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DATA EVALUATION RECORD 030703

Study Type: Subchronic Oral (Dietary) Toxicity
Species: Dog Guideline: §82-1b

EPA Numbers: EPA MRID# 00106277
EPA Pesticide Chemical Code 030703
Toxicology Chemical No. 592 (acid), 780A (Na salt)

Test Material: Alanap S

Synonyms: Naptalam

Title of Report: FINAL REPORT
13-WEEK Dietary Feeding - Dogs

Sponsor: Uniroyal Incorporated

Testing Facility: Hazleton Laboratories, Incorporated
Falls Church, Virginia

Study Number: Project No. 798-140

Author(s): G.C. Holsing, Ph.D.

Report Issued: March 1, 1968

Executive Summary: In a 13 week subchronic feeding study (MRID# 00106277), male and female adult beagle dogs (unknown source) received either 0, 300, 1000, or 3000-5000 ppm of Alanap S (equal to 11.4, 29.7, and 124.7 mg/kg/day in males and 9.7, 29.9, and 123.6 mg/kg/day in females).

Systemic toxicity was noted at the high dose (3000-5000 ppm) in the form of reduced body weight gains, reduced food efficiency and increased absolute and relative liver weights. **The LOEL for Systemic Toxicity is 3000 ppm and the NOEL for Systemic Toxicity is 1000 ppm based on reduced body weight gains, reduced food efficiency and increased absolute and relative liver weights.**

The study is classified as Core-Supplementary Data and does not satisfy the guideline requirements (§82-1b) for a subchronic oral toxicity study in non-rodents. This study cannot be upgraded due to numerous reporting and study deficiencies.

A. Materials and Methods: A copy of the Materials and Methods section from the investigators report is attached.

1. Test compound: Alanap S (Naptalam)
Description - Fine, pale tan powder with a faint unpleasant odor
Lot # - C-465
Purity - assumed 100%
Received - July 27, 1967
Contaminants - none reported

2. Vehicle(s): None used

3. Test animals: Species: young adult male and female dogs
Strain: beagle
Age: not provided
Weight: 6.9-15.9 kg at study initiation
Source: not provided

4. Animal assignment

Animals were assigned to the following test groups; no indication as to method of assignment was provided:

Test Group	Dose in Diet (ppm)	# males	#females
1 Control	None	3	3
2 Low (LDT)	300	3	3
3 Mid (MDT)	1000	3	3
4 High (HDT)	3000 to 5000*	3	3

*** study made reference to at least 3 dosages, 3000, 4000, and 5000 ppm; however, information on this was illegible**

5. Diet preparation

Diet was prepared weekly, no storage method provided. There was no indication if samples of dietary admix were analyzed for stability and concentration.

6. Animal Husbandry

Animals were housed in metal cages and received Ground Wayne Dog Meal and water *ad libitum*. No other information was provided.

7. Clinical Observations

Animals were inspected daily for *appearance, behavior, appetite, elimination and signs of compound effect*. They were weighed weekly and food consumption was determined weekly.

8. Ophthalmological examination

Ophthalmological examinations were not performed as they are not required in subchronic studies.

9. Hematology and Clinical Chemistry

Blood was collected before treatment and at 1 and 3 months for hematology and clinical chmeistry analysis from all animals.

a. Hematology

The following parameters were measured:

Erythrocyte count (RBC)*
Leukocyte count (WBC)*
Leukocyte differential count*
Hematocrit (HCT)*
Hemoglobin (HGB)*
*** Required for subchronic studies**

The following parameters required for subchronic studies were not determined:

Platelet count*

b. Clinical Chemistry

The following parameters were measured:

Blood sugar (Glucose)*
Blood urea nitrogen*
Serum glutamic-pyruvic transaminase (Serum alanine aminotransferase, SGPT)*
Serum glutamic-oxaloacetic transaminase (Serum aspartate aminotransferase, SGOT)*
Alkaline phosphatase (ALK)
Serum electrolytes (Sodium*, Potassium*, Chloride*)
Total serum Protein (TP)*
Albumin*
*** Required for subchronic studies**

The following parameters required in subchronic studies were not determined:

Calcium*, Blood creatinine*, Phosphorous*, Cholesterol*

10. Urinalysis^

Urine was collected prior to study initiation and at 1 and 3 months; there was no indication if animals were fasted. The following parameters were examined:

Appearance (volume also?)	Protein
pH	Bilirubin
Specific gravity	Occult Blood
Sugar (Glucose)	Sediment (microscopic)
Acetone (Ketones)	

^Not required for subchronic studies

11. Sacrifice and Pathology

All animals that died and that were sacrificed on schedule were subject to gross pathological examination and the following tissues were collected for histological examination, the bolded organs, in addition, were weighed (the organs with **M** were examined microscopically in the control and high dose groups only):

Brain*+
Pituitary*
Eyes (optic nerve?)*#**M**
Thyroids*++**M**
Lung*
Heart*
Liver*+**M**
Gall bladder*
Spleen M
Kidneys*+**M**
Adrenal gland*
Stomach*
Pancreas***M**
Duodenum*, Jejunum*, Ileum*, Colon*
Urinary bladder*
Ovaries*+
Bone*# (costochondral junction)
Bone marrow* (sternum)
Testes*+

The following required for subchronic studies were not examined: Aorta*, Salivary glands*, Periph. nerve*#, Esophagus*, Spinal cord (3 levels)*#, Lymph nodes*, Thymus*, Cecum*, Lacrimal gland#, Mammary gland*#, Rectum*, Parathyroids*++ (possibly determined with thyroids), Skeletal muscle*#, Trachea*, Uterus*, Skin*#,All gross lesions and masses*

* Required for subchronic and chronic studies.
# In subchronic studies, examined only if indicated by signs of toxicity or target organ involvement.
+ Organ weight required in subchronic studies.
++ Organ weight required for non-rodent studies.

12. Statistics

There was no indication of statistical procedures utilized.

13. Compliance

No statements of data confidentiality claims, compliance with GLP's quality assurance or flagging criteria were provided.

B. RESULTS:

1. Clinical Observations

a. Clinical signs of toxicity/mortality

No clinical signs of toxicity were reported.

b. Body weight

Only individual animal data were provided. The following table presents body weight gain data (kg) calculated by the reviewer from the individual animal data:

Weeks:		Control	300	1000	3000
1-13	M	0.4	1.3	0.6	0
	F	0.5	1.2	0.5	0.3

Although only 3 animals per sex per dose group were used, it is apparent that the high dose group gained less weight than the control.

c. Food consumption, food efficiency and compound intake

Only individual animal data were provided. The following table presents food consumption data (kg/wk) calculated by the reviewer from the individual animal data:

Weeks:		Control	300	1000	3000
1-13	M	2.4	2.9	2.4	2.5
	F	2.1	2.1	1.9	2.0

The following table presents the food efficiency calculated by the reviewer from the above data:

Weeks:		Control	300	1000	3000
1-13	M	1.3	3.5	2.0	0
	F	1.9	4.4	2.0	1.2

Although food consumption seemed relatively unaffected, the food efficiency was reduced compared to control in the high dose group.

The following table presents the compound intake (mg/kg/day) calculated by the reviewer from the individual animal data:

	Low	Mid	High
M	11.4	29.7	124.7
F	9.7	29.9	123.6

2. Hematology and Clinical Chemistry

a. Hematology

No treatment related effects were noted; the following table presents data from the tables provided in the investigators report:

DOG NO.	SEX	TIME INTERVAL months	HCT. %	HGB. g.%	RBC $\times 10^6$/cmm	WBC $\times 10^3$/cmm	DOG NO.	SEX	TIME INTERVAL months	HCT. %	HGB. g.%	RBC $\times 10^6$/cmm	WBC $\times 10^3$/cmm
			CONTROL										CONTROL
12117	M	0	44.0	15.1	5.26	16.1	12185	F	0	50.0	18.2	6.92	10.5
		1	44.0	16.1	6.04	16.8			1	45.0	17.6	5.78	8.3
		3	45.0	16.3	6.77	15.6			3	50.0	17.0	7.62	9.2
12288	M	0	51.0	18.4	6.83	11.8	12189	F	0	58.0	18.9	7.81	11.5
		1	51.0	19.5	6.69	9.1			1	53.0	20.6	5.70	8.6
		3	54.0	18.3	7.70	9.1			3	51.0	17.6	7.71	9.0
12303	M	0	49.0	16.7	6.53	15.3	12246	F	0	47.0	16.5	7.22	14.0
		1	48.0	18.4	6.18	8.7			1	47.0	18.2	6.36	11.3
		3	48.0	16.8	7.53	14.8			3	49.0	16.5	7.03	24.9
			300 PPM										300 PPM
12144	M	0	42.0	15.4	5.13	17.7	12186	F	0	55.0	19.7	7.90	10.7
		1	39.0	15.9	5.06	15.0			1	50.0	18.7	4.91	7.6
		3	46.0	15.7	6.45	8.7			3	48.0	17.0	7.58	11.7
12302	M	0	54.0	18.6	5.03	10.6	12188	F	0	55.0	19.5	7.62	14.6
		1	45.0	16.9	4.24	8.9			1	50.0	19.6	5.29	11.7
		3	51.0	17.6	7.36	7.8			3	51.0	18.1	7.67	15.2
12305	M	0	50.0	18.4	6.63	13.8	12328	F	0	46.0	16.5	6.28	11.8
		1	46.0	17.6	6.58	12.1			1	50.0	19.4	4.81	7.1
		3	47.0	16.1	6.85	16.4			3	50.0	17.6	7.97	15.8

DOG NO.	SEX	TIME INTERVAL months	HCT. %	HGB. g.%	RBC x10⁶/cmm	WBC x10³/cmm
1000 PPM						
12304	M	0	49.0	18.2	5.96	12.2
		1	44.0	17.1	3.92	10.6
		3	42.0	14.1	6.04	11.5
12307	M	0	53.0	19.5	6.40	13.1
		1	49.0	19.7	5.81	8.7
		3	47.0	16.5	6.89	8.8
12316	M	0	47.0	16.9	6.77	15.0
		1	44.0	17.6	4.03	20.2
		3	49.0	16.3	7.27	30.8
		REPEAT				32.2
3000 TO 5000 PPM						
12282	M	0	52.0	19.5	7.16	16.8
		1	51.0	19.4	5.50	10.5
		3	47.0	16.8	6.64	9.6
12306	M	0	47.0	17.2	5.89	12.7
		1	45.0	17.4	4.32	9.2
		3	41.0	14.3	5.69	10.9
12315	M	0	47.0	16.7	6.20	12.7
		1	52.0	19.6	6.96	10.4
		3	50.0	17.4	7.36	12.3

DOG NO.	SEX	TIME INTERVAL months	HCT. %	HGB. g.%	RBC x10⁶/cmm	WBC x10³/cmm
1000 PPM						
12251	F	0	49.0	17.6	6.63	11.0
		1	48.0	17.6	5.04	8.6
		3	48.0	16.3	6.98	9.5
12253	F	0	47.0	16.5	6.73	10.4
		1	47.0	18.6	4.96	8.4
		3	47.0	16.3	6.78	10.4
12327	F	0	44.0	14.4	5.04	12.6
		1	45.0	17.8	5.21	11.8
		3	48.0	15.2	6.27	13.3
3000 TO 5000 PPM						
12244	F	0	47.0	16.7	7.12	12.7
		1	49.0	19.6	6.20	11.0
		3	47.0	16.8	7.67	8.8
12254	F	0	51.0	17.8	6.09	8.8
		1	46.0	17.4	5.20	9.5
		3	47.0	15.9	6.84	8.5
12278	F	0	46.0	17.2	5.97	17.1
		1	44.0	17.4	5.68	11.2
		3	45.0	15.9	7.03	8.4

b. Clinical Chemistry

No treatment related effects were noted; the following table presents data from the tables provided in the investigators report:

ALANAP S [redacted] 9 DOG SUBCHRONIC

DOG NO.	S E X	TIME INTERVAL weeks	[redacted] mg. %	BUN mg.%	% BSP RETENT. 30 min.	AS-PT B-P units	AG-DT B-P units	ALK. PO4 B-L-B units	PROTH. TIME secs.	NA mEq/l	K mEq/L	CL mEq/L
						CONTROL						
12117	M	0	69	16.0		20	35	5.4	152	4.85	123
		1	101	15.0		10	30	1.6	148	5.00	123
		3	110	15.0		24	115	1.4	152	5.20	123
12208	M	0	84	16.0		23	18	1.3	148	5.00	117
		1	90	13.0		12	25	0.5	145	5.45	116
		3	88	15.5		17	25	.5	149	5.60	117
12303	M	0	75	15.0		25	19	1.8	144	4.80	118
		1	95	17.0		13	26	0.7	146	4.50	121
		3	90	16.0		17	16	0.8	146	4.90	114
12165	F	0	105	11.5		11	30	2.5	149	4.00	120
		1	84	15.0		9	30	1.1	148	4.90	119
		3	88	14.0		13	20	0.8	149	4.80	117
12189	F	0	105	18.0		14	32	2.3	152	4.55	113
		1	91	16.0		8	25	1.0	147	5.30	117
		3	86	17.0		13	20	0.7	148	4.80	116
12246	F	0	120	16.5		17	29	2.5	154	4.35	120
		1	107	17.0		14	28	1.0	155	5.20	124
		3	76	17.0		14	22	1.5	149	4.55	121
						300 PPM						
12144	M	0	80	11.0		19	31	2.9	148	5.20	117
		1	96	12.0		9	30	1.0	145	5.25	116
		3	87	10.0		16	22	0.9	143	5.20	116
12302	M	0	70	18.5		25	18	3.5	143	4.55	117
		1	95	15.0		9	24	1.9	145	5.60	119
		3	94	15.0		13	21	1.6	145	5.20	116
12305	M	0	80	16.0		16	18	1.5	144	4.05	117
		1	99	14.0		13	16	0.8	145	4.55	119
		3	91	17.0		16	29	1.0	150	4.80	116
[redacted]	F	0	91	19.5		20	28	1.4	149	4.10	117
		1	102	10.5		10	32	0.8	149	5.10	117
		3	86	11.0		17	33	0.7	150	5.00	117
12168	F	0	115	14.0		11	30	2.9	150	3.75	116
		1	104	15.5		14	32	1.2	149	5.05	119
		3	95	15.0		13	33	0.9	149	4.60	115
12328	F	0	75	12.5		26	28	2.4	155	4.60	116
		1	97	14.0		12	27	1.4	149	5.90	114
		3	84	13.0		18	35	1.0	149	5.00	115

ALANAP S

DOG SUBCHRONIC

DOG NO.	SEX	TIME INTERVAL months	WEIGHT kg	RUN mg.%	% BSP RETENT. 30 min.	SG-PT K-U units	SG-GT K-U units	ALK. PO4 K-L-B units	PROTH. TIME secs.	NA mEq/L	K mEq/L	Cl mEq/L
						1000 PPM						
12304	M	0	75	13.0		30	19	1.0		144	4.60	116
		1	105	14.5		12	27	0.7		148	5.20	117
		3	91	17.0		18	27	0.7		148	4.55	116
12307	M	0	76	12.0		23	17	1.9		144	4.30	116
		1	100	12.5		8	22	1.1		148	5.75	116
		3	91	13.0		16	36	0.9		149	5.30	116
12316	M	0	97	14.0		21	20	2.5		149	5.00	122
		1	86	14.0		14	26	0.9		149	5.00	116
		3	96	13.0		6	32	0.8		149	5.35	115
12251	F	0	94	20.5		13	28	3.7		150	4.60	119
		1	99	18.5		7	27	1.6		149	4.80	121
		3	101	18.0		10	34	1.4		149	4.50	117
12253	F	0	94	11.5		16	21	2.4		147	5.20	117
		1	105	11.0		12	24	1.0		148	5.75	115
		3	116	13.0		20	32	0.9		152	4.40	114
12327	F	0	90	7.0		14	24	2.8		155	4.30	117
		1	91	12.5		8	26	1.2		148	5.10	118
		3	93	12.0		8	27	1.2		152	4.60	117
						3000 TO 5000 PPM						
12282	M	0	76	14.5		22	23	1.8		152	4.35	122
		1	120	17.0		9	31	1.2		153	5.90	123
		3	95	16.0		23	32	1.7		154	4.50	119
12306	M	0	80	10.0		26	22	1.3		149	3.95	124
		1	98	12.0		14	22	0.8		149	5.00	120
		3	95	10.0		12	28	1.0		149	4.80	115
12315	M	0	90	13.0		32	30	3.0		148	4.20	116
		1	105	16.0		12	35	1.2		148	5.20	116
		3	102	18.0		16	33	1.2		152	4.70	117
12244	F	0	90	17.5		16	30	3.5		151	4.25	116
		1	115	20.0		12	30	2.1		150	4.65	121
		3	99	21.0		9	32	2.0		152	4.95	116
12254	F	0	87	15.0		27	23	2.0		151	4.65	120
		1	90	17.0		16	34	1.4		150	4.80	121
		3	91	19.0		18	39	2.2		152	4.40	117
12278	F	0	71	23.5		34	30	2.9		153	4.25	120
		1	106	23.0		11	27	1.6		151	4.50	124
		3	104	24.0		16	30	2.3		152	4.60	120

ALANAP S

DOG SUBCHRONIC

DOG NO.	SEX	TIME INTERVAL (months)	TOTAL PROTEIN g. %	ALBUMIN g. %	DOG NO.	SEX	TIME INTERVAL (months)	TOTAL PROTEIN g. %	ALBUMIN g. %
				CONTROL					CONTROL
12117	M	0	6.5	2.0	12185	F	0	6.5	1.9
		1	6.4	1.7			1	7.0	1.5
		3	6.8	2.4			3	7.0	2.2
12288	M	0	7.3	2.1	12189	F	0	6.7	2.2
		1	6.5	1.9			1	6.7	2.0
		3	7.1	2.3			3	6.8	2.4
12303	M	0	7.1	1.7	12246	F	0	6.5	2.0
		1	6.4	1.5			1	7.1	1.7
		3	6.6	2.2			3	7.1	2.2
				300 PPM					300 PPM
12144	M	0	6.3	1.8	12186	F	0	7.6	1.8
		1	6.1	1.5			1	6.2	1.7
		3	6.2	2.2			3	6.6	2.5
12302	M	0	7.6	1.8	12188	F	0	7.5	2.8
		1	7.3	1.7			1	7.0	2.0
		3	7.6	2.4			3	7.0	2.7
12305	M	0	6.7	2.1	12328	F	0	6.8	2.2
		1	6.6	1.9			1	6.7	2.1
		3	7.2	2.3			3	7.1	3.1
				1000 PPM					1000 PPM
12304	M	0	7.0	1.9	12251	F	0	6.5	2.1
		1	6.8	1.9			1	6.6	2.2
		3	6.6	2.6			3	6.8	2.8
12307	M	0	7.0	1.9	12253	F	0	6.6	2.2
		1	6.9	1.7			1	6.5	2.1
		3	6.7	2.5			3	6.9	2.4
12316	M	0	6.2	1.7	12327	F	0	6.7	2.0
		1	6.6	1.2			1	6.5	1.9
		3	6.5	2.2			3	6.5	2.5
				3000 TO 5000 PPM					
12282	M	0	7.1	2.0	12244	F	0	6.4	2.0
		1	7.2	1.7			1	6.6	1.6
		3	6.6	2.5			3	6.9	2.6
12306	M	0	7.7	2.0	12254	F	0	6.6	2.0
		1	7.1	1.4			1	6.6	1.6
		3	7.3	2.4			3	7.1	2.4
12315	M	0	6.0	1.6	12278	F	0	7.0	1.7
		1	6.3	1.7			1	6.6	1.5
		3	6.5	2.3			3	6.9	2.6

3. Urinalysis

No treatment related effects were noted; the following table presents data from the tables provided in the investigators report:

DOG NO.	SEX	TIME INTERVAL months	APPEAR.	[redacted]	SP. GR.	SUGAR	ACE-TONE	PRO-TEIN	BILI-RUBIN	OCCULT BLOOD
									CONTROL	
12117	M	INITIAL	V T	YEL	7	1.041	0	0	1	0	0
		1	T	YEL	6	1.040	0	0	1	T	0
		3	VT	DY	7	1.034	0	0	1	T	T
12288	M	INITIAL	T	YLL	7	1.022	0	0	0	1	0
		1	T	YEL	7	1.041	0	0	1	T	0
		3	T	YEL	8	1.030	0	0	1	1	0
12303	M	INITIAL	V T	YEL	7	1.040	0	0	1	1	0
		1	T	YEL	7	1.056	0	0	1	T	0
		3	T	YEL	5	1.025	0	0	T	T	0
12185	F	INITIAL	T	YEL	7	1.030	0	0	1	0	0
		1	V T	YLL	8	1.036	0	0	1	0	0
		3	T	YEL	7	1.040	0	0	1	0	0
12189	F	INITIAL	V T	YEL	7	1.030	0	0	T	0	0
		1	V T	YEL	7	1.030	0	0	1	T	1
		3	T	YEL	7	1.040	0	0	1	0	0
12246	F	INITIAL	T	YEL	6	1.040	0	0	1	0	T
		1	T	YEL	6	1.045	0	0	1	0	0
		3	T	YEL	5	1.060	0	0	1	0	T
		REPLAT				1.033					

DOG NO.	SEX	TIME INTERVAL months	APPEAR.	pH	SP. GR.	SUGAR	ACE-TONE	PRO-TEIN	BILI-RUBIN	OCCULT BLOOD
									300 PPM	
12144	M	INITIAL	V T YEL	7	1.051	0	0	1	0	0
		1	T YEL	5	1.041	0	0	T	0	0
		3	T YEL	7	1.040	0	0	1	1	0
12302	M	INITIAL	T YEL	6	1.045	0	0	1	1	0
		1	V T YEL	7	1.025	0	0	1	T	0
		3	T YEL	6	1.038	0	0	1	1	0
12305	M	INITIAL	T YEL	6	1.037	0	0	1	1	0
		1	T YEL	6	1.040	0	0	1	1	0
		3	T YEL	5	1.050	0	0	1	T	0
12186	F	INITIAL	V T YEL	9	1.032	0	0	1	0	0
		1	T YEL	9	1.025	0	0	T	0	0
		3	T YEL	8	1.036	0	0	1	0	0
12188	F	INITIAL	T YEL	8	1.030	0	0	1	0	0
		1	T YEL	6	1.040	0	0	T	0	0
		3	T YEL	6	1.035	0	0	T	0	0
12328	F	INITIAL	T YEL	6	1.060	0	0	1	0	0
		1	T YEL	6	1.035	0	0	T	0	T
		3	T YEL	6	1.039	0	0	T	0	0
					1000 PPM					
12304	M	INITIAL	V T YEL	8	1.035	0	0	1	1	0
		1	T YEL	6	1.030	0	0	T	T	0
		3	T YEL	5	1.045	0	0	T	2	0
12307	M	INITIAL	T YEL	7	1.035	0	0	1	T	0
		1	T YEL	5	1.030	0	0	1	T	0
		3	T YEL	6	1.045	0	0	T	2	0
12316	M	INITIAL	T YEL	7	1.050	0	0	1	0	0
		1	T YEL	7	1.010	0	0	T	0	T
		3	T YEL	7	1.010	0	0	0	T	0

DOG NO.	SEX	TIME INTERVAL months	APPEAR.	pH	SP. GR.	SUGAR	ACETONE	PROTEIN	BILIRUBIN	OCCULT BLOOD
			1000 PPM							
12251	F	INITIAL	T YEL	7	1.050	0	0	1	0	0
		1	T YEL	7	1.050	0	0	1	1	0
		3	T YEL	6	1.048	0	0	T	T	0
12253	F	INITIAL	T P YEL	7	1.015	0	0	T	0	0
		1	V T YEL	6	1.035	0	0	T	1	0
		3	T YEL	7	1.030	0	0	1	0	0
12327	F	INITIAL	T YEL	8	1.021	0	0	T	0	0
		1	T YEL	8	1.035	0	0	T	1	0
		3	T YEL	9	1.050	0	0	1	0	0
			3000 TO 5000 PPM							
12282	M	INITIAL	V T YEL	7	1.038	0	0	1	1	0
		1	T YEL	6	1.045	0	0	1	1	0
		3	T YEL	6	1.028	0	0	1	1	0
12306	M	INITIAL	T YEL	8	1.032	0	0	T	T	0
		1	T YEL	7	1.040	0	0	1	1	0
		3	V T YEL	5	*1.060	0	0	1	2	0
		REPLAT			1.014					
12315	M	INITIAL	T YEL	6	1.048	0	0	T	0	0
		1	T YEL	6	1.050	0	0	T	1	0
		3	V T YEL	6	*1.060	0	0	1	1	0
		REPEAT			1.040					
12244	F	INITIAL	T YEL	7	1.042	0	0	1	0	0
		1	T YEL	8	1.020	0	0	1	1	0
		3	T YEL	6	1.050	0	0	1	1	0
12254	F	INITIAL	T P YEL	6	1.026	0	0	0	0	0
		1	T YEL	9	1.025	0	0	T	T	0
		3	T YEL	7	1.025	0	0	T	0	0
12278	F	INITIAL	T YEL	6	1.040	0	0	0	0	0
		1	T YEL	6	1.040	0	0	T	1	0
		3	T YEL	5	1.030	0	0	T	0	0

4. Sacrifice and Pathology

a. Organ weight

According to the investigators, no treatment related effects were noted; however, it appears that there is a dose related increase in liver weight, both absolute and relative. The following table presents data from the tables provided in the investigators report:

Organ:	Control	Low	Mid	High
Thyroid				
M	0.979/0.0080[1]	0.790/0.0073	1.116/0.0100	0.910/0.0085
F	0.936/0.0095	0.959/0.0106	0.986/0.0110	1.006/0.0125
Heart				
M	98.333/0.8227	91.100/0.8470	91.533/0.8171	90.633/0.8462
F	82.133/0.8398	79.500/0.8735	81.200/0.8856	70.366/0.8950
Liver				
M	306.333/2.5488	316.666/2.9521	334.666/2.9842	377.666/3.5576
F	260.333/2.6399	262.666/2.8196	266.000/2.9125	301.333/3.7894
Spleen				
M	35.633/0.2935	26.666/0.2489	28.433/0.2568	30.466/0.2915
F	28.133/0.2818	25.833/0.2844	23.066/0.2509	23.600/0.3022
Kidneys				
M	61.900/0.5169	57.266/0.5320	59.166/0.5305	55.066/0.5175
F	48.766/0.4995	47.999/0.5297	42.999/0.4723	41.133/0.5222
Adrenals				
M	1.270/0.0106	1.029/0.0095	1.326/0.0119	1.110/0.0105
F	1.033/0.0105	1.093/0.0121	0.993/0.0109	0.999/0.0129
Testes	27.333/0.2324	23.300/0.2163	21.399/0.1927	22.833/0.2159

[1] = absolute/relative

Data extracted from Report 798-140, Table 5.

b. Gross pathology

No treatment related effects were noted (individual animal data only were provided). Observations were singular in nature.

c. Microscopic pathology

No treatment related effects were noted (individual animal data only were provided). Observations were singular in nature.

C. Discussion and Conclusions

Systemic toxicity was noted at the high dose (3000-5000 ppm) in the form of reduced body weight gains, reduced food efficiency and increased absolute and relative liver weights.

Systemic Toxicity NOEL = 1000 ppm
Systemic Toxicity LOEL = 3000 ppm

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INTRODUCTION

The purpose of this study was to characterize and evaluate the subacute oral toxicity of Alanap S in dogs. The study was started on August 30, 1967, and terminated on December 13, 1967.

MATERIAL

Identification: Alanap S (Lot No. C-465).

Received: July 27, 1967, from UniRoyal Incorporated.

Description: Fine, pale tan powder with a faint unpleasant odor.

Purity: Assumed 100%.

METHODS

Experimental Animals

Breed: Young adult purebred beagles.

Number: Twelve males and 12 females.

Body Weight (at initiation): 6.9 to 15.9 kg.

Housing: [redacted] individually in metal cages.

Diet: [redacted] Wayne Dog Meal and water ad libitum.

Dosage Levels

GROUP NO.	NO. OF ANIMALS male	NO. OF ANIMALS female	DIETARY LEVEL ppm
1 (Control)	3	3	0
2	3	3	1000
3	3	3	3000
4	3	3	10000

1.4

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Diet Preparation

The test material was incorporated into the basal diet on a weight per weight basis and thoroughly mixed in a twin-shell blender to provide the appropriate dietary levels. Fresh compound/diet mixtures were prepared weekly.

Compound Administration

The compound/diet mixtures were available to the compound treated dogs continuously for 13 weeks. The control dogs received the basal diet only.

Observations and Records

Daily: Appearance, behavior, appetite, elimination, and signs of compound effect.

Weekly: Body weights and food and compound consumption.

Clinical Laboratory Studies

Performed: Once initially and at one and three months

Hematology: Erythrocyte counts, total and differential leukocyte counts, and hematocrit and hemoglobin determinations.

Biochemistry: Blood sugar, blood urea nitrogen, serum glutamic-pyruvic transaminase, serum glutamic-oxaloacetic transaminase, alkaline phosphatase, serum electrolytes, total protein, and albumin.

Urine Analyses: Appearance, pH, specific gravity, sugar, acetone, protein, bilirubin, occult blood, and microscopic examination of the sediment.

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Terminal Studies

Terminal Sacrifice: All dogs after 13 weeks of dietary feeding.

Gross Necropsies: On all sacrificed dogs.

Organ Weights: Thyroids, heart, liver, spleen, kidneys, adrenals, and testes.

Tissues Preserved: In 10% neutral buffered formalin - brain, pituitary, eyes, thyroids, lung, heart, liver, gallbladder, spleen, kidneys, adrenals, stomach, pancreas, duodenum, jejunum, ileum, colon, urinary bladder, ovaries, bone (costochondral junction), and bone marrow (sternum). In Bouin's fixative - testes.

Microscopic Examination: All cited tissues from the control and high level dogs, and eyes, thyroids, liver, kidney, and pancreas from all dogs at each of the two lower levels as well as the spleen of one animal from each of the two lower levels.

Tissue Storage: Wet tissues and paraffin blocks are being stored at Hazleton Laboratories, Inc., for possible future reference.

RESULTS

[redacted] Behavior, Body Weight Changes, Signs of Compound Effect

Weekly body weights and food and compound consumption are presented in Table No. 1.

The control dogs maintained normal appearance and behavior, ate well, and had normal elimination during the study. Four dogs showed body weight, the gains ranging from 0.6 to 1.8 kg., and the other two dogs lost 0.4 and 0.5 kg.

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Chemical:	**Benzoic acid, 2-((1-naphthalenylamino)ca**
PC Code:	**030702**
HED File Code	**13000 Tox Reviews**
Memo Date:	**07/15/94 12:00:00 AM**
File ID:	**00000000**
Accession Number:	**412-04-0046**

HED Records Reference Center
03/25/2004