male	Female		Dietary Constituents 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.

Industrial BIO-TEST Laboratories, Inc.

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TOXSTUDIES1967

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:

TOXSTUDIES1968

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):

TOXSTUDIES1969

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, jejunum, ileum)
Esophagus	Spinal Cord
Gall Bladder	Spleen
Gonads	Stomach (cardia, fundus, pylorus)
Heart	Trachea
Kidneys	Thyroid Gland
Liver	Uterus
Lungs	Urinary Bladder
Lymph Nodes (cervical, mesenteric)	
Muscle (skeletal)	

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

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TOXSTUDIES1970

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.

TOXSTUDIES1971

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 0	1	2	3	4	5	6	7	8	9	10	11	12	13	Overall Weight Gain
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

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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														Overall Weight Gain
				0	1	2	3	4	5	6	7	8	9	10	11	12	13	
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

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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.

TOXSTUDIES1974

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	307	325	334
5		292	294	259	330	352	312	303	372
6		274	285	259	283	318	340	310	280
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.

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TOXSTUDIES1975

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	*	**	
9		214	255	232	289	321	309	283	
10		264	226	222	263	270	286	282	
11		287	208	210	268	304	337	328	
12		280	312	305	278	345	259	288	
13		269	187	219	195	340	343	296	
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.

TOXSTUDIES1976

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.

TOXSTUDIES1977

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	18.3	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

TOXSTUDIES1978

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	6.59	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

TOXSTUDIES1979

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 (Days 1-28)	9-M	13.3	14.3	15.9
		10-M	14.5	14.0	14.2
		11-M	14.8	13.8	15.0
	30 (Days 29-90)	12-M	15.3	14.4	15.0
		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 (Days 1-28)	17-M	14.9	14.0	15.3
		18-M	13.7	13.7	13.9
	300 (Days 29-90)	19-M	13.3	13.2	14.2
		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

TOXSTUDIES1980

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	45
		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

0366433

TOXSTUDIES1981

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	9-M	60	54	50
	(Days 1-28)	10-M	65	61	74
		11-M	65	56	63
	30	12-M	57	65	67
	(Days 29-90)	13-F	64	57	60
		14-F	57	62	63
		15-F	42	56	58
		16-F	69	56	53
T-II	10	17-M	56	58	51
	(Days 1-28)	18-M	58	70	71
	300	19-M	70	60	62
	(Days 29-90)	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

0366434

TOXSTUDIES1982

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

0366435

TOXSTUDIES1983

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	9-M	0	0	0
	(Days 1-28)	10-M	0	0	0
		11-M	0	0	0
	30	12-M	0	0	0
	(Days 29-90)	13-F	0	0	0
		14-F	0	0	0
		15-F	0	0	0
		16-F	0	0	0
T-II	10	17-M	0	0	0
	(Days 1-28)	18-M	0	0	0
	300	19-M	0	0	0
	(Days 29-90)	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

0366436

TOXSTUDIES1984

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)	9-M	5	5	
		10-M	3	7	
		11-M	7	10	
	30 (Days 29-90)	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)	17-M	2	3	
		18-M	1	0	
	300 (Days 29-90)	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	

TOXSTUDIES1985

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	9-M	0	1	0
	(Days 1-28)	10-M	0	0	0
		11-M	0	0	0
	30	12-M	0	0	0
	(Days 29-90)	13-F	0	0	0
		14-F	1	0	0
		15-F	0	0	0
		16-F	0	0	0
T-II	10	17-M	0	0	0
	(Days 1-28)	18-M	1	0	0
	300	19-M	0	0	0
	(Days 29-90)	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

TOXSTUDIES1986

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.

TOXSTUDIES1987

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 (Days 1-28) 30 (Days 29-90)	9-M	7	14	11
		10-M	8	13	12
		11-M	9	13	10
		12-M	8	12	11
		13-F	11	18	14
		14-F	9	16	13
		15-F	9	15	11
		16-F	11	16	16
T-II	10 (Days 1-28) 300 (Days 29-90)	17-M	7	13	10
		18-M	6	8	9
		19-M	8	10	10
		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 Gochman.

0366440

TOXSTUDIES1988

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	105	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

TOXSTUDIES1989

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.

0366442

TOXSTUDIES1990

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	9-M	25	26	25
	(Days 1-28)	10-M	17	23	21
		11-M	22	33	22
	30	12-M	16	22	23
	(Days 29-90)	13-F	20	29	32
		14-F	22	30	25
		15-F	20	26	31
		16-F	28	31	31
T-II	10	17-M	21	29	27
	(Days 1-28)	18-M	71	28	22
	300	19-M	56	27	29
	(Days 29-90)	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	24

note: fluorometric method by Levine and Hill.

0366443

TOXSTUDIES1991

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) 30 (Days 29-90)	9-M	35	41	66
		10-M	20	9	20
		11-M	33	33	42
		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) 300 (Days 29-90)	17-M	29	27	38
		18-M	30	26	27
		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.

0366444

TOXSTUDIES1992

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.

TOXSTUDIES1993

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	9-M	0	1-10	11-50
	(Days 1-28)	10-M	1-10	1-10	1-10
		11-M	1-10	1-10	1-10
	30	12-M	1-10	1-10	1-10
	(Days 29-90)	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	17-M	11-50	1-10	1-10
	(Days 1-28)	18-M	51-200	0	1-10
	300	19-M	1-10	1-10	0
	(Days 29-90)	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

0366446

TOXSTUDIES1994

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) 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	0	0	0
		32-F	0	0	0

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

0366447

TOXSTUDIES1995

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 (Days 1-28) 30 (Days 29-90)	9-M	8	8	7
		10-M	7	8	8
		11-M	7	8	8
		12-M	7	8	8
		13-F	8	6	7
		14-F	7	8	6
		15-F	8	8	7
		16-F	8	8	8
T-II	10 (Days 1-28) 300 (Days 29-90)	17-M	8	7	8
		18-M	8	6	8
		19-M	8	8	7
		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.

0366448

TOXSTUDIES1996

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[illegible]
		2-M	1.005	1.041	1.0[illegible]
		3-M	1.032	1.045	1.0[illegible]
		4-M	1.019	1.010	1.0[illegible]
		5-F	1.012	1.022	1.0[illegible]
		6-F	1.015	1.026	1.0[illegible]
		7-F	1.019	1.012	1.0[illegible]
		8-F	1.022	1.032	1.0[illegible]
T-I	1 (Days 1-28)	9-M	1.010	1.017	1.0[illegible]
		10-M	1.015	1.024	1.0[illegible]
		11-M	1.032	1.034	1.0[illegible]
	30 (Days 29-90)	12-M	1.048	1.019	1.0[illegible]
		13-F	1.026	1.007	1.0[illegible]
		14-F	1.036	1.026	1.0[illegible]
		15-F	1.038	1.026	1.0[illegible]
		16-F	1.038	1.024	1.0[illegible]
T-II	10 (Days 1-28)	17-M	1.029	1.015	1.0[illegible]
		18-M	1.034	1.029	1.0[illegible]
	300 (Days 29-90)	19-M	1.029	1.019	1.0[illegible]
		20-M	1.034	1.022	1.0[illegible]
		21-F	1.032	1.026	1.0[illegible]
		22-F	1.036	1.015	1.0[illegible]
		23-F	1.036	1.026	1.032
		24-F	1.036	1.019	1.0[illegible]
T-III	100	25-M	1.034	1.015	1.0[illegible]
		26-M	1.019	1.017	1.0[illegible]
		27-M	1.029	1.022	1.0[illegible]
		28-M	1.029	1.029	1.0[illegible]
		29-F	1.029	1.012	1.0[illegible]
		30-F	1.038	1.010	1.0[illegible]
		31-F	1.045	1.010	1.0[illegible]
		32-F	1.034	1.024	1.0[illegible]

TOXSTUDIES1997

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	45	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	5
T-I	1	9-M	0	0	0
	(Days 1-28)	10-M	0	0	3
		11-M	0	0	2
	30	12-M	0	0	2
	(Days 29-90)	13-F	>500	0	40
		14-F	0	12-15	4
		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	8
	300	19-M	0	0	0
	(Days 29-90)	20-M	0	3-5	0
		21-F	4-6	90-100	90
		22-F	0	0	3
		23-F	0	10-12	20
		24-F	2-4	90-100	40
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	8
		31-F	0	0	3
		32-F	0	0	15

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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

TOXSTUDIES1999

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	9-M	1-3	1-3	1-3
	(Days 1-28)	10-M	1-3	1-3	1-3
		11-M	1-3	1-3	1-3
	30	12-M	1-3	1-3	1-3
	(Days 29-90)	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	17-M	1-3	1-3	1-3
	(Days 1-28)	18-M	1-3	1-3	1-3
	300	19-M	1-3	1-3	1-3
	(Days 29-90)	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

TOXSTUDIES2000

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.

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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	9-M	254.7	23.8
	(Days 1-28)	10-M	199.7	29.8
		11-M	275.0	25.7
	30	12-M	258.3	26.1
	(Days 29-90)	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	17-M	281.2	26.7
	(Days 1-28)	18-M	236.1	29.5
	300	19-M	224.7	30.0
	(Days 29-90)	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

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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 (Days 1-28)	9-M	47.2	4.41
		10-M	29.7	4.43
		11-M	56.2	5.25
	30 (Days 29-90)	12-M	60.1	6.07
		13-F	39.6	4.71
		14-F	44.3	5.54
		15-F	44.4	5.41
		16-F	47.9	4.94
T-II	10 (Days 1-28)	17-M	46.0	4.38
		18-M	49.8	6.22
	300 (Days 29-90)	19-M	39.0	5.20
		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

TOXSTUDIES2003

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 (Days 1-28)	9-M	88.1	8.23
		10-M	47.1	7.03
		11-M	66.6	6.22
	30 (Days 29-90)	12-M	67.8	6.85
		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 (Days 1-28)	17-M	75.1	7.15
		18-M	64.3	8.04
	300 (Days 29-90)	19-M	52.3	6.97
		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

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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

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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

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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 (Days 1-28)	9-M	17.5	1.64
		10-M	7.3	1.09
		11-M	6.7	0.626
	30 (Days 29-90)	12-M	11.4	1.15
		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 (Days 1-28)	17-M	14.2	1.35
		18-M	5.9	0.738
	300 (Days 29-90)	19-M	3.5	0.467
		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

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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

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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	0.0616
		11-M	1.130	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

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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	0.060	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

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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

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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.

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TOXSTUDIES2012

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	-	-	-	-	-

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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)	+

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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)	+

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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 eosinophils (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)	+

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