Toxicology Research Laboratory

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19. ABSTRACT (*Continue on reverse if necessary and identify by block number*)

This study evaluated the toxicity of WR238605 Succinate in rats following six months of daily oral (gavage) administration. WR238605 Succinate is an 8-aminoquinoline derivative which has demonstrated antimalarial potential in preclinical studies. Dose levels studied were 0 (vehicle control), 0.5, 2.0 and 9.0 mg base/kg/day, and were based on a three month toxicity study with a three month recovery period in rats (UIC/TRL Study No. 098) in which anemia and lung lesions were seen at 6 and 18 mg base/kg/day whereas 0.5 mg base/kg/day was the no-observed effect level. In the present study, the animals were ≈ 7 weeks old, and weighed 216 - 289 g (males) and 160 - 204 g (females) upon initiation of drug treatment.

The primary toxicities of WR238605 Succinate were to RBCs, the lungs and the liver. Mortality occurred in one high dose male rat. Treatment-related clinical signs in high dose animals included rough coat, hunched posture, labored breathing (males), and piloerection (females). Body weight gains were significantly reduced in high dose animals and mid dose males. Also, food consumption was decreased in high dose animals. High dose males, and mid and high dose females had decreased RBC counts, HCT and HGB concentration, suggestive of mild anemia. The anemia may have been hemolytic in origin due to the presence of Heinz bodies and increased methemoglobin levels. Microscopic lesions observed in the spleen, bone marrow, kidneys and adrenal glands may have been secondary to anemia and/or hemolysis. High dose animals had elevations in mature neutrophil and lymphocyte numbers. Mild thrombocytopenia was seen in mid and high dose males. Pulmonary lesions in male and female rats in the mid and high dose groups consisted of foamy macrophage accumulation, chronic interstitial inflammation, and hemorrhage (high dose groups only). Apoptosis, pigmentation and fatty change in the centrilobular region of the liver were seen in high dose males, but not in females, and were accompanied by decreased serum GLOB, BUN and increased TBA. Similar clinical chemistry changes were seen in high dose females. The no-effect level (NOEL) for WR238605 Succinate is considered to be at or near the low dose of 0.5 mg base/kg/day.

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Title Page

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Volume 2 of 2

Study Report for Task Order No. UIC-15B

SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS

Sponsor: US Army Medical Materiel Development Activity

Test Article: WR238605 Succinate

Contract No.: DAMD17-92-C-2001

Study Director

Barry S. Levine, D.Sc., D.A.B.T.

In-Life Phase Completed On

February 2, 1996

Performing Laboratory

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The views, opinions, and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy, or decision, unless so designated by other documentation.

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VOLUME 2

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APPENDIX G

INDIVIDUAL HEMATOLOGY DATA

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Hematology Test Directory

STUDY: UIC-15B

NO.	ABBR. / UNITS	DESCRIPTION / PRECISION	CALCULATED	OPERAND A	OPERAND B	---LOWER LIMIT--- MALE	FEMALE	---UPPER LIMIT--- MALE	FEMALE
1.	RBC	Erythrocytes							
	10^6/mm^3	0.00	NO			6.50	6.50	9.00	9.00
2.	HGB	Hemoglobin							
	g/dL	0.0	NO			13.0	13.0	17.0	17.0
3.	HCT	Hematocrit							
	%	0.0	NO			40.0	40.0	50.0	50.0
4.	MCV	Mean Corpuscular Volume							
	fL	0.0	NO			50.0	50.0	65.0	65.0
5.	MCH	Mean Corpuscular Hemoglobin							
	pg	0.0	NO			18.0	18.0	23.0	23.0
6.	MCHC	Mean Corpus. Hemo. Conc.							
	g/dL	0.0	NO			32.0	32.0	39.0	39.0
7.	RETICS	Reticulocytes							
	% RBCs	0.0	NO			0.0	0.0	1.0	1.0
8.	HEINZ BOD.	Heinz Bodies							
	% RBCs	0.0	NO			0.0	0.0	1.0	1.0
9.	% METHGB	% Methemoglobin							
	% HGB	0.0	NO			0.0	0.0	1.5	1.5
10.	PLT	Platelets							
	10^3/mm^3	Integer	NO			800	800	1400	1400
11.	WBC	Leukocytes							
	10^3/mm^3	0.0	NO			9.0	6.0	18.0	15.0
12.	APTT	Act. Partial Thrombo. Time							
	sec	0.0	NO			7.0	7.0	12.0	12.0

(END OF REPORT)

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152 MORPHOLOGY DICTIONARY

	ABBR	DESCRIPTION
1.	AN	Anisocytosis
2.	HC	Hypochromia
3.	NR	Nucleated Red Blood Cells
4.	PC	Polychromasia
5.	BS	Basophilic Stippling
6.	MI	Microcytes
7.	OV	Ovalocytes
8.	SK	Sickle Cells
9.	HB	Heinz Bodies
10.	MA	Macrocytes
11.	PK	Poikilocytes
12.	SP	Spherocytes
13.	HJ	Howell-Jolly Bodies
14.	NN	Normocytic & Normochromic
15.	TG	Target Cells
16.	LP	Large Platelets
17.	CP	Clumped Platelets
18.	RF	Rouleaux Formation
19.	NRC	Normal Red Blood Cells
20.	TX	Toxic Granule
21.	PY	Pyknotic Cells
22.	RL	Reactive Lymphocytes
23.	VA	Vacuoles

152 DETAIL DICTIONARY

	ABBR	DESCRIPTION
1.	1	Slight
2.	2	Moderate
3.	3	Mod. to Marked
4.	4	Marked

(END OF REPORT)

HISTORICAL DATABASE REPORT

		MCHC	MCV	PLT	PT	RBC	RETICS	WBC
RAT CD Male								
control data1	MEAN	35.5	59.0	1127	--	7.36	0.7	18.0
	SD	1.06	3.36	195.2	--	0.759	0.52	3.47
	N	145	145	145	--	145	108	145
RAT CD Female								
control data1	MEAN	36.8	58.9	1192	--	7.01	0.5	16.1
	SD	1.08	2.46	150.6	--	0.634	0.34	3.86
	N	145	145	145	--	145	105	145
RAT CD Both								
control data1	MEAN	36.1	59.0	1159	--	7.18	0.6	17.1
	SD	1.25	2.94	177.1	--	0.720	0.45	3.79
	N	290	290	290	--	290	213	290
RAT CD Male								
control data2	MEAN	35.4	53.4	1027	14.0	8.42	0.5	15.4
	SD	0.92	1.53	130.1	0.68	0.443	0.32	2.63
	N	90	90	90	10	90	86	90
RAT CD Female								
control data2	MEAN	36.1	56.0	1013	14.1	7.81	0.7	12.8
	SD	1.01	1.75	134.0	0.67	0.342	0.39	3.92
	N	90	90	90	10	90	80	90
RAT CD Both								
control data2	MEAN	35.7	54.7	1020	14.0	8.12	0.6	14.1
	SD	1.02	2.10	131.9	0.66	0.499	0.37	3.57
	N	180	180	180	20	180	166	180

(--)-Data Unavailable
control data1-40-120 days
control data2-120-300 days

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HISTORICAL DATABASE REPORT

		% METHGB	APTT	FBGN	HB	HCT	HEINZ BOD.	HGB	MCH
RAT CD Male									
control data1	MEAN	0.7	--	--	0.1	43.2	--	15.3	20.9
	SD	0.27	--	--	0.05	3.25	--	1.26	0.97
	N	74	--	--	8	145	--	145	145
RAT CD Female									
control data1	MEAN	0.8	--	--	0.1	41.2	--	15.2	21.7
	SD	0.35	--	--	0.05	3.13	--	1.23	0.65
	N	75	--	--	7	145	--	145	145
RAT CD Both									
control data1	MEAN	0.7	--	--	0.1	42.2	--	15.2	21.3
	SD	0.31	--	--	0.05	3.33	--	1.25	0.91
	N	149	--	--	15	290	--	290	290
RAT CD Male									
control data2	MEAN	0.8	18.6	231	0.3	44.9	--	15.9	18.9
	SD	0.27	2.90	18.6	0.11	2.30	--	0.81	0.73
	N	60	30	10	5	90	--	90	90
RAT CD Female									
control data2	MEAN	0.7	16.6	159	0.1	43.7	0.1	15.8	20.2
	SD	0.37	1.67	16.3	0.04	1.94	0.00	0.68	0.64
	N	54	30	10	5	90	2	90	90
RAT CD Both									
control data2	MEAN	0.7	17.6	195	0.2	44.3	0	15.8	19.5
	SD	0.32	2.54	40.8	0.12	2.21	0.0	0.75	0.95
	N	114	60	20	10	180	2	180	180

(--)-Data Unavailable
control data1-40-120 days
control data2-120-300 days

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Erythrocytes

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: RBC

SEX: MALE

UNITS: 10^6/mm^3

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-M:0 mg base/kg/day			
401	8.22	8.90	8.49
402	7.87	8.75	8.84
403	7.71	8.20	8.11
404	6.91	7.70	8.28
405	7.79	8.25	8.44
406	7.33	8.26	8.02
407	7.87	8.90	8.65
408	6.84	7.09	7.89
409	7.21	8.16	8.69
410	7.85	8.42	8.44
MEAN	7.56	8.26	8.39
SD	0.460	0.556	0.308
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	7.71	7.83	8.02
452	7.84	8.40	8.23
453	7.87	8.72	9.21
454	7.43	8.06	7.72
455	7.28	8.25	7.98
456	7.34	7.78	7.80
457	7.82	8.94	8.20
458	7.77	8.02	8.40
459	8.16	8.61	8.55
460	7.69	8.47	8.48
MEAN	7.69	8.31	8.26
SD	0.270	0.387	0.434
N	10	10	10

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Erythrocytes

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: RBC

SEX: MALE

UNITS: 10^6/mm^3

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	7.55	8.30	8.49
502	7.14	8.16	8.16
503	7.51	8.21	8.52
504	7.16	8.20	7.87
505	7.36	8.13	8.33
506	7.36	7.87	8.32
507	7.15	8.20	8.34
508	7.02	8.40	8.64
509	7.45	7.79	8.07
510	7.44	8.07	8.05
MEAN	7.31	8.13	8.28
SD	0.183	0.184	0.240
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	7.41	8.37	8.59
552	7.15	7.80	7.89
553	7.12	8.14	8.83
554	6.63	7.19	7.51
555	6.75	8.16	8.14
556	7.52	9.09	8.77
557	7.64	8.47	8.50
558	7.49	6.91	--
559	7.36	8.25	8.79
560	6.86	7.55	7.80
561	--	--	8.70
MEAN	7.19	7.99	8.35
SD	0.350	0.645	0.479
N	10	10	10

(--) - Data Unavailable

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Hemoglobin

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: HGB

SEX: MALE

UNITS: g/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-M:0 mg base/kg/day			
401	16.8	16.6	15.1
402	15.4	15.9	15.6
403	16.0	16.2	15.0
404	16.4	15.0	15.8
405	14.6	15.3	14.7
406	14.9	15.7	14.6
407	16.0	16.8	15.8
408	14.9	13.7	14.6
409	16.1	16.0	15.5
410	16.2	15.8	15.4
MEAN	15.7	15.7	15.2
SD	0.73	0.89	0.47
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	16.7	14.9	14.6
452	16.5	16.9	15.7
453	14.5	16.3	16.5
454	15.0	16.1	14.6
455	15.7	16.4	15.9
456	16.0	15.9	15.5
457	15.9	16.6	14.5
458	16.2	16.4	16.1
459	15.8	15.9	14.9
460	16.3	16.6	16.3
MEAN	15.9	16.2	15.5
SD	0.67	0.56	0.76
N	10	10	10

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Hemoglobin

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: HGB

SEX: MALE

UNITS: g/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	14.9	15.4	15.0
502	15.2	16.2	15.6
503	15.4	16.3	16.0
504	14.8	16.4	14.7
505	15.4	15.8	15.0
506	15.4	15.6	15.7
507	15.7	16.3	15.8
508	15.0	16.1	15.6
509	16.0	16.3	15.9
510	15.7	15.4	15.1
MEAN	15.4	16.0	15.4
SD	0.38	0.39	0.45
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	12.9	14.9	13.9
552	13.9	14.9	14.1
553	14.6	14.7	14.6
554	14.1	14.1	13.8
555	14.0	15.4	14.8
556	14.8	15.8	14.9
557	15.4	15.5	14.2
558	14.0	13.7	--
559	14.5	15.2	14.5
560	14.2	14.5	13.7
561	--	--	14.4
MEAN	14.2	14.9	14.3
SD	0.66	0.65	0.42
N	10	10	10

(--) - Data Unavailable

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Hematocrit

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: HCT

SEX: MALE

UNITS: %

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-M:0 mg base/kg/day			
401	47.7	46.7	44.8
402	44.7	44.8	45.8
403	44.7	44.6	43.2
404	41.7	41.2	46.0
405	43.8	42.7	43.9
406	43.0	43.9	42.4
407	45.5	46.3	44.7
408	40.4	37.6	41.4
409	43.6	43.6	46.2
410	46.7	44.8	44.6
MEAN	44.2	43.6	44.3
SD	2.19	2.65	1.59
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	44.3	41.1	42.3
452	48.3	47.9	47.4
453	45.6	46.2	47.4
454	44.4	44.3	42.2
455	45.9	47.0	46.9
456	45.4	43.9	44.8
457	44.6	45.6	43.4
458	45.5	47.0	45.8
459	45.9	43.8	43.3
460	47.8	47.9	47.9
MEAN	45.8	45.5	45.1
SD	1.34	2.18	2.23
N	10	10	10

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Hematocrit

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: HCT

SEX: MALE

UNITS: %

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	43.1	43.7	44.1
502	42.3	44.6	45.8
503	45.2	46.1	48.6
504	41.4	45.2	42.7
505	43.1	44.1	43.4
506	44.9	45.5	47.8
507	44.3	46.0	46.8
508	41.3	45.4	45.6
509	47.6	47.0	48.5
510	43.7	44.2	44.8
MEAN	43.7	45.2	45.8
SD	1.91	1.03	2.09
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	41.5	42.4	42.3
552	43.8	43.8	42.8
553	40.0	41.2	43.3
554	41.9	41.3	42.4
555	38.9	44.4	43.6
556	43.2	46.2	44.3
557	44.5	45.0	41.8
558	43.6	40.4	--
559	41.9	42.7	43.1
560	41.4	42.1	41.7
561	--	--	43.1
MEAN	42.1	43.0	42.8
SD	1.75	1.85	0.81
N	10	10	10

(--) - Data Unavailable

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpuscular Volume

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: MCV

SEX: MALE

UNITS: fL

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-M:0 mg base/kg/day			
401	58.0	52.5	52.8
402	56.8	51.2	51.8
403	58.0	54.4	53.3
404	60.3	53.5	55.6
405	56.2	51.8	52.0
406	58.7	53.1	52.9
407	57.8	52.0	51.7
408	59.1	53.0	52.5
409	60.5	53.4	53.2
410	59.5	53.2	52.8
MEAN	58.5	52.8	52.9
SD	1.41	0.94	1.11
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	57.5	52.5	52.7
452	61.6	57.0	57.6
453	57.9	53.0	51.5
454	59.8	55.0	54.7
455	63.0	57.0	58.8
456	61.9	56.4	57.4
457	57.0	51.0	52.9
458	58.6	58.6	54.5
459	56.3	50.9	50.6
460	62.2	56.6	56.5
MEAN	59.6	54.8	54.7
SD	2.44	2.75	2.79
N	10	10	10

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpuscular Volume

STUDY ID: UIC-158
STUDY NO: 152
ABBR: MCV

SEX: MALE

UNITS: fL

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	57.1	52.7	51.9
502	59.2	54.7	56.1
503	60.2	56.2	57.0
504	57.8	55.1	54.3
505	58.6	54.2	52.1
506	61.0	57.8	57.5
507	62.0	56.1	56.1
508	58.8	54.0	52.8
509	63.9	60.3	60.1
510	58.7	54.8	55.7
MEAN	59.7	55.6	55.4
SD	2.07	2.16	2.61
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	56.0	50.7	49.2
552	61.3	56.2	54.2
553	56.2	50.6	49.0
554	63.2	57.4	56.5
555	57.6	54.4	53.6
556	57.4	50.8	50.5
557	58.2	53.1	49.2
558	58.2	58.5	--
559	56.9	51.8	49.0
560	60.3	55.8	53.5
561	--	--	49.5
MEAN	58.5	53.9	51.4
SD	2.34	2.95	2.76
N	10	10	10

(--) - Data Unavailable

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpuscular Hemoglobin

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: MCH

SEX: MALE

UNITS: pg

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-M:0 mg base/kg/day			
401	20.4	18.7	17.8
402	19.6	18.2	17.6
403	20.8	19.8	18.5
404	23.7	19.5	19.1
405	20.3	18.5	17.4
406	20.3	19.0	18.2
407	20.3	18.9	18.3
408	21.8	19.3	18.5
409	22.3	19.6	17.8
410	20.6	18.8	18.2
MEAN	21.0	19.0	18.1
SD	1.23	0.51	0.50
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	23.9	19.0	18.2
452	21.0	20.1	19.1
453	21.4	18.7	17.9
454	22.6	20.0	18.9
455	21.6	19.9	19.9
456	23.3	20.4	19.9
457	20.3	18.6	17.7
458	20.8	20.4	19.2
459	19.4	18.5	17.4
460	21.2	19.6	19.2
MEAN	21.6	19.5	18.7
SD	1.37	0.75	0.89
N	10	10	10

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpuscular Hemoglobin

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: MCH

SEX: MALE

UNITS: pg

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	19.7	18.6	17.7
502	21.3	19.9	19.1
503	20.5	19.9	18.8
504	20.7	20.0	18.7
505	20.9	19.4	18.0
506	22.6	19.8	18.9
507	22.0	19.9	18.9
508	21.4	19.2	18.1
509	21.5	20.9	19.7
510	22.2	19.1	18.8
MEAN	21.3	19.7	18.7
SD	0.87	0.63	0.59
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	20.9	17.8	16.2
552	22.5	19.1	17.9
553	20.5	18.1	16.5
554	21.3	19.6	18.4
555	20.7	18.9	18.2
556	19.7	17.4	17.0
557	20.2	18.3	16.7
558	21.1	19.8	--
559	19.7	18.4	16.5
560	20.7	19.2	17.6
561	--	--	16.6
MEAN	20.7	18.7	17.2
SD	0.82	0.79	0.80
N	10	10	10

(--) - Data Unavailable

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpus. Hemo. Conc.

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: MCHC

SEX: MALE

UNITS: g/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-M:0 mg base/kg/day			
401	35.2	35.5	33.7
402	34.5	35.5	34.1
403	35.8	36.3	34.7
404	39.3	36.4	34.3
405	36.6	35.8	33.5
406	34.7	35.8	34.4
407	35.2	36.3	35.3
408	36.9	36.4	35.3
409	36.9	36.7	33.5
410	34.7	35.3	34.5
MEAN	36.0	36.0	34.3
SD	1.48	0.48	0.66
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	40.9	36.3	34.5
452	34.2	35.3	33.1
453	36.6	35.3	34.8
454	37.2	36.3	34.6
455	34.2	34.9	33.9
456	37.0	36.2	34.6
457	35.7	36.4	33.4
458	35.6	34.9	35.2
459	34.4	36.3	34.4
460	34.1	34.7	34.0
MEAN	36.0	35.7	34.3
SD	2.10	0.70	0.65
N	10	10	10

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpus. Hemo. Conc.

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: MCHC

SEX: MALE

UNITS: g/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	34.6	35.2	34.0
502	35.9	36.3	34.1
503	34.1	35.4	32.9
504	35.7	36.3	34.4
505	35.7	35.8	34.6
506	36.5	34.3	32.8
507	35.4	35.4	33.8
508	36.3	35.5	34.2
509	33.6	34.7	32.8
510	37.8	34.8	33.7
MEAN	35.6	35.4	33.7
SD	1.23	0.66	0.67
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	36.8	35.1	32.9
552	36.5	34.0	32.9
553	36.5	35.7	33.7
554	33.7	34.1	32.5
555	36.0	34.7	33.9
556	34.3	34.2	33.6
557	34.6	34.4	34.0
558	35.7	33.9	--
559	34.6	35.6	33.6
560	34.3	34.4	32.9
561	--	--	33.4
MEAN	35.3	34.6	33.3
SD	1.12	0.65	0.51
N	10	10	10

(--) - Data Unavailable

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Reticulocytes

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: RETICS

SEX: MALE

UNITS: % RBCs

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-M:0 mg base/kg/day			
401	0.6	0.1	0.7
402	0.7	0.1	0.6
403	1.2	0.5	0.7
404	0.4	0.3	0.6
405	0.8	0.4	1.2
406	0.5	0.5	0.7
407	1.2	0.9	0.2
408	0.8	0.7	0.6
409	0.7	0.4	0.8
410	0.5	0.5	0.7
MEAN	0.7	0.4	0.7
SD	0.28	0.25	0.24
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	0.3	1.5	0.3
452	0.8	0.2	0.9
453	1.0	0.9	0.2
454	0.6	0.1	0.6
455	0.9	0.9	0.3
456	1.1	0.6	1.1
457	0.8	0.3	1.3
458	0.8	0.8	0.7
459	0.9	0.7	0.2
460	0.4	1.0	0.8
MEAN	0.8	0.7	0.6
SD	0.25	0.42	0.39
N	10	10	10

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Reticulocytes

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: RETICS

SEX: MALE

UNITS: % RBCs

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	0.6	0.5	0.6
502	1.3	0.4	1.0
503	0.5	1.0	0.9
504	0.3	0.7	0.7
505	0.5	0.2	0.2
506	0.9	0.3	0.9
507	0.8	0.9	0.6
508	1.5	0.3	0.9
509	0.5	0.3	0.4
510	0.8	0.3	0.6
MEAN	0.8	0.5	0.7
SD	0.38	0.28	0.25
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	1.6	1.2	1.6
552	1.4	1.7	1.1
553	1.5	0.6	1.1
554	1.4	0.4	1.1
555	2.3	0.8	1.0
556	0.6	1.0	0.7
557	1.2	0.8	0.4
558	1.7	1.7	--
559	1.8	1.0	2.0
560	2.0	2.0	2.1
561	--	--	1.7
MEAN	1.6	1.1	1.3
SD	0.46	0.52	0.55
N	10	10	10

(--) - Data Unavailable

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Heinz Bodies

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: HEINZ BOD.

SEX: MALE

UNITS: % RBCs

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-M:0 mg base/kg/day			
401	0.0	0.0	0.0
402	0.0	0.0	0.0
403	0.0	0.0	0.0
404	0.0	0.0	0.0
405	0.0	0.0	0.0
406	0.0	0.0	0.0
407	0.0	0.0	0.0
408	0.0	0.0	0.0
409	0.0	0.0	0.0
410	0.0	0.0	0.0
MEAN	0.0	0.0	0.0
SD	0.00	0.00	0.00
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	0.0	0.0	0.2
452	0.0	0.0	0.0
453	0.0	0.0	0.0
454	0.0	0.0	0.0
455	0.0	0.0	0.0
456	0.0	0.0	0.0
457	0.0	0.0	0.2
458	0.0	0.0	0.0
459	0.0	0.0	0.0
460	0.0	0.0	0.0
MEAN	0.0	0.0	0.0
SD	0.00	0.00	0.08
N	10	10	10

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Heinz Bodies

STUDY ID: UIC-158
STUDY NO: 152
ABBR: HEINZ BOD.

SEX: MALE

UNITS: % RBCs

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	0.0	0.0	0.0
502	0.0	0.0	0.2
503	0.0	0.0	0.0
504	0.0	0.0	0.0
505	0.0	0.0	0.0
506	0.0	0.0	0.0
507	0.0	0.0	0.0
508	0.0	0.0	0.0
509	0.0	0.0	0.0
510	0.0	0.0	0.0
MEAN	0.0	0.0	0.0
SD	0.00	0.00	0.06
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	0.0	0.0	0.0
552	0.0	0.0	0.0
553	0.0	0.3	0.0
554	0.0	0.0	0.0
555	0.0	0.0	0.0
556	0.0	0.0	0.0
557	0.0	0.2	0.0
558	0.0	0.0	--
559	0.0	0.0	0.0
560	0.0	0.4	0.1
561	--	--	0.0
MEAN	0.0	0.1	0.0
SD	0.00	0.15	0.03
N	10	10	10

(--) - Data Unavailable

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: % Methemoglobin

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: % METHGB

SEX: MALE

UNITS: % HGB

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-M:0 mg base/kg/day			
401	0.6	0.6	0.7
402	0.4	0.9	0.4
403	0.5	0.7	0.6
404	0.6	0.9	0.5
405	0.8	1.4	0.7
406	0.8	0.6	0.4
407	0.7	0.8	0.5
408	1.2	0.8	0.7
409	0.4	0.9	0.5
410	0.4	0.7	0.6
MEAN	0.6	0.8	0.6
SD	0.25	0.23	0.12
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	0.6	0.4	0.4
452	0.6	1.0	0.8
453	0.6	0.6	0.2
454	1.0	0.4	0.4
455	1.0	1.2	0.6
456	0.7	1.2	0.9
457	1.0	1.2	0.4
458	1.1	0.5	0.7
459	0.3	0.7	0.7
460	0.5	1.1	0.9
MEAN	0.7	0.8	0.6
SD	0.27	0.34	0.24
N	10	10	10

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: % Methemoglobin

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: % METHGB

SEX: MALE

UNITS: % HGB

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	1.3	3.7	2.5
502	1.2	2.3	2.1
503	0.7	1.9	2.0
504	1.3	2.1	2.7
505	1.3	1.8	2.2
506	1.1	2.0	2.2
507	1.2	3.0	2.2
508	1.4	2.1	1.6
509	1.2	2.6	2.5
510	1.2	2.1	2.6
MEAN	1.2	2.4	2.3
SD	0.19	0.59	0.33
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	6.4	5.9	4.7
552	6.9	7.9	7.8
553	7.5	10.1	9.4
554	6.1	7.6	6.8
555	8.7	5.8	6.0
556	6.1	5.7	7.7
557	7.0	7.3	7.6
558	4.0	6.7	--
559	6.4	9.3	9.5
560	5.8	7.1	7.3
561	--	--	7.4
MEAN	6.5	7.3	7.4
SD	1.22	1.47	1.43
N	10	10	10

(--) - Data Unavailable

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Platelets

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: PLT

SEX: MALE

UNITS: 10^3/mm^3

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-M:0 mg base/kg/day			
401	867	1014	647
402	1016	1000	1016
403	964	979	1055
404	1006	1021	901
405	1119	1303	1411
406	939	986	1003
407	1034	1106	1042
408	760	1040	997
409	906	958	920
410	934	1006	1014
MEAN	955	1041	1001
SD	99.1	100.4	187.1
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	884	856	962
452	1020	961	961
453	1031	1024	856
454	896	947	845
455	1079	988	987
456	957	923	807
457	942	960	1128
458	1248	1240	1148
459	1103	948	968
460	1027	1008	1073
MEAN	1019	986	974
SD	108.7	100.9	116.8
N	10	10	10

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Platelets

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: PLT

SEX: MALE

UNITS: 10^3/mm^3

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	1005	1021	1180
502	1098	1016	1022
503	931	874	986
504	832	928	881
505	969	961	1077
506	955	953	1006
507	916	736	611
508	995	954	1045
509	800	847	843
510	945	1029	1060
MEAN	945	932	971
SD	85.0	91.4	158.6
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	880	817	523
552	1151	918	945
553	1137	995	861
554	894	798	795
555	1024	886	910
556	1064	920	972
557	933	827	842
558	1070	1064	--
559	982	937	1002
560	843	694	781
561	--	--	611
MEAN	998	886	824
SD	108.6	106.0	154.9
N	10	10	10

(--) - Data Unavailable

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Act. Partial Thrombo. Time

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: APTT

SEX: MALE

UNITS: sec

Animal ID	Week 27
GROUP: 1-M:0 mg base/kg/day	
401	15.0
402	20.8
403	19.0
404	22.8
405	11.5
406	22.9
407	18.7
408	16.3
409	18.2
410	16.5
MEAN	18.2
SD	3.54
N	10
GROUP: 2-M:0.5 mg base/kg/day	
451	17.5
452	20.2
453	19.2
454	18.8
455	19.3
456	21.3
457	19.4
458	20.3
459	21.4
460	20.7
MEAN	19.8
SD	1.21
N	10

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Act. Partial Thrombo. Time

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: APTT

SEX: MALE

UNITS: sec

Animal ID	Week 27
GROUP: 3-M:2.0 mg base/kg/day	
501	21.4
502	18.8
503	17.6
504	18.2
505	20.2
506	19.1
507	18.0
508	20.4
509	20.0
510	18.9
MEAN	19.3
SD	1.21
N	10
GROUP: 4-M:9.0 mg base/kg/day	
551	18.1
552	18.4
553	14.5
554	17.7
555	16.5
556	18.3
557	17.8
558	--
559	16.7
560	16.6
561	18.4
MEAN	17.3
SD	1.24
N	10

(--) - Data Unavailable

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Leukocytes

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: WBC

SEX: MALE

UNITS: 10^3/mm^3

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-M:0 mg base/kg/day			
401	15.4	19.3	14.5
402	14.8	14.8	13.6
403	13.6	14.5	13.5
404	21.9	23.0	18.2
405	20.1	18.2	17.8
406	14.7	17.0	16.3
407	17.4	15.7	12.7
408	16.3	14.2	13.8
409	18.8	16.2	17.4
410	12.3	12.1	11.1
MEAN	16.5	16.5	14.9
SD	3.01	3.08	2.40
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	21.2	21.5	23.5
452	19.5	20.2	23.6
453	13.9	15.8	14.6
454	12.3	10.6	11.3
455	19.9	18.7	19.9
456	17.2	18.4	17.0
457	14.5	13.7	14.5
458	12.5	14.3	13.4
459	18.5	16.4	15.1
460	20.6	21.7	19.1
MEAN	17.0	17.1	17.2
SD	3.43	3.62	4.21
N	10	10	10

WBC corrected for NRBC = or > 10

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Leukocytes

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: WBC

SEX: MALE

UNITS: 10^3/mm^3

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	16.4	17.2	15.4
502	15.4	18.9	17.7
503	22.3	24.1	27.5
504	19.4	25.2	17.5
505	17.6	20.0	17.4
506	14.8	20.8	21.1
507	22.0	22.4	22.5
508	23.7	21.0	18.3
509	19.1	19.5	18.1
510	17.1	17.0	17.0
MEAN	18.8	20.6	19.3
SD	3.07	2.70	3.54
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	28.6	30.8	34.7
552	26.1	36.3	24.6
553	26.3	24.8	29.8
554	33.3	31.3	27.8
555	18.3	19.1	14.8
556	31.9	24.9	21.6
557	25.2	26.2	23.4
558	17.1	17.8	--
559	20.4	23.6	20.5
560	35.5	32.6	31.9
561	--	--	33.9
MEAN	26.3	26.7	26.3
SD	6.28	5.95	6.44
N	10	10	10

WBC corrected for NRBC = or > 10

(--) - Data Unavailable

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WHITE DIFFERENTIAL DATA

STUDY ID: UIC-158
STUDY NO: 152

GROUP: 1-M : 0 mg base/kg/day

SEX: MALE

Animal ID		Week 4		Week 13		Week 26	
		CNT	ABS	CNT	ABS	CNT	ABS
401	Nucleated Red Cells	0		0		0	
	M. Neutrophils	18	2.8	13	2.5	12	1.7
	I. Neutrophils	0	0.0	2	0.4	0	0.0
	Lymphocytes	78	12.0	82	15.8	80	11.6
	Monocytes	3	0.5	2	0.4	3	0.4
	Eosinophils	1	0.2	1	0.2	5	0.7
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		15.4		19.3		14.5
402	Nucleated Red Cells	0		0		0	
	M. Neutrophils	8	1.2	25	3.7	21	2.9
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	89	13.2	73	10.8	75	10.2
	Monocytes	3	0.4	2	0.3	2	0.3
	Eosinophils	0	0.0	0	0.0	2	0.3
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		14.8		14.8		13.6
403	Nucleated Red Cells	0		0		0	
	M. Neutrophils	15	2.0	9	1.3	12	1.6
	I. Neutrophils	1	0.1	0	0.0	0	0.0
	Lymphocytes	81	11.0	88	12.8	85	11.5
	Monocytes	3	0.4	2	0.3	1	0.1
	Eosinophils	0	0.0	1	0.1	2	0.3
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		13.6		14.5		13.5
404	Nucleated Red Cells	0		0		0	
	M. Neutrophils	14	3.1	10	2.3	9	1.6
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	84	18.4	89	20.5	89	16.2
	Monocytes	2	0.4	0	0.0	1	0.2
	Eosinophils	0	0.0	1	0.2	1	0.2
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		21.9		23.0		18.2

WBC corrected for NRBC = or > 10

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: U1C-15B
STUDY NO: 152

GROUP: 1-M : 0 mg base/kg/day

SEX: MALE

Animal ID		Week 4		Week 13		Week 26	
		CNT	ABS	CNT	ABS	CNT	ABS
405	Nucleated Red Cells	0		0		0	
	M. Neutrophils	18	3.6	7	1.3	3	0.5
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	79	15.9	92	16.7	97	17.3
	Monocytes	3	0.6	1	0.2	0	0.0
	Eosinophils	0	0.0	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		20.1		18.2		17.8
406	Nucleated Red Cells	0		0		0	
	M. Neutrophils	18	2.6	21	3.6	20	3.3
	I. Neutrophils	1	0.1	1	0.2	0	0.0
	Lymphocytes	76	11.2	76	12.9	78	12.7
	Monocytes	5	0.7	1	0.2	2	0.3
	Eosinophils	0	0.0	1	0.2	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		14.7		17.0		16.3
407	Nucleated Red Cells	0		0		0	
	M. Neutrophils	26	4.5	17	2.7	16	2.0
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	65	11.3	80	12.6	76	9.7
	Monocytes	5	0.9	2	0.3	5	0.6
	Eosinophils	4	0.7	1	0.2	3	0.4
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		17.4		15.7		12.7
408	Nucleated Red Cells	0		0		0	
	M. Neutrophils	9	1.5	16	2.3	21	2.9
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	88	14.3	81	11.5	72	9.9
	Monocytes	3	0.5	2	0.3	4	0.6
	Eosinophils	0	0.0	1	0.1	3	0.4
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		16.3		14.2		13.8

WBC corrected for NRBC = or > 10

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-15B
STUDY NO: 152 GROUP: 1-M : 0 mg base/kg/day SEX: MALE

Animal ID		Week 4		Week 13		Week 26	
		CNT	ABS	CNT	ABS	CNT	ABS
409	Nucleated Red Cells	0		0		0	
	M. Neutrophils	26	4.9	4	0.6	10	1.7
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	73	13.7	94	15.2	90	15.7
	Monocytes	1	0.2	2	0.3	0	0.0
	Eosinophils	0	0.0	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		18.8		16.2		17.4
410	Nucleated Red Cells	0		0		0	
	M. Neutrophils	13	1.6	18	2.2	22	2.4
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	82	10.1	78	9.4	71	7.9
	Monocytes	4	0.5	3	0.4	3	0.3
	Eosinophils	1	0.1	1	0.1	4	0.4
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		12.3		12.1		11.1

WBC corrected for NRBC = or > 10

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WHITE DIFFERENTIAL DATA

STUDY ID: UIC-15B
STUDY NO: 152 GROUP: 2-M : 0.5 mg base/kg/day SEX: MALE

Animal ID		Week 4		Week 13		Week 26	
		CNT	ABS	CNT	ABS	CNT	ABS
451	Nucleated Red Cells	0		0		0	
	M. Neutrophils	16	3.4	15	3.2	25	5.9
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	74	15.7	83	17.8	73	17.2
	Monocytes	7	1.5	2	0.4	1	0.2
	Eosinophils	3	0.6	0	0.0	1	0.2
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		21.2		21.5		23.5
452	Nucleated Red Cells	0		0		0	
	M. Neutrophils	18	3.5	23	4.6	20	4.7
	I. Neutrophils	0	0.0	1	0.2	0	0.0
	Lymphocytes	75	14.6	69	13.9	77	18.2
	Monocytes	7	1.4	4	0.8	0	0.0
	Eosinophils	0	0.0	3	0.6	3	0.7
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		19.5		20.2		23.6
453	Nucleated Red Cells	0		0		0	
	M. Neutrophils	18	2.5	24	3.8	28	4.1
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	77	10.7	75	11.9	69	10.1
	Monocytes	5	0.7	1	0.2	1	0.1
	Eosinophils	0	0.0	0	0.0	2	0.3
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		13.9		15.8		14.6
454	Nucleated Red Cells	0		0		1	
	M. Neutrophils	21	2.6	18	1.9	19	2.1
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	78	9.6	82	8.7	79	8.9
	Monocytes	1	0.1	0	0.0	2	0.2
	Eosinophils	0	0.0	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		12.3		10.6		11.3

WBC corrected for NRBC = or > 10

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-15B
STUDY NO: 152 GROUP: 2-M : 0.5 mg base/kg/day SEX: MALE

Animal ID		Week 4		Week 13		Week 26	
		CNT	ABS	CNT	ABS	CNT	ABS
455	Nucleated Red Cells	0		0		0	
	M. Neutrophils	9	1.8	10	1.9	23	4.6
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	86	17.1	88	16.5	72	14.3
	Monocytes	5	1.0	2	0.4	5	1.0
	Eosinophils	0	0.0	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		19.9		18.7		19.9
456	Nucleated Red Cells	0		0		0	
	M. Neutrophils	9	1.5	13	2.4	19	3.2
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	87	15.0	85	15.6	77	13.1
	Monocytes	4	0.7	0	0.0	3	0.5
	Eosinophils	0	0.0	2	0.4	1	0.2
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		17.2		18.4		17.0
457	Nucleated Red Cells	0		0		0	
	M. Neutrophils	8	1.2	15	2.1	17	2.5
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	83	12.0	81	11.1	76	11.0
	Monocytes	7	1.0	4	0.5	5	0.7
	Eosinophils	2	0.3	0	0.0	2	0.3
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		14.5		13.7		14.5
458	Nucleated Red Cells	0		0		0	
	M. Neutrophils	8	1.0	6	0.9	10	1.3
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	91	11.4	91	13.0	84	11.3
	Monocytes	0	0.0	2	0.3	2	0.3
	Eosinophils	1	0.1	1	0.1	4	0.5
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		12.5		14.3		13.4

WBC corrected for NRBC = or > 10

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WHITE DIFFERENTIAL DATA

STUDY ID: UIC-15B
STUDY NO: 152

GROUP: 2-M : 0.5 mg base/kg/day

SEX: MALE

Animal ID		Week 4		Week 13		Week 26	
		CNT	ABS	CNT	ABS	CNT	ABS
459	Nucleated Red Cells	0		0		0	
	M. Neutrophils	11	2.0	10	1.6	14	2.1
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	85	15.7	85	13.9	84	12.7
	Monocytes	3	0.6	4	0.7	2	0.3
	Eosinophils	1	0.2	1	0.2	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		18.5		16.4		15.1
460	Nucleated Red Cells	0		0		0	
	M. Neutrophils	10	2.1	10	2.2	16	3.1
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	87	17.9	87	18.9	80	15.3
	Monocytes	2	0.4	3	0.7	3	0.6
	Eosinophils	1	0.2	0	0.0	1	0.2
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		20.6		21.7		19.1

WBC corrected for NRBC = or > 10

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-15B
STUDY NO: 152

GROUP: 3-M : 2.0 mg base/kg/day

SEX: MALE

Animal ID		Week 4		Week 13		Week 26	
		CNT	ABS	CNT	ABS	CNT	ABS
501	Nucleated Red Cells	0		0		0	
	M. Neutrophils	18	3.0	19	3.3	18	2.8
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	76	12.5	78	13.4	80	12.3
	Monocytes	6	1.0	1	0.2	1	0.2
	Eosinophils	0	0.0	2	0.3	1	0.2
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		16.4		17.2		15.4
502	Nucleated Red Cells	0		0		0	
	M. Neutrophils	20	3.1	11	2.1	16	2.8
	I. Neutrophils	1	0.2	0	0.0	0	0.0
	Lymphocytes	79	12.2	85	16.1	81	14.3
	Monocytes	0	0.0	4	0.8	2	0.4
	Eosinophils	0	0.0	0	0.0	1	0.2
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		15.4		18.9		17.7
503	Nucleated Red Cells	0		0		0	
	M. Neutrophils	18	4.0	13	3.1	27	7.4
	I. Neutrophils	1	0.2	0	0.0	0	0.0
	Lymphocytes	77	17.2	85	20.5	70	19.3
	Monocytes	4	0.9	1	0.2	1	0.3
	Eosinophils	0	0.0	1	0.2	2	0.6
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		22.3		24.1		27.5
504	Nucleated Red Cells	0		0		0	
	M. Neutrophils	11	2.1	13	3.3	9	1.6
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	88	17.1	85	21.4	91	15.9
	Monocytes	1	0.2	2	0.5	0	0.0
	Eosinophils	0	0.0	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		19.4		25.2		17.5

WBC corrected for NRBC = or > 10

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WHITE DIFFERENTIAL DATA

STUDY ID: UIC-15B
STUDY NO: 152 GROUP: 3-M : 2.0 mg base/kg/day SEX: MALE

Animal ID		Week 4		Week 13		Week 26	
		CNT	ABS	CNT	ABS	CNT	ABS
505	Nucleated Red Cells	0		0		1	
	M. Neutrophils	10	1.8	17	3.4	13	2.3
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	88	15.5	80	16.0	82	14.3
	Monocytes	2	0.4	1	0.2	3	0.5
	Eosinophils	0	0.0	2	0.4	2	0.3
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		17.6		20.0		17.4
506	Nucleated Red Cells	0		0		0	
	M. Neutrophils	12	1.8	11	2.3	17	3.6
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	86	12.7	85	17.7	81	17.1
	Monocytes	2	0.3	3	0.6	2	0.4
	Eosinophils	0	0.0	1	0.2	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		14.8		20.8		21.1
507	Nucleated Red Cells	0		1		0	
	M. Neutrophils	20	4.4	14	3.1	13	2.9
	I. Neutrophils	0	0.0	1	0.2	0	0.0
	Lymphocytes	77	16.9	83	18.6	86	19.4
	Monocytes	3	0.7	2	0.4	1	0.2
	Eosinophils	0	0.0	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		22.0		22.4		22.5
508	Nucleated Red Cells	0		0		1	
	M. Neutrophils	31	7.3	23	4.8	11	2.0
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	66	15.6	72	15.1	89	16.3
	Monocytes	3	0.7	5	1.1	0	0.0
	Eosinophils	0	0.0	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		23.7		21.0		18.3

WBC corrected for NRBC = or > 10

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-15B
STUDY NO: 152 GROUP: 3-M : 2.0 mg base/kg/day SEX: MALE

Animal ID		Week 4		Week 13		Week 26	
		CNT	ABS	CNT	ABS	CNT	ABS
509	Nucleated Red Cells	0		0		0	
	M. Neutrophils	24	4.6	18	3.5	20	3.6
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	72	13.8	81	15.8	80	14.5
	Monocytes	4	0.8	1	0.2	0	0.0
	Eosinophils	0	0.0	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		19.1		19.5		18.1
510	Nucleated Red Cells	0		0		0	
	M. Neutrophils	22	3.8	20	3.4	19	3.2
	I. Neutrophils	1	0.2	0	0.0	0	0.0
	Lymphocytes	76	13.0	80	13.6	80	13.6
	Monocytes	0	0.0	0	0.0	1	0.2
	Eosinophils	1	0.2	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		17.1		17.0		17.0

WBC corrected for NRBC = or > 10

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WHITE DIFFERENTIAL DATA

STUDY ID: UIC-15B
STUDY NO: 152

GROUP: 4-M : 9.0 mg base/kg/day

SEX: MALE

Animal ID		Week 4		Week 13		Week 26	
		CNT	ABS	CNT	ABS	CNT	ABS
551	Nucleated Red Cells	0		1		0	
	M. Neutrophils	8	2.3	17	5.2	12	4.2
	I. Neutrophils	0	0.0	1	0.3	0	0.0
	Lymphocytes	89	25.5	76	23.4	85	29.5
	Monocytes	3	0.9	6	1.8	3	1.0
	Eosinophils	0	0.0	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		28.6		30.8		34.7
552	Nucleated Red Cells	0		0		0	
	M. Neutrophils	13	3.4	10	3.6	14	3.4
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	84	21.9	85	30.9	83	20.4
	Monocytes	3	0.8	4	1.5	3	0.7
	Eosinophils	0	0.0	1	0.4	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		26.1		36.3		24.6
553	Nucleated Red Cells	0		0		2	
	M. Neutrophils	12	3.2	12	3.0	16	4.8
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	86	22.6	86	21.3	79	23.5
	Monocytes	2	0.5	2	0.5	5	1.5
	Eosinophils	0	0.0	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		26.3		24.8		29.8
554	Nucleated Red Cells	0		0		0	
	M. Neutrophils	22	7.3	11	3.4	19	5.3
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	74	24.6	86	26.9	80	22.2
	Monocytes	4	1.3	3	0.9	1	0.3
	Eosinophils	0	0.0	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		33.3		31.3		27.8

WBC corrected for NRBC = or > 10

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WHITE DIFFERENTIAL DATA

STUDY ID: UIC-15B
STUDY NO: 152

GROUP: 4-M : 9.0 mg base/kg/day

SEX: MALE

Animal ID		Week 4		Week 13		Week 26	
		CNT	ABS	CNT	ABS	CNT	ABS
555	Nucleated Red Cells	0		0		0	
	M. Neutrophils	17	3.1	19	3.6	19	2.8
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	81	14.8	79	15.1	76	11.2
	Monocytes	2	0.4	2	0.4	5	0.7
	Eosinophils	0	0.0	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		18.3		19.1		14.8
556	Nucleated Red Cells	0		0		0	
	M. Neutrophils	20	6.4	18	4.5	16	3.5
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	78	24.9	82	20.4	77	16.6
	Monocytes	1	0.3	0	0.0	6	1.3
	Eosinophils	1	0.3	0	0.0	1	0.2
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		31.9		24.9		21.6
557	Nucleated Red Cells	0		0		0	
	M. Neutrophils	11	2.8	22	5.8	15	3.5
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	81	20.4	77	20.2	82	19.2
	Monocytes	7	1.8	0	0.0	3	0.7
	Eosinophils	1	0.3	1	0.3	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		25.2		26.2		23.4
558	Nucleated Red Cells	0		0		0	
	M. Neutrophils	22	3.8	33	5.9	0	--
	I. Neutrophils	0	0.0	0	0.0	0	--
	Lymphocytes	75	12.8	65	11.6	0	--
	Monocytes	3	0.5	2	0.4	0	--
	Eosinophils	0	0.0	0	0.0	0	--
	Basophils	0	0.0	0	0.0	0	--
	Atypical Lymphocytes	0	0.0	0	0.0	0	--
	WBC		17.1		17.8		--

WBC corrected for NRBC = or > 10

(--) - Data Unavailable

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-15B
STUDY NO: 152

GROUP: 4-M : 9.0 mg base/kg/day

SEX: MALE

Animal ID		Week 4		Week 13		Week 26	
		CNT	ABS	CNT	ABS	CNT	ABS
559	Nucleated Red Cells	0		0		0	
	M. Neutrophils	11	2.2	9	2.1	21	4.3
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	83	16.9	87	20.5	77	15.8
	Monocytes	6	1.2	4	0.9	1	0.2
	Eosinophils	0	0.0	0	0.0	1	0.2
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		20.4		23.6		20.5
560	Nucleated Red Cells	0		0		0	
	M. Neutrophils	18	6.4	20	6.5	18	5.7
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	79	28.0	78	25.4	77	24.6
	Monocytes	3	1.1	2	0.7	3	1.0
	Eosinophils	0	0.0	0	0.0	2	0.6
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		35.5		32.6		31.9
561	Nucleated Red Cells	0		0		0	
	M. Neutrophils	0	--	0	--	14	4.7
	I. Neutrophils	0	--	0	--	1	0.3
	Lymphocytes	0	--	0	--	82	27.8
	Monocytes	0	--	0	--	3	1.0
	Eosinophils	0	--	0	--	0	0.0
	Basophils	0	--	0	--	0	0.0
	Atypical Lymphocytes	0	--	0	--	0	0.0
	WBC		--		--		33.9

WBC corrected for NRBC = or > 10

(--) - Data Unavailable

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: UIC-15B
STUDY NO: 152
GROUP: 1-M : 0 mg base/kg/day
SEX: MALE

Animal ID	Week 4	Week 13	Week 26
401	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
402	Normal Red Blood Cells	Normal Red Blood Cells	Anisocytosis,Slight
403	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
404	Anisocytosis,Slight	Normal Red Blood Cells	Normal Red Blood Cells
405	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
406	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
407	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
408	Clumped Platelets, Slight	Normal Red Blood Cells	Clumped Platelets, Slight;Normal Red Blood Cells
409	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
410	Normal Red Blood Cells	Polychromasia,Slight Anisocytosis,Slight	Normal Red Blood Cells

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: UIC-15B
STUDY NO: 152
SEX: MALE
GROUP: 2-M : 0.5 mg base/kg/day

Animal ID	Week 4	Week 13	Week 26
451	Normal Red Blood Cells	Anisocytosis,Slight	Anisocytosis,Slight.
452	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
453	Normal Red Blood Cells	Anisocytosis,Slight; Hyper-Segmented Neutrophils,Slight	Normal Red Blood Cells
454	Normal Red Blood Cells	Anisocytosis,Slight	Normal Red Blood Cells
455	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
456	Normal Red Blood Cells	Poikilocytes,Slight	Normal Red Blood Cells
457	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
458	Normal Red Blood Cells	Poikilocytes,Slight; Anisocytosis,Slight	Normal Red Blood Cells
459	Normal Red Blood Cells	Anisocytosis,Slight	Anisocytosis,Slight; Poikilocytes,Slight
460	Polychromasia,Slight	Normal Red Blood Cells	Normal Red Blood Cells

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: UIC-15B
STUDY NO: 152

SEX: MALE

GROUP: 3-M : 2.0 mg base/kg/day

Animal ID	Week 4	Week 13	Week 26
501	Normal Red Blood Cells	Normal Red Blood Cells	Poikilocytes,Slight
502	Normal Red Blood Cells	Normal Red Blood Cells	Anisocytosis,Slight
503	Normal Red Blood Cells	Normal Red Blood Cells	Anisocytosis,Slight
504	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
505	Normal Red Blood Cells	Anisocytosis,Slight	Normal Red Blood Cells
506	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
507	Normal Red Blood Cells	Poikilocytes,Slight	Normal Red Blood Cells
508	Normal Red Blood Cells	Normal Red Blood Cells	Anisocytosis,Slight
509	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
510	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: UIC-15B
STUDY NO: 152

SEX: MALE

GROUP: 4-M : 9.0 mg base/kg/day

Animal ID	Week 4	Week 13	Week 26
551	Normal Red Blood Cells	Normal Red Blood Cells	Clumped Platelets, Slight;Normal Red Blood Cells
552	Anisocytosis,Slight	Anisocytosis,Slight	Normal Red Blood Cells
553	Normal Red Blood Cells	Normal Red Blood Cells	Poikilocytes,Slight
554	Normal Red Blood Cells	Normal Red Blood Cells	Poikilocytes,Slight
555	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
556	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
557	Polychromasia,Slight	Poikilocytes,Slight; Anisocytosis,Slight	Normal Red Blood Cells
558	Polychromasia,Slight	Normal Red Blood Cells	--
559	Normal Red Blood Cells	Anisocytosis,Slight	Normal Red Blood Cells
560	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
561	--	--	Normal Red Blood Cells

(--) - Data Unavailable

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Erythrocytes

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: RBC

SEX: FEMALE

UNITS: 10^6/mm^3

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	7.32	7.99	7.56
427	7.37	7.93	7.86
428	7.18	7.98	8.25
429	7.40	7.76	7.52
430	7.42	7.43	7.06
431	7.20	7.94	7.65
432	7.65	8.58	8.08
433	7.09	7.27	7.43
434	7.66	7.84	7.44
435	7.61	8.28	8.07
MEAN	7.39	7.90	7.69
SD	0.201	0.375	0.367
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	7.34	8.83	7.85
477	8.04	8.44	7.68
478	7.23	7.49	7.15
479	7.26	7.57	7.42
480	7.35	7.71	7.66
481	7.12	7.12	7.02
482	7.63	7.75	7.84
483	7.34	7.41	7.55
484	7.19	7.82	7.58
485	7.59	7.49	7.63
MEAN	7.41	7.76	7.54
SD	0.275	0.509	0.272
N	10	10	10

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Erythrocytes

STUDY ID: U1C-15B
STUDY NO: 152
ABBR: RBC

SEX: FEMALE

UNITS: 10^6/mm^3

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	6.82	7.49	7.79
527	7.36	7.34	7.63
528	7.29	7.79	7.47
529	6.79	6.84	7.08
530	6.91	7.07	7.22
531	7.23	7.07	6.99
532	7.66	8.07	7.39
533	6.93	7.76	7.34
534	7.32	6.99	7.35
535	6.90	7.36	7.02
MEAN	7.12	7.38	7.33
SD	0.290	0.400	0.261
N	10	10	10
GROUP: 4-F:9.0 mg base/kg/day			
576	6.71	7.34	7.40
577	6.63	7.13	6.95
578	6.72	8.02	7.51
579	6.57	7.55	7.84
580	6.29	7.15	7.20
581	6.70	7.02	7.07
582	6.57	6.73	6.91
583	6.99	7.51	7.91
584	6.76	7.30	7.56
585	6.11	7.06	7.08
MEAN	6.61	7.28	7.34
SD	0.248	0.355	0.358
N	10	10	10

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Hemoglobin

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: HGB

SEX: FEMALE

UNITS: g/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	16.5	16.3	15.0
427	16.4	15.9	15.8
428	16.1	15.7	16.1
429	15.3	15.5	14.7
430	15.6	14.9	14.4
431	15.7	16.0	15.4
432	16.0	16.2	15.3
433	15.2	14.8	14.9
434	16.8	16.8	15.4
435	16.1	16.0	15.3
MEAN	16.0	15.8	15.2
SD	0.52	0.62	0.50
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	15.1	16.5	15.0
477	16.7	16.2	15.0
478	15.6	14.9	14.4
479	15.9	15.4	15.2
480	15.9	15.8	14.9
481	15.1	14.7	14.9
482	15.6	15.2	14.9
483	15.8	15.2	15.4
484	15.0	15.1	15.0
485	15.9	14.9	14.8
MEAN	15.7	15.4	15.0
SD	0.51	0.59	0.26
N	10	10	10

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Hemoglobin

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: HGB

SEX: FEMALE
UNITS: g/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	14.7	14.9	14.9
527	16.0	14.9	15.2
528	15.3	15.1	15.1
529	14.8	13.9	14.3
530	15.2	14.6	14.7
531	15.3	14.4	14.4
532	17.3	17.2	15.4
533	14.8	14.9	14.4
534	15.7	18.1@	14.9
535	15.3	15.0	14.3
MEAN	15.4	15.0	14.8
SD	0.77	0.91	0.40
N	10	9	10
GROUP: 4-F:9.0 mg base/kg/day			
576	15.0	15.4	15.0
577	14.5	14.4	13.4
578	13.9	15.0	13.3
579	14.8	15.4	15.1
580	14.1	14.4	14.2
581	14.5	14.7	14.3
582	14.7	13.2	12.9
583	14.3	14.5	14.4
584	14.7	14.9	14.9
585	13.8	14.4	13.8
MEAN	14.4	14.6	14.1
SD	0.40	0.63	0.76
N	10	10	10

@ - Excluded - apparent outlier (> 3 SDs from the mean)

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Hematocrit

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: HCT

SEX: FEMALE

UNITS: %

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	42.3	44.3	43.8
427	43.3	44.0	45.2
428	41.4	43.3	46.0
429	41.4	42.0	41.6
430	43.7	42.6	41.7
431	41.3	43.5	43.1
432	45.1	45.6	45.1
433	40.5	40.1	41.6
434	46.6	47.0	45.7
435	43.4	43.8	44.5
MEAN	42.9	43.6	43.8
SD	1.91	1.89	1.74
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	40.4	46.4	43.0
477	44.9	44.5	41.9
478	42.4	42.8	42.2
479	42.5	42.6	43.2
480	42.0	42.3	43.6
481	43.2	42.4	43.8
482	44.1	43.2	44.1
483	42.5	41.4	44.2
484	40.8	43.2	42.9
485	42.2	40.8	42.7
MEAN	42.5	43.0	43.2
SD	1.35	1.57	0.77
N	10	10	10

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Hematocrit

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: HCT

SEX: FEMALE

UNITS: %

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	38.9	40.5	43.5
527	42.9	42.4	44.6
528	40.4	41.9	41.2
529	38.8	37.8	40.2
530	39.9	40.2	42.3
531	41.0	39.3	40.8
532	44.3	46.4	43.5
533	38.5	41.4	40.8
534	42.7	39.8	42.6
535	40.0	41.7	41.5
MEAN	40.7	41.1	42.1
SD	1.97	2.31	1.44
N	10	10	10
GROUP: 4-F:9.0 mg base/kg/day			
576	40.7	43.7	44.8
577	39.8	41.9	40.9
578	37.7	43.0	38.7
579	40.1	44.8	45.3
580	37.2	40.0	40.2
581	40.3	41.3	41.8
582	38.8	37.1	37.9
583	38.7	40.8	41.4
584	41.4	43.7	44.7
585	36.2	39.8	40.3
MEAN	39.1	41.6	41.6
SD	1.67	2.31	2.58
N	10	10	10

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpuscular Volume

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: MCV

SEX: FEMALE

UNITS: fL

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	57.8	55.4	57.9
427	58.8	55.5	57.5
428	57.7	54.3	55.8
429	55.9	54.1	55.3
430	58.9	57.3	59.1
431	57.4	54.8	56.3
432	59.0	53.1	55.8
433	57.1	55.2	56.0
434	60.8	59.9	61.4
435	57.0	52.9	55.1
MEAN	58.0	55.3	57.0
SD	1.37	2.07	1.99
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	55.0	52.5	54.8
477	55.8	52.7	54.6
478	58.6	57.1	59.0
479	58.5	56.3	58.2
480	57.1	54.9	56.9
481	60.7	59.6	62.4
482	57.8	55.7	56.3
483	57.9	55.9	58.5
484	56.7	55.2	56.6
485	55.6	54.5	56.0
MEAN	57.4	55.4	57.3
SD	1.70	2.07	2.31
N	10	10	10

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpuscular Volume

STUDY ID: UIC-158
STUDY NO: 152
ABBR: MCV

SEX: FEMALE

UNITS: fL

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	57.0	54.1	55.8
527	58.3	57.8	58.5
528	55.4	53.8	55.2
529	57.1	55.3	56.8
530	57.7	56.9	58.6
531	56.7	55.6	58.4
532	57.8	57.5	58.9
533	55.6	53.4	55.6
534	58.3	56.9	58.0
535	58.0	56.7	59.1
MEAN	57.2	55.8	57.5
SD	1.04	1.60	1.49
N	10	10	10
GROUP: 4-F:9.0 mg base/kg/day			
576	60.7	59.5	60.5
577	60.0	58.8	58.8
578	56.1	53.6	51.5
579	61.0	59.3	57.8
580	59.1	55.9	55.8
581	60.1	58.8	59.1
582	59.1	55.1	54.8
583	55.4	54.3	52.3
584	61.2	59.9	59.1
585	59.2	56.4	56.9
MEAN	59.2	57.2	56.7
SD	1.97	2.36	3.03
N	10	10	10

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpuscular Hemoglobin

STUDY ID: UIC-158
STUDY NO: 152
ABBR: MCH

SEX: FEMALE

UNITS: pg

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	22.5	20.4	19.8
427	22.3	20.1	20.1
428	22.4	19.7	19.5
429	20.7	20.0	19.5
430	21.0	20.1	20.4
431	21.8	20.2	20.1
432	20.9	18.9	18.9
433	21.4	20.4	20.1
434	21.9	21.4	20.7
435	21.2	19.3	19.0
MEAN	21.6	20.1	19.8
SD	0.66	0.68	0.58
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	20.6	18.7	19.1
477	20.8	19.2	19.5
478	21.6	19.9	20.1
479	21.9	20.3	20.5
480	21.6	20.5	19.5
481	21.2	20.6	21.2
482	20.4	19.6	19.0
483	21.5	20.5	20.4
484	20.9	19.3	19.8
485	20.9	19.9	19.4
MEAN	21.1	19.9	19.9
SD	0.49	0.64	0.69
N	10	10	10

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpuscular Hemoglobin

STUDY ID: UIC-158
STUDY NO: 152
ABBR: MCH

SEX: FEMALE

UNITS: pg

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	21.6	19.9	19.1
527	21.7	20.3	19.9
528	21.0	19.4	20.2
529	21.8	20.3	20.2
530	22.0	20.7	20.4
531	21.2	20.4	20.6
532	22.6	21.3	20.8
533	21.4	19.2	19.6
534	21.4	25.9@	20.3
535	22.2	20.4	20.4
MEAN	21.7	20.2	20.2
SD	0.48	0.64	0.50
N	10	9	10
GROUP: 4-F:9.0 mg base/kg/day			
576	22.4	21.0	20.3
577	21.9	20.2	19.3
578	20.7	18.7	17.7
579	22.5	20.4	19.3
580	22.4	20.1	19.7
581	21.6	20.9	20.2
582	22.4	19.6	18.7
583	20.5	19.3	18.2
584	21.7	20.4	19.7
585	22.6	20.4	19.5
MEAN	21.9	20.1	19.3
SD	0.75	0.71	0.84
N	10	10	10

@ - [Excluded - apparent outlier (> 3 SDs from the mean)

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpus. Hemo. Conc.

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: MCHC

SEX: FEMALE

UNITS: g/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	39.0	36.8	34.2
427	37.9	36.1	35.0
428	38.9	36.3	35.0
429	37.0	36.9	35.3
430	35.7	35.0	34.5
431	38.0	36.8	35.7
432	35.5	35.5	33.9
433	37.5	36.9	35.8
434	36.1	35.7	33.7
435	37.1	36.5	34.4
MEAN	37.3	36.3	34.8
SD	1.23	0.66	0.73
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	37.4	35.6	34.9
477	37.2	36.4	35.8
478	36.8	34.8	34.1
479	37.4	36.2	35.2
480	37.9	37.4	34.2
481	35.0	34.7	34.0
482	35.4	35.2	33.8
483	37.2	36.7	34.8
484	36.8	35.0	35.0
485	37.7	36.5	34.7
MEAN	36.9	35.9	34.7
SD	0.95	0.92	0.62
N	10	10	10

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpus. Hemo. Conc.

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: MCHC

SEX: FEMALE

UNITS: g/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	37.8	36.8	34.3
527	37.3	35.1	34.1
528	37.9	36.0	36.7
529	38.1	36.8	35.6
530	38.1	36.3	34.8
531	37.3	36.6	35.3
532	39.1	37.1	35.4
533	38.4	36.0	35.3
534	36.8	45.5@	35.0
535	38.3	36.0	34.5
MEAN	37.9	36.3	35.1
SD	0.66	0.61	0.75
N	10	9	10
GROUP: 4-F:9.0 mg base/kg/day			
576	36.9	35.2	33.5
577	36.4	34.4	32.8
578	36.9	34.9	34.4
579	36.9	34.4	33.3
580	37.9	36.0	35.3
581	36.0	35.6	34.2
582	37.9	35.6	34.0
583	37.0	35.5	34.8
584	35.5	34.1	33.3
585	38.1	36.2	34.2
MEAN	37.0	35.2	34.0
SD	0.85	0.72	0.76
N	10	10	10

@ - Excluded - apparent outlier (> 3 SDs from the mean)

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Reticulocytes

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: RETICS

SEX: FEMALE

UNITS: % RBCs

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	0.7	0.3	1.2
427	0.5	0.4	0.8
428	0.4	0.6	0.8
429	0.9	0.7	1.1
430	0.3	0.5	1.3
431	0.4	0.4	1.4
432	0.5	0.2	1.1
433	0.7	0.9	1.0
434	0.8	0.3	1.4
435	0.6	0.5	1.2
MEAN	0.6	0.5	1.1
SD	0.19	0.21	0.22
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	0.6	0.5	1.2
477	0.8	0.4	0.5
478	0.8	0.4	1.6
479	0.3	0.6	0.9
480	0.5	0.3	1.0
481	1.0	1.1	1.2
482	0.8	0.9	1.0
483	0.8	0.4	0.3
484	0.7	0.4	1.1
485	0.3	0.8	1.0
MEAN	0.7	0.6	1.0
SD	0.23	0.27	0.36
N	10	10	10

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Reticulocytes

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: RETICS

SEX: FEMALE

UNITS: % RBCs

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	0.8	1.4	1.5
527	0.6	1.4	0.9
528	0.5	0.0	0.8
529	0.8	0.5	0.8
530	0.2	0.4	0.7
531	1.1	0.4	0.3
532	1.3	0.4	0.5
533	1.0	0.5	1.6
534	1.5	0.2	1.4
535	0.8	0.9	0.7
MEAN	0.9	0.6	0.9
SD	0.38	0.47	0.44
N	10	10	10
GROUP: 4-F:9.0 mg base/kg/day			
576	1.1	0.2	1.5
577	0.9	2.0	2.5
578	2.3	0.7	1.5
579	1.1	1.1	2.1
580	0.8	0.8	1.7
581	2.0	0.9	1.1
582	2.0	1.5	2.2
583	1.4	0.8	1.3
584	1.2	0.9	1.2
585	1.6	1.0	1.4
MEAN	1.4	1.0	1.7
SD	0.51	0.48	0.47
N	10	10	10

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Heinz Bodies

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: HEINZ BOD.

SEX: FEMALE

UNITS: % RBCs

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	0.0	0.0	0.0
427	0.0	0.1	0.0
428	0.0	0.0	0.0
429	0.0	0.0	0.0
430	0.0	0.0	0.0
431	0.0	0.0	0.0
432	0.0	0.0	0.0
433	0.0	0.0	0.0
434	0.0	0.0	0.0
435	0.0	0.0	0.0
MEAN	0.0	0.0	0.0
SD	0.00	0.03	0.00
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	0.0	0.1	0.0
477	0.0	0.0	0.0
478	0.0	0.0	0.0
479	0.0	0.0	0.0
480	0.0	0.0	0.0
481	0.0	0.0	0.0
482	0.0	0.0	0.0
483	0.0	0.0	0.0
484	0.0	0.0	0.0
485	0.0	0.0	0.0
MEAN	0.0	0.0	0.0
SD	0.00	0.03	0.00
N	10	10	10

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Heinz Bodies

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: HEINZ BOD.

SEX: FEMALE

UNITS: % RBCs

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	0.0	0.0	0.0
527	0.0	0.0	0.0
528	0.0	0.0	0.0
529	0.0	0.0	0.0
530	0.0	0.0	0.0
531	0.0	0.0	0.0
532	0.0	0.0	0.0
533	0.0	0.0	0.0
534	0.0	0.0	0.0
535	0.0	0.0	0.0
MEAN	0.0	0.0	0.0
SD	0.00	0.00	0.00
N	10	10	10
GROUP: 4-F:9.0 mg base/kg/day			
576	0.0	0.0	0.2
577	0.0	0.0	0.0
578	0.0	0.0	0.5
579	0.0	0.4	0.0
580	0.0	0.0	0.0
581	0.0	0.2	0.1
582	0.0	0.1	0.1
583	0.0	0.1	0.1
584	0.0	0.0	0.0
585	0.0	0.2	0.0
MEAN	0.0	0.1	0.1
SD	0.00	0.13	0.16
N	10	10	10

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: % Methemoglobin

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: % METHGB

SEX: FEMALE

UNITS: % HGB

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	0.6	0.3	0.4
427	1.0	0.4	0.8
428	0.6	1.0	0.0
429	0.6	0.0	0.3
430	0.9	0.5	0.8
431	0.8	0.3	1.4
432	0.9	0.4	0.0
433	0.7	0.3	1.5
434	0.8	0.7	0.6
435	0.7	0.4	0.6
MEAN	0.8	0.4	0.6
SD	0.14	0.27	0.51
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	0.7	0.4	0.5
477	0.7	0.7	1.0
478	0.8	0.1	0.7
479	0.6	0.7	0.6
480	0.4	-0.1	0.1
481	0.7	0.9	0.7
482	0.8	0.1	0.7
483	0.5	0.6	0.1
484	0.8	0.6	1.0
485	1.2	0.8	0.8
MEAN	0.7	0.5	0.6
SD	0.21	0.34	0.32
N	10	10	10

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: % Methemoglobin

STUDY ID: UIC-158
STUDY NO: 152
ABBR: % METHGB

SEX: FEMALE

UNITS: % HGB

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	1.2	1.8	0.9
527	0.9	1.2	1.4
528	1.2	1.5	2.5
529	1.2	1.9	1.2
530	1.3	1.4	2.0
531	1.8	2.2	2.6
532	1.0	1.8	2.1
533	1.1	1.7	1.9
534	1.2	1.7	2.4
535	0.9	1.2	1.3
MEAN	1.2	1.6	1.8
SD	0.26	0.32	0.60
N	10	10	10
GROUP: 4-F:9.0 mg base/kg/day			
576	5.4	6.3	6.4
577	4.8	5.9	5.5
578	7.7	8.6	8.8
579	6.1	7.5	8.6
580	8.3	9.1	12.7
581	5.4	7.0	6.7
582	5.1	6.4	7.1
583	7.1	6.4	8.6
584	3.8	5.6	6.5
585	5.6	7.5	8.7
MEAN	5.9	7.0	8.0
SD	1.39	1.15	2.04
N	10	10	10

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Platelets

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: PLT

SEX: FEMALE

UNITS: 10^3/mm^3

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	1161	1094	1034
427	1175	1034	1050
428	957	870	807
429	1056	904	858
430	1072	851	892
431	1336	1213	1281
432	845	638	963
433	1180	955	1022
434	977	917	901
435	1129	1064	989
MEAN	1089	954	980
SD	139.2	158.7	133.1
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	1253	1060	1126
477	1223	1215	1089
478	973	933	798
479	856	726	729
480	1087	996	898
481	912	803	752
482	1029	946	1046
483	1190	1050	852
484	1090	903	964
485	1046	867	772
MEAN	1066	950	903
SD	130.9	139.7	146.2
N	10	10	10

880 - 1400

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Platelets

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: PLT

SEX: FEMALE

UNITS: 10^3/mm^3

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	398	793	1014
527	960	856	930
528	975	940	987
529	1042	905	969
530	824	780	815
531	954	838	814
532	1082	1003	990
533	1114	824	841
534	1169	978	1109
535	985	948	946
MEAN	950	887	942
SD	216.9	79.0	94.9
N	10	10	10
GROUP: 4-F:9.0 mg base/kg/day			
576	1176	1180	1095
577	1048	1072	1077
578	1064	971	766
579	1253	1121	1022
580	962	851	920
581	1105	987	883
582	1245	1366	1192
583	1070	825	905
584	1209	1166	1080
585	1046	998	855
MEAN	1118	1054	980
SD	97.6	162.9	133.1
N	10	10	10

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Act. Partial Thrombo. Time

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: APTT

SEX: FEMALE

UNITS: sec

Animal ID	Week 27
GROUP: 1-F:0 mg base/kg/day	
426	15.4
427	16.1
428	13.7
429	13.6
430	16.9
431	17.0
432	18.0
433	15.8
434	20.1
435	16.7
MEAN	16.3
SD	1.93
N	10
GROUP: 2-F:0.5 mg base/kg/day	
476	17.7
477	25.8
478	19.1
479	13.2
480	11.8
481	18.3
482	18.4
483	19.5
484	12.7
485	27.3
MEAN	18.4
SD	5.16
N	10

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Act. Partial Thrombo. Time

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: APTT

SEX: FEMALE

UNITS: sec

Animal ID	Week 27
GROUP: 3-F:2.0 mg base/kg/day	
526	20.6
527	18.2
528	19.3
529	18.9
530	21.1
531	19.5
532	22.8
533	17.8
534	10.2
535	20.7
MEAN	18.9
SD	3.40
N	10
GROUP: 4-F:9.0 mg base/kg/day	
576	18.5
577	20.8
578	19.2
579	11.9
580	17.4
581	15.4
582	14.0
583	18.5
584	20.6
585	13.3
MEAN	17.0
SD	3.13
N	10

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Leukocytes

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: WBC

SEX: FEMALE

UNITS: 10^3/mm^3

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	12.6	15.1	12.9
427	12.4	13.5	8.3
428	21.7	24.4	18.2
429	14.1	14.4	9.3
430	12.4	12.5	9.4
431	16.1	17.4	16.0
432	14.8	10.4	9.2
433	18.1	15.3	14.7
434	15.7	10.9	10.2
435	21.0	18.9	17.8
MEAN	15.9	15.3	12.6
SD	3.41	4.16	3.82
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	16.7	15.8	10.3
477	16.9	16.7	8.9
478	20.2	22.9	10.4
479	16.6	17.3	12.5
480	14.3	13.6	11.8
481	12.2	11.9	11.6
482	20.8	19.7	18.2
483	14.5	12.1	7.1
484	13.0	12.5	10.3
485	13.7	11.6	8.7
MEAN	15.9	15.4	11.0
SD	2.91	3.79	3.01
N	10	10	10

WBC corrected for NRBC = or > 10

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Leukocytes

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: WBC

SEX: FEMALE

UNITS: 10^3/mm^3

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	13.0	13.8	12.4
527	10.6	10.6	10.9
528	15.2	14.6	9.6
529	18.9	13.0	11.9
530	13.1	12.4	10.6
531	15.2	13.2	9.8
532	17.2	12.7	9.8
533	17.9	17.3	10.2
534	15.1	17.3	14.5
535	12.4	14.4	10.0
MEAN	14.9	13.9	11.0
SD	2.63	2.10	1.55
N	10	10	10
GROUP: 4-F:9.0 mg base/kg/day			
576	25.7	14.9	15.8
577	28.5	25.5	25.1
578	34.9	36.5	24.8
579	36.5	28.4	23.4
580	21.5	21.5	17.8
581	32.8	24.4	21.8
582	27.5	27.9	20.8
583	28.9	35.9	22.3
584	19.9	27.8	20.1
585	19.7	19.5	16.0
MEAN	27.6	26.2	20.8
SD	6.01	6.74	3.37
N	10	10	10

WBC corrected for NRBC = or > 10

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WHITE DIFFERENTIAL DATA

STUDY ID: UIC-15B
STUDY NO: 152

GROUP: 1-F : 0 mg base/kg/day

SEX: FEMALE

Animal ID		Week 4		Week 13		Week 26	
		CNT	ABS	CNT	ABS	CNT	ABS
426	Nucleated Red Cells	0		0		1	
	M. Neutrophils	23	2.9	9	1.4	10	1.3
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	74	9.3	88	13.3	87	11.2
	Monocytes	3	0.4	1	0.2	1	0.1
	Eosinophils	0	0.0	2	0.3	2	0.3
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		12.6		15.1		12.9
427	Nucleated Red Cells	0		0		0	
	M. Neutrophils	9	1.1	10	1.4	12	1.0
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	90	11.2	85	11.5	83	6.9
	Monocytes	0	0.0	3	0.4	4	0.3
	Eosinophils	1	0.1	2	0.3	1	0.1
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		12.4		13.5		8.3
428	Nucleated Red Cells	0		0		0	
	M. Neutrophils	31	6.7	17	4.1	30	5.5
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	67	14.5	81	19.8	68	12.4
	Monocytes	2	0.4	2	0.5	1	0.2
	Eosinophils	0	0.0	0	0.0	1	0.2
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		21.7		24.4		18.2
429	Nucleated Red Cells	0		0		0	
	M. Neutrophils	20	2.8	11	1.6	26	2.4
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	78	11.0	86	12.4	73	6.8
	Monocytes	1	0.1	2	0.3	1	0.1
	Eosinophils	1	0.1	1	0.1	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		14.1		14.4		9.3

WBC corrected for NRBC = or > 10

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WHITE DIFFERENTIAL DATA

STUDY ID: UIC-15B
STUDY NO: 152

GROUP: 1-F : 0 mg base/kg/day

SEX: FEMALE

Animal ID		Week 4		Week 13		Week 26	
		CNT	ABS	CNT	ABS	CNT	ABS
430	Nucleated Red Cells	0		0		0	
	M. Neutrophils	9	1.1	7	0.9	24	2.3
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	86	10.7	91	11.4	74	7.0
	Monocytes	3	0.4	2	0.3	1	0.1
	Eosinophils	2	0.2	0	0.0	1	0.1
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		12.4		12.5		9.4
431	Nucleated Red Cells	0		0		0	
	M. Neutrophils	15	2.4	9	1.6	10	1.6
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	84	13.5	87	15.1	85	13.6
	Monocytes	0	0.0	3	0.5	3	0.5
	Eosinophils	1	0.2	1	0.2	2	0.3
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		16.1		17.4		16.0
432	Nucleated Red Cells	0		0		0	
	M. Neutrophils	7	1.0	7	0.7	16	1.5
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	90	13.3	90	9.4	82	7.5
	Monocytes	1	0.1	2	0.2	1	0.1
	Eosinophils	2	0.3	1	0.1	1	0.1
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		14.8		10.4		9.2
433	Nucleated Red Cells	0		0		0	
	M. Neutrophils	10	1.8	9	1.4	15	2.2
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	85	15.4	90	13.8	81	11.9
	Monocytes	2	0.4	0	0.0	3	0.4
	Eosinophils	2	0.4	1	0.2	1	0.1
	Basophils	1	0.2	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		18.1		15.3		14.7

WBC corrected for NRBC = or > 10

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WHITE DIFFERENTIAL DATA

STUDY ID: UIC-15B
STUDY NO: 152

GROUP: 1-F : 0 mg base/kg/day

SEX: FEMALE

Animal ID		Week 4		Week 13		Week 26	
		CNT	ABS	CNT	ABS	CNT	ABS
434	Nucleated Red Cells	0		0		2	
	M. Neutrophils	19	3.0	18	2.0	10	1.0
	I. Neutrophils	1	0.2	0	0.0	0	0.0
	Lymphocytes	78	12.2	80	8.7	86	8.8
	Monocytes	2	0.3	2	0.2	4	0.4
	Eosinophils	0	0.0	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		15.7		10.9		10.2
435	Nucleated Red Cells	0		0		0	
	M. Neutrophils	19	4.0	6	1.1	19	3.4
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	78	16.4	93	17.6	81	14.4
	Monocytes	2	0.4	1	0.2	0	0.0
	Eosinophils	1	0.2	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		21.0		18.9		17.8

WBC corrected for NRBC = or > 10

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WHITE DIFFERENTIAL DATA

STUDY ID: UIC-15B
STUDY NO: 152 GROUP: 2-F : 0.5 mg base/kg/day SEX: FEMALE

Animal ID		Week 4		Week 13		Week 26	
		CNT	ABS	CNT	ABS	CNT	ABS
476	Nucleated Red Cells	0		0		0	
	M. Neutrophils	13	2.2	5	0.8	10	1.0
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	84	14.0	92	14.5	85	8.8
	Monocytes	2	0.3	2	0.3	3	0.3
	Eosinophils	1	0.2	1	0.2	2	0.2
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		16.7		15.8		10.3
477	Nucleated Red Cells	0		0		0	
	M. Neutrophils	3	0.5	3	0.5	17	1.5
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	95	16.1	94	15.7	81	7.2
	Monocytes	2	0.3	3	0.5	1	0.1
	Eosinophils	0	0.0	0	0.0	1	0.1
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		16.9		16.7		8.9
478	Nucleated Red Cells	0		0		0	
	M. Neutrophils	15	3.0	13	3.0	6	0.6
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	84	17.0	83	19.0	92	9.6
	Monocytes	1	0.2	3	0.7	1	0.1
	Eosinophils	0	0.0	1	0.2	1	0.1
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		20.2		22.9		10.4
479	Nucleated Red Cells	0		0		0	
	M. Neutrophils	22	3.7	7	1.2	17	2.1
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	75	12.5	93	16.1	82	10.3
	Monocytes	2	0.3	0	0.0	1	0.1
	Eosinophils	1	0.2	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		16.6		17.3		12.5

WBC corrected for NRBC = or > 10

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-15B
STUDY NO: 152

GROUP: 2-F : 0.5 mg base/kg/day

SEX: FEMALE

Animal ID		Week 4		Week 13		Week 26	
		CNT	ABS	CNT	ABS	CNT	ABS
480	Nucleated Red Cells	0		0		1	
	M. Neutrophils	17	2.4	14	1.9	7	0.8
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	79	11.3	84	11.4	90	10.6
	Monocytes	3	0.4	1	0.1	2	0.2
	Eosinophils	1	0.1	1	0.1	1	0.1
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		14.3		13.6		11.8
481	Nucleated Red Cells	0		0		3	
	M. Neutrophils	4	0.5	11	1.3	23	2.7
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	93	11.3	86	10.2	74	8.6
	Monocytes	2	0.2	2	0.2	3	0.3
	Eosinophils	1	0.1	1	0.1	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		12.2		11.9		11.6
482	Nucleated Red Cells	1		0		0	
	M. Neutrophils	7	1.5	5	1.0	16	2.9
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	86	17.9	91	17.9	83	15.1
	Monocytes	7	1.5	3	0.6	1	0.2
	Eosinophils	0	0.0	1	0.2	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		20.8		19.7		18.2
483	Nucleated Red Cells	0		0		0	
	M. Neutrophils	6	0.9	15	1.8	11	0.8
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	94	13.6	82	9.9	86	6.1
	Monocytes	0	0.0	1	0.1	2	0.1
	Eosinophils	0	0.0	2	0.2	1	0.1
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		14.5		12.1		7.1

WBC corrected for NRBC = or > 10

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-15B
STUDY NO: 152

GROUP: 2-F : 0.5 mg base/kg/day

SEX: FEMALE

Animal ID		Week 4		Week 13		Week 26	
		CNT	ABS	CNT	ABS	CNT	ABS
484	Nucleated Red Cells	0		0		0	
	M. Neutrophils	10	1.3	11	1.4	10	1.0
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	85	11.1	85	10.6	87	9.0
	Monocytes	4	0.5	4	0.5	1	0.1
	Eosinophils	1	0.1	0	0.0	2	0.2
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		13.0		12.5		10.3
485	Nucleated Red Cells	0		0		0	
	M. Neutrophils	10	1.4	13	1.5	7	0.6
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	88	12.1	83	9.6	89	7.7
	Monocytes	2	0.3	2	0.2	3	0.3
	Eosinophils	0	0.0	2	0.2	1	0.1
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		13.7		11.6		8.7

WBC corrected for NRBC = or > 10

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-15B
STUDY NO: 152

GROUP: 3-F : 2.0 mg base/kg/day

SEX: FEMALE

Animal ID		Week 4		Week 13		Week 26	
		CNT	ABS	CNT	ABS	CNT	ABS
526	Nucleated Red Cells	0		0		0	
	M. Neutrophils	6	0.8	17	2.3	20	2.5
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	89	11.6	81	11.2	78	9.7
	Monocytes	2	0.3	2	0.3	0	0.0
	Eosinophils	3	0.4	0	0.0	2	0.2
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		13.0		13.8		12.4
527	Nucleated Red Cells	0		0		0	
	M. Neutrophils	10	1.1	21	2.2	22	2.4
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	87	9.2	79	8.4	77	8.4
	Monocytes	2	0.2	0	0.0	0	0.0
	Eosinophils	1	0.1	0	0.0	1	0.1
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		10.6		10.6		10.9
528	Nucleated Red Cells	0		0		0	
	M. Neutrophils	20	3.0	22	3.2	22	2.1
	I. Neutrophils	0	0.0	1	0.1	0	0.0
	Lymphocytes	76	11.6	73	10.7	77	7.4
	Monocytes	1	0.2	1	0.1	0	0.0
	Eosinophils	3	0.5	3	0.4	1	0.1
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		15.2		14.6		9.6
529	Nucleated Red Cells	0		0		1	
	M. Neutrophils	13	2.5	19	2.5	31	3.7
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	86	16.3	80	10.4	66	7.9
	Monocytes	1	0.2	1	0.1	3	0.4
	Eosinophils	0	0.0	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		18.9		13.0		11.9

WBC corrected for NRBC = or > 10

DRAFT

WHITE DIFFERENTIAL DATA

STUDY IO: UIC-15B
STUDY NO: 152

GROUP: 3-F : 2.0 mg base/kg/day

SEX: FEMALE

Animal IO		Week 4		Week 13		Week 26	
		CNT	ABS	CNT	ABS	CNT	ABS
530	Nucleated Red Cells	1		0		0	
	M. Neutrophils	12	1.6	24	3.0	28	3.0
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	83	10.9	73	9.1	71	7.5
	Monocytes	3	0.4	2	0.2	1	0.1
	Eosinophils	2	0.3	1	0.1	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		13.1		12.4		10.6
531	Nucleated Red Cells	0		0		0	
	M. Neutrophils	14	2.1	11	1.5	13	1.3
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	86	13.1	85	11.2	81	7.9
	Monocytes	0	0.0	4	0.5	4	0.4
	Eosinophils	0	0.0	0	0.0	2	0.2
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		15.2		13.2		9.8
532	Nucleated Red Cells	0		0		0	
	M. Neutrophils	14	2.4	19	2.4	23	2.3
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	85	14.6	77	9.8	75	7.4
	Monocytes	1	0.2	4	0.5	1	0.1
	Eosinophils	0	0.0	0	0.0	1	0.1
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		17.2		12.7		9.8
533	Nucleated Red Cells	0		0		0	
	M. Neutrophils	20	3.6	18	3.1	20	2.0
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	76	13.6	81	14.0	74	7.5
	Monocytes	2	0.4	1	0.2	4	0.4
	Eosinophils	2	0.4	0	0.0	2	0.2
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		17.9		17.3		10.2

WBC corrected for NRBC = or > 10

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-15B
STUDY NO: 152

GROUP: 3-F : 2.0 mg base/kg/day

SEX: FEMALE

Animal ID		Week 4		Week 13		Week 26	
		CNT	ABS	CNT	ABS	CNT	ABS
534	Nucleated Red Cells	0		0		0	
	M. Neutrophils	10	1.5	9	1.6	22	3.2
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	87	13.1	87	15.1	77	11.2
	Monocytes	3	0.5	3	0.5	0	0.0
	Eosinophils	0	0.0	1	0.2	1	0.1
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		15.1		17.3		14.5
535	Nucleated Red Cells	0		0		0	
	M. Neutrophils	7	0.9	15	2.2	21	2.1
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	92	11.4	82	11.8	77	7.7
	Monocytes	1	0.1	2	0.3	2	0.2
	Eosinophils	0	0.0	1	0.1	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		12.4		14.4		10.0

WBC corrected for NRBC = or > 10

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-15B
STUDY NO: 152

GROUP: 4-F : 9.0 mg base/kg/day

SEX: FEMALE

Animal ID		Week 4		Week 13		Week 26	
		CNT	ABS	CNT	ABS	CNT	ABS
576	Nucleated Red Cells	0		0		0	
	M. Neutrophils	26	6.7	18	2.7	18	2.8
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	71	18.2	80	11.9	82	13.0
	Monocytes	3	0.8	1	0.1	0	0.0
	Eosinophils	0	0.0	1	0.1	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		25.7		14.9		15.8
577	Nucleated Red Cells	0		0		0	
	M. Neutrophils	19	5.4	23	5.9	10	2.5
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	77	21.9	72	18.4	89	22.3
	Monocytes	4	1.1	5	1.3	1	0.3
	Eosinophils	0	0.0	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		28.5		25.5		25.1
578	Nucleated Red Cells	0		0		1	
	M. Neutrophils	13	4.5	9	3.3	11	2.7
	I. Neutrophils	0	0.0	1	0.4	0	0.0
	Lymphocytes	81	28.3	89	32.5	86	21.3
	Monocytes	5	1.7	1	0.4	3	0.7
	Eosinophils	1	0.3	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		34.9		36.5		24.8
579	Nucleated Red Cells	0		0		0	
	M. Neutrophils	10	3.7	13	3.7	14	3.3
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	87	31.8	87	24.7	86	20.1
	Monocytes	3	1.1	0	0.0	0	0.0
	Eosinophils	0	0.0	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		36.5		28.4		23.4

WBC corrected for NRBC = or > 10

DRAFT

WHITE DIFFERENTIAL DATA

STUDY IO: UIC-158
STUDY NO: 152

GROUP: 4-F : 9.0 mg base/kg/day

SEX: FEMALE

Animal IO		Week 4		Week 13		Week 26	
		CNT	ABS	CNT	ABS	CNT	ABS
580	Nucleated Red Cells	0		0		0	
	M. Neutrophils	20	4.3	5	1.1	19	3.4
	I. Neutrophils	0	0.0	1	0.2	0	0.0
	Lymphocytes	80	17.2	91	19.6	77	13.7
	Monocytes	0	0.0	1	0.2	2	0.4
	Eosinophils	0	0.0	2	0.4	2	0.4
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		21.5		21.5		17.8
581	Nucleated Red Cells	0		0		0	
	M. Neutrophils	9	3.0	8	2.0	19	4.1
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	90	29.5	89	21.7	81	17.7
	Monocytes	1	0.3	3	0.7	0	0.0
	Eosinophils	0	0.0	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		32.8		24.4		21.8
582	Nucleated Red Cells	0		0		0	
	M. Neutrophils	9	2.5	7	2.0	13	2.7
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	88	24.2	90	25.1	87	18.1
	Monocytes	3	0.8	1	0.3	0	0.0
	Eosinophils	0	0.0	2	0.6	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		27.5		27.9		20.8
583	Nucleated Red Cells	0		0		0	
	M. Neutrophils	20	5.8	5	1.8	29	6.5
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	78	22.5	93	33.4	70	15.6
	Monocytes	2	0.6	2	0.7	0	0.0
	Eosinophils	0	0.0	0	0.0	1	0.2
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		28.9		35.9		22.3

WBC corrected for NRBC = or > 10

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: UIC-15B
STUDY NO: 152

GROUP: 4-F : 9.0 mg base/kg/day

SEX: FEMALE

Animal ID		Week 4		Week 13		Week 26	
		CNT	ABS	CNT	ABS	CNT	ABS
584	Nucleated Red Cells	0		0		1	
	M. Neutrophils	21	4.2	11	3.1	17	3.4
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	75	14.9	87	24.2	81	16.3
	Monocytes	3	0.6	2	0.6	2	0.4
	Eosinophils	1	0.2	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		19.9		27.8		20.1
585	Nucleated Red Cells	0		0		0	
	M. Neutrophils	18	3.5	10	2.0	24	3.8
	I. Neutrophils	3	0.6	1	0.2	0	0.0
	Lymphocytes	77	15.2	88	17.2	75	12.0
	Monocytes	2	0.4	1	0.2	1	0.2
	Eosinophils	0	0.0	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		19.7		19.5		16.0

WBC corrected for NRBC = or > 10

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: UIC-15B
STUDY NO: 152
GROUP: 1-F : 0 mg base/kg/day
SEX: FEMALE

Animal ID	Week 4	Week 13	Week 26
426	Normal Red Blood Cells	Normal Red Blood Cells	Polychromasia,Slight Anisocytosis,Slight
427	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
428	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
429	Normal Red Blood Cells	Normal Red Blood Cells	Anisocytosis;Slight
430	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
431	Normal Red Blood Cells	Poikilocytes,Slight	Polychromasia;Slight
432	Normal Red Blood Cells;Clumped Platelets,Slight	Normal Red Blood Cells;Clumped Platelets,Slight	Normal Red Blood Cells
433	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
434	Normal Red Blood Cells	Normal Red Blood Cells	Poikilocytes,Slight; Anisocytosis,Slight
435	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: UIC-15B
STUDY NO: 152

SEX: FEMALE

GROUP: 2-F : 0.5 mg base/kg/day

Animal ID	Week 4	Week 13	Week 26
476	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
477	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
478	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
479	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
480	Normal Red Blood Cells	Normal Red Blood Cells	Poikilocytes,Slight
481	Normal Red Blood Cells	Normal Red Blood Cells	Anisocytosis,Slight
482	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
483	Normal Red Blood Cells	Normal Red Blood Cells	Anisocytosis,Slight
484	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
485	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: UIC-15B
STUDY NO: 152
SEX: FEMALE
GROUP: 3-F : 2.0 mg base/kg/day

Animal ID	Week 4	Week 13	Week 26
526	Normal Red Blood Cells;Clumped Platelets,Slight	Normal Red Blood Cells;Clumped Platelets,Slight	Poikilocytes,Slight
527	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
528	Normal Red Blood Cells;Clumped Platelets,Slight	Anisocytosis,Slight	Normal Red Blood Cells
529	Polychromasia,Slight	Normal Red Blood Cells	Normal Red Blood Cells
530	Normal Red Blood Cells;Clumped Platelets,Slight	Normal Red Blood Cells	Normal Red Blood Cells
531	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
532	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
533	Normal Red Blood Cells	Anisocytosis,Slight	Normal Red Blood Cells
534	Normal Red Blood Cells	Anisocytosis,Slight	Normal Red Blood Cells
535	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells

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RBC MORPHOLOGY OBSERVATIONS

STUDY ID: UIC-158
STUDY NO: 152

GROUP: 4-F : 9.0 mg base/kg/day

SEX: FEMALE

Animal ID	Week 4	Week 13	Week 26
576	Anisocytosis,Slight	Normal Red Blood Cells	Polychromasia,Slight Anisocytosis,Slight
577	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
578	Normal Red Blood Cells	Normal Red Blood Cells	Anisocytosis,Slight; Clumped Platelets, Slight
579	Normal Red Blood Cells	Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
580	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
581	Normal Red Blood Cells	Anisocytosis,Slight	Normal Red Blood Cells
582	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
583	Normal Red Blood Cells	Normal Red Blood Cells	Polychromasia,Slight
584	Normal Red Blood Cells	Normal Red Blood Cells	Polychromasia,Slight Anisocytosis,Slight
585	Normal Red Blood Cells	Normal Red Blood Cells	Anisocytosis,Slight

DRAFT

APPENDIX H

OPHTHALMOLOGY REPORT

ANIMAL EYE ASSOCIATES

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DRAFT

April 16, 1996

OPHTHALMIC REPORT

UIC/TRL Study No. 152

SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS

During Week -1 (July 25, 1995), a sufficient number of rats were given ophthalmic examinations by indirect ophthalmoscopy to result in eighty males and eighty females which were within normal limits.

During Week 13 (October 31, 1995) and Week 26 (January 30, 1996), all surviving animals which were used in the above-referenced study were re-examined. Treatment-related lesions were not apparent at either time point. A few sporadic observations were seen in the various groups (including control animals), but were not considered biologically significant with respect to drug treatment.

Sincerely,

Samuel J. Vainisi, D.V.M.
Professor of Comparative
Ophthalmology, Univ. of IL at Chicago

Diplomate, American College of
Veterinary Ophthalmologists

SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS

Male Ophthalmic Examinations

DRAFT

DOSE (mg base/kg/day)	ANIMAL NUMBER	PRETEST		WEEK 13		WEEK 26	
		R.E.	L.E.	R.E.	L.E.	R.E.	L.E
0	401	WNL	WNL	WNL	WNL	WNL	WNL
	402	WNL	WNL	WNL	WNL	WNL	WNL
	403	WNL	WNL	WNL	WNL	WNL	WNL
	404	WNL	WNL	WNL	WNL	WNL	WNL
	405	WNL	WNL	WNL	WNL	WNL	WNL
	406	WNL	WNL	WNL	WNL	WNL	WNL
	407	WNL	WNL	WNL	WNL	WNL	WNL
	408	WNL	WNL	WNL	WNL	WNL	WNL
	409	WNL	WNL	WNL	WNL	WNL	WNL
	410	WNL	WNL	WNL	WNL	WNL	WNL
	411	WNL	WNL	WNL	WNL	WNL	WNL
	412	WNL	WNL	WNL	WNL	WNL	WNL
	413	WNL	WNL	WNL	WNL	WNL	WNL
	414	WNL	WNL	WNL	WNL	WNL	WNL
	415	WNL	WNL	WNL	WNL	WNL	WNL
	416	WNL	WNL	WNL	WNL	WNL	WNL
	417	WNL	WNL	WNL	WNL	WNL	WNL
	418	WNL	WNL	WNL	WNL	WNL	WNL
	419	WNL	WNL	WNL	WNL	WNL	WNL
	420	WNL	WNL	WNL	WNL	WNL	WNL
0.5	451	WNL	WNL	WNL	WNL	WNL	WNL
	452	WNL	WNL	WNL	WNL	WNL	WNL
	453	WNL	WNL	WNL	WNL	WNL	WNL
	454	WNL	WNL	WNL	WNL	WNL	WNL
	455	WNL	WNL	WNL	WNL	WNL	WNL
	456	WNL	WNL	WNL	WNL	WNL	WNL
	457	WNL	WNL	WNL	WNL	WNL	WNL
	458	WNL	WNL	WNL	WNL	WNL	WNL
	459	WNL	WNL	WNL	WNL	WNL	WNL
	460	WNL	WNL	WNL	WNL	WNL	WNL
	461	WNL	WNL	WNL	WNL	WNL	WNL
	462	WNL	WNL	WNL	WNL	WNL	WNL
	463	WNL	WNL	WNL	WNL	WNL	WNL
	464	WNL	WNL	WNL	WNL	WNL	WNL
	465	WNL	WNL	WNL	WNL	WNL	WNL
	466	WNL	WNL	WNL	WNL	WNL	WNL
	467	WNL	WNL	WNL	WNL	WNL	WNL
	468	WNL	WNL	WNL	WNL	WNL	WNL
	469	WNL	WNL	WNL	WNL	WNL	WNL
	470	WNL	WNL	WNL	WNL	SR	WNL

R.E. = Right eye
L.E. = Left eye
WNL = Within normal limits
CA = Choroidal atrophy
CE = Corneal erosion
MRA = Mild retinal atrophy
MRD = Mild retinal degeneration
RDG = Retinal degeneration, generalized
RDD = Retinal degeneration, diffused
RDL = Retinal degeneration, linear
RDM = Retinal degeneration, moderate
SR = Sector retinopathy
FD = Found dead

SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS

Male Ophthalmic Examinations (Continued)

DRAFT

DOSE (mg base/kg/day)	ANIMAL NUMBER	PRETEST		WEEK 13		WEEK 26	
		R.E.	L.E.	R.E.	L.E.	R.E.	L.E
2	501	WNL	WNL	WNL	WNL	WNL	WNL
	5[illegible]7	WNL	WNL	WNL	WNL	WNL	WNL
	5[illegible]7	WNL	WNL	WNL	WNL	WNL	WNL
	501	WNL	WNL	WNL	WNL	WNL	CE
	503	WNL	WNL	WNL	WNL	WNL	WNL
	503	WNL	WNL	WNL	WNL	WNL	WNL
	5[illegible]7	WNL	WNL	WNL	WNL	WNL	WNL
	5[illegible]7	WNL	WNL	WNL	WNL	WNL	WNL
	50[illegible]	WNL	WNL	WNL	WNL	WNL	WNL
	557	WNL	WNL	WNL	WNL	WNL	WNL
	557	WNL	WNL	WNL	WNL	WNL	WNL
	512	WNL	WNL	WNL	WNL	WNL	WNL
	513	WNL	WNL	WNL	WNL	WNL	WNL
	513	WNL	WNL	WNL	WNL	WNL	WNL
	513	WNL	WNL	WNL	WNL	WNL	WNL
	513	WNL	WNL	WNL	WNL	WNL	WNL
	519	WNL	WNL	WNL	WNL	WNL	WNL
	518	WNL	WNL	WNL	WNL	WNL	WNL
	519	WNL	WNL	WNL	WNL	WNL	WNL
	520	WNL	WNL	WNL	WNL	WNL	WNL
9	501	WNL	WNL	WNL	WNL	WNL	WNL
	562	WNL	WNL	WNL	WNL	WNL	WNL
	501	WNL	WNL	WNL	WNL	WNL	WNL
	557	WNL	WNL	WNL	WNL	WNL	WNL
	555	WNL	WNL	WNL	WNL	WNL	WNL
	557	WNL	WNL	WNL	WNL	WNL	WNL
	557	WNL	WNL	WNL	WNL	WNL	WNL
	557	WNL	WNL	WNL	WNL	FD	FD
	559	WNL	WNL	WNL	WNL	WNL	WNL
	560	WNL	WNL	WNL	WNL	WNL	WNL
	501	WNL	WNL	WNL	WNL	WNL	WNL
	562	WNL	WNL	WNL	WNL	WNL	WNL
	513	WNL	WNL	WNL	WNL	WNL	WNL
	564	WNL	WNL	WNL	WNL	WNL	WNL
	560	WNL	WNL	WNL	WNL	WNL	WNL
	566	WNL	WNL	WNL	WNL	WNL	WNL
	567	WNL	WNL	WNL	WNL	WNL	WNL
	568	WNL	WNL	WNL	WNL	CA,RDG	WNL
	569	WNL	WNL	WNL	WNL	WNL	WNL
	570	WNL	WNL	WNL	WNL	WNL	WNL

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MRD = Mild retinal degeneration
RDG = Retinal degeneration, generalized
RDD = Retinal degeneration, diffused
RDL = Retinal degeneration, linear
RDM = Retinal degeneration, moderate
SR = Sector retinopathy
FD = Found dead

SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS

Female Ophthalmic Examinations

DRAFT

DOSE (mg base/kg/day)	ANIMAL NUMBER.	PRETEST		WEEK 13		WEEK 26	
		R.E.	L.E.	R.E.	L.E.	R.E.	L.E
0	426	WNL	WNL	WNL	WNL	WNL	WNL
	429	WNL	WNL	WNL	WNL	WNL	WNL
	429	WNL	WNL	WNL	WNL	WNL	WNL
	429	WNL	WNL	WNL	WNL	WNL	WNL
	430	WNL	WNL	WNL	RDD	WNL	RDM,CA
	432	WNL	WNL	WNL	WNL	WNL	WNL
	432	WNL	WNL	WNL	WNL	WNL	WNL
	430	WNL	WNL	WNL	WNL	WNL	WNL
	434	WNL	WNL	WNL	WNL	WNL	WNL
	435	WNL	WNL	WNL	WNL	WNL	WNL
	436	WNL	WNL	WNL	WNL	WNL	WNL
	437	WNL	WNL	WNL	WNL	WNL	WNL
	438	WNL	WNL	WNL	WNL	WNL	WNL
	439	WNL	WNL	WNL	WNL	WNL	WNL
	440	WNL	WNL	WNL	WNL	WNL	WNL
	441	WNL	WNL	WNL	WNL	WNL	WNL
	442	WNL	WNL	WNL	WNL	WNL	WNL
	443	WNL	WNL	WNL	WNL	WNL	WNL
	444	WNL	WNL	WNL	WNL	WNL	WNL
	445	WNL	WNL	WNL	WNL	WNL	WNL
0.5	476	WNL	WNL	WNL	WNL	WNL	WNL
	477	WNL	WNL	WNL	WNL	WNL	WNL
	478	WNL	WNL	WNL	WNL	WNL	WNL
	479	WNL	WNL	WNL	WNL	WNL	WNL
	480	WNL	WNL	WNL	WNL	WNL	WNL
	481	WNL	WNL	WNL	WNL	WNL	WNL
	482	WNL	WNL	WNL	WNL	WNL	WNL
	483	WNL	WNL	WNL	WNL	WNL	WNL
	484	WNL	WNL	WNL	WNL	WNL	WNL
	485	WNL	WNL	WNL	WNL	WNL	WNL
	486	WNL	WNL	WNL	WNL	WNL	WNL
	487	WNL	WNL	WNL	WNL	WNL	WNL
	488	WNL	WNL	WNL	WNL	WNL	WNL
	489	WNL	WNL	WNL	WNL	WNL	WNL
	490	WNL	WNL	WNL	WNL	WNL	WNL
	491	WNL	WNL	WNL	WNL	WNL	WNL
	492	WNL	WNL	WNL	WNL	WNL	WNL
	493	WNL	WNL	WNL	WNL	WNL	WNL
	494	WNL	WNL	WNL	WNL	WNL	WNL
	495	WNL	WNL	RDL	WNL	CA	WNL

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RDD = Retinal degeneration, diffused
RDL = Retinal degeneration, linear
RDM = Retinal degeneration, moderate
SR = Sector retinopathy
FD = Found dead

SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS

Female Ophthalmic Examinations (Continued)

DRAFT

DOSE (mg base/kg/day)	ANIMAL NUMBER	PRETEST		WEEK 13		WEEK 26	
		R.E.	L.E.	R.E.	L.E.	R.E.	L.E
2.0	526	WNL	WNL	WNL	WNL	WNL	WNL
	587	WNL	WNL	WNL	WNL	WNL	WNL
	526	WNL	WNL	WNL	WNL	WNL	WNL
	589	WNL	WNL	WNL	WNL	WNL	WNL
	534	WNL	WNL	WNL	WNL	WNL	WNL
	591	WNL	WNL	WNL	WNL	WNL	WNL
	532	WNL	WNL	WNL	RDD	WNL	WNL
	583	WNL	WNL	WNL	WNL	WNL	WNL
	534	WNL	WNL	WNL	WNL	WNL	WNL
	535	WNL	WNL	WNL	WNL	WNL	WNL
	589	WNL	WNL	WNL	WNL	WNL	WNL
	537	WNL	WNL	WNL	WNL	WNL	WNL
	534	WNL	WNL	WNL	WNL	WNL	WNL
	589	WNL	WNL	WNL	WNL	WNL	WNL
	590	WNL	WNL	WNL	WNL	WNL	WNL
	583	WNL	WNL	WNL	WNL	WNL	WNL
	542	WNL	WNL	WNL	WNL	WNL	WNL
	543	WNL	WNL	WNL	WNL	WNL	WNL
	591	WNL	WNL	WNL	WNL	WNL	WNL
	589	WNL	WNL	WNL	WNL	WNL	WNL
9.0	526	WNL	WNL	WNL	WNL	WNL	WNL
	577	WNL	WNL	WNL	WNL	WNL	WNL
	593	WNL	WNL	WNL	WNL	WNL	WNL
	591	WNL	WNL	WNL	WNL	WNL	WNL
	534	WNL	WNL	WNL	WNL	WNL	WNL
	583	WNL	WNL	WNL	WNL	WNL	WNL
	589	WNL	WNL	WNL	WNL	WNL	WNL
	583	WNL	WNL	WNL	WNL	WNL	WNL
	584	WNL	WNL	WNL	WNL	WNL	WNL
	589	WNL	WNL	WNL	WNL	WNL	WNL
	534	WNL	WNL	WNL	WNL	WNL	WNL
	587	WNL	WNL	WNL	WNL	WNL	WNL
	589	WNL	WNL	WNL	WNL	WNL	WNL
	589	WNL	WNL	WNL	WNL	WNL	WNL
	590	WNL	WNL	WNL	RDL	CA,MRA	CA,MRD
	591	WNL	WNL	WNL	WNL	WNL	WNL
	592	WNL	WNL	WNL	WNL	WNL	WNL
	593	WNL	WNL	WNL	WNL	WNL	WNL
	594	WNL	WNL	WNL	WNL	WNL	WNL
	595	WNL	WNL	WNL	WNL	WNL	WNL

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CA = Choroidal atrophy
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RDL = Retinal degeneration, linear
RDM = Retinal degeneration, moderate
SR = Sector retinopathy
FD = Found dead

DRAFT

APPENDIX I

INDIVIDUAL ORGAN WEIGHTS

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

INDIVIDUAL ORGAN WEIGHTS

DRAFT

STUDY: 152
SEX: MALE
GROUP: 1-M - 0 mg base/kg/day
ALL FATES DAYS: 183-185 ALL BALANCES

ANIMAL ID:	401	402	403	404	405	406	407	408	409
BALANCE NO.:	2027	2027	2027	2027	2027	2027	2027	2027	2027
BODY WEIGHT (G)	723	719	653	725	681	772	726	736	809
Adrenal Glands (G)	0.059	0.071	0.051	0.069	0.053	0.069	0.058	0.061	0.053
% BRAIN WEIGHT	2.94	3.17	2.54	3.04	2.47	3.11	2.72	2.58	2.40
Brain (G)	2.007	2.237	2.011	2.272	2.144	2.217	2.134	2.363	2.211
Heart (G)	1.760	1.875	1.865	1.861	1.845	1.939	1.957	1.728	2.276
% BRAIN WEIGHT	87.69	83.82	92.74	81.91	86.05	87.46	91.71	73.13	102.94
Kidneys (G)	3.894	4.266	3.334	4.114	4.557	4.506	3.767	4.785	4.209
% BRAIN WEIGHT	194.02	190.70	165.79	181.07	212.55	203.25	176.52	202.50	190.37
Lungs/Bronchi (G)	2.223	2.165	2.316	2.864	2.030	2.177	2.637	2.816	2.577
% BRAIN WEIGHT	110.76	96.78	115.17	126.06	94.68	98.20	123.57	119.17	116.55
Liver (G)	23.110	26.518	21.228	22.456	28.975	21.348	22.182	27.988	28.566
% BRAIN WEIGHT	1151.47	1185.43	1055.59	988.38	1351.45	962.92	1039.46	1184.43	1291.99
Spleen (G)	0.909	0.863	0.871	0.975	1.023	1.031	0.770	1.019	1.048
% BRAIN WEIGHT	45.29	38.58	43.31	42.91	47.71	46.50	36.08	43.12	47.40
Testes with Epididymides (G)	6.310	5.383	4.793	5.744	4.806	5.394	5.083	5.706	5.553
% BRAIN WEIGHT	314.40	240.63	238.34	252.82	224.16	243.30	238.19	241.47	251.15

INDIVIDUAL ORGAN WEIGHTS

DRAFT

STUDY: 152
SEX: MALE
GROUP: 1-M - 0 mg base/kg/day
ALL FATES DAYS: 183-185 ALL BALANCES

ANIMAL ID:	410	411	412	413	414	415	416	417	418
BALANCE NO.:	2027	2027	2027	2027	2027	2027	2027	2027	2027
BODY WEIGHT (G)	745	643	664	726	737	598	810	648	751
Adrenal Glands (G)	0.079	0.059	0.067	0.068	0.071	0.052	0.053	0.057	0.075
% BRAIN WEIGHT	3.32	2.84	3.13	2.95	2.59	2.47	2.43	2.58	3.20
Brain (G)	2.376	2.079	2.141	2.307	2.741	2.104	2.179	2.211	2.345
Heart (G)	1.691	1.625	1.720	2.012	1.948	1.508	1.885	1.402	2.141
% BRAIN WEIGHT	71.17	78.16	80.34	87.21	71.07	71.67	86.51	63.41	91.30
Kidneys (G)	4.475	4.409	3.843	4.313	4.306	3.524	4.036	3.947	4.942
% BRAIN WEIGHT	188.34	212.07	179.50	186.95	157.10	167.49	185.22	178.52	210.75
Lungs/Bronchi (G)	2.248	1.864	2.292	2.290	2.334	2.010	2.213	2.229	1.921
% BRAIN WEIGHT	94.61	89.66	107.05	99.26	85.15	95.53	101.56	100.81	81.92
Liver (G)	24.771	23.079	23.647	27.733	31.109	23.130	26.579	20.832	25.932
% BRAIN WEIGHT	1042.55	1110.10	1104.48	1202.12	1134.95	1099.33	1219.78	942.20	1105.84
Spleen (G)	0.799	0.796	0.900	1.027	1.577	0.816	0.952	1.038	1.112
% BRAIN WEIGHT	33.63	38.29	42.04	44.52	57.53	38.78	43.69	46.95	47.42
Testes with Epididymides (G)	5.588	5.444	6.083	4.913	6.149	5.266	5.704	4.466	5.069
% BRAIN WEIGHT	235.19	261.86	284.12	212.96	224.33	250.29	261.77	201.99	216.16

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

INDIVIDUAL ORGAN WEIGHTS

DRAFT

STUDY: 152
SEX: MALE

GROUP: 1-M - 0 mg base/kg/day
ALL FATES DAYS: 183-185 ALL BALANCES

ANIMAL ID:	419	420
BALANCE NO.:	2027	2027
BODY WEIGHT (G)	756	686
Adrenal Glands (G)	0.049	0.058
% BRAIN WEIGHT	2.22	2.68
Brain (G)	2.204	2.165
Heart (G)	1.917	1.615
% BRAIN WEIGHT	86.98	74.60
Kidneys (G)	4.116	3.963
% BRAIN WEIGHT	186.75	183.05
Lungs/Bronchi (G)	2.782	2.340
% BRAIN WEIGHT	126.23	108.08
Liver (G)	27.417	25.298
% BRAIN WEIGHT	1243.97	1168.50
Spleen (G)	1.144	0.716
% BRAIN WEIGHT	51.91	33.07
Testes with Epididymides (G)	4.718	5.185
% BRAIN WEIGHT	214.07	239.49

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 152
SEX: MALE
GROUP: 2-M - 0.5 mg base/kg/day
ALL FATES DAYS: 183-185 ALL BALANCES

DRAFT

ANIMAL ID:	451	452	453	454	455	456	457	458	459
BALANCE NO.:	2027	2027	2027	2027	2027	2027	2027	2027	2027
BODY WEIGHT (G)	760	670	548	653	761	715	787	731	676
Adrenal Glands (G)	0.087	0.066	0.038	0.099	0.074	0.070	0.054	0.074	0.070
% BRAIN WEIGHT	3.91	2.82	1.93	4.78	3.11	3.07	2.39	3.42	3.00
Brain (G)	2.226	2.344	1.965	2.073	2.377	2.278	2.255	2.162	2.333
Heart (G)	1.657	1.981	1.381	1.979	1.963	1.672	1.840	1.630	1.909
% BRAIN WEIGHT	74.44	84.51	70.28	95.47	82.58	73.40	81.60	75.39	81.83
Kidneys (G)	4.201	4.330	3.835	4.435	4.805	3.645	4.586	4.375	3.601
% BRAIN WEIGHT	188.72	184.73	195.17	213.94	202.15	160.01	203.37	202.36	154.35
Lungs/Bronchi (G)	2.337	2.235	2.761	2.406	2.697	2.340	2.754	2.082	3.187
% BRAIN WEIGHT	104.99	95.35	140.51	116.06	113.46	102.72	122.13	96.30	136.61
Liver (G)	25.321	25.139	15.508	22.658	25.532	24.655	25.651	26.304	21.903
% BRAIN WEIGHT	1137.51	1072.48	789.21	1093.01	1074.13	1082.31	1137.52	1216.65	938.83
Spleen (G)	0.949	1.044	0.716	1.072	1.392	0.975	1.022	0.814	0.776
% BRAIN WEIGHT	42.63	44.54	36.44	51.71	58.56	42.80	45.32	37.65	33.26
Testes with Epididymides (G)	5.279	5.652	5.066	5.849	6.103	5.053	5.434	5.048	5.052
% BRAIN WEIGHT	237.15	241.13	257.81	282.15	256.75	221.82	240.98	233.49	216.55

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 152
SEX: MALE

GROUP: 2-M - 0.5 mg base/kg/day
ALL FATES DAYS: 183-185 ALL BALANCES

DRAFT

ANIMAL ID:	460	461	462	463	464	465	466	467	468
BALANCE NO.:	2027	2027	2027	2027	2027	2027	2027	2027	2027
BODY WEIGHT (G)	673	710	750	697	731	709	763	585	745
Adrenal Glands (G)	0.063	0.060	0.070	0.058	0.064	0.069	0.058	0.066	0.055
% BRAIN WEIGHT	3.01	2.77	3.11	2.53	3.00	3.17	2.54	3.03	2.61
Brain (G)	2.092	2.164	2.252	2.290	2.132	2.177	2.286	2.181	2.109
Heart (G)	1.781	1.655	2.028	1.797	1.690	1.637	1.804	1.609	1.674
% BRAIN WEIGHT	85.13	76.48	90.05	78.47	79.27	75.20	78.92	73.77	79.37
Kidneys (G)	4.276	3.800	4.298	4.671	4.234	3.448	4.266	4.225	3.883
% BRAIN WEIGHT	204.40	175.60	190.85	203.97	198.59	158.38	186.61	193.72	184.12
Lungs/Bronchi (G)	2.537	2.980	2.381	2.502	1.973	2.434	2.647	2.576	2.284
% BRAIN WEIGHT	121.27	137.71	105.73	109.26	92.54	111.81	115.79	118.11	108.30
Liver (G)	27.841	27.778	25.059	24.371	24.511	22.002	24.863	18.961	24.488
% BRAIN WEIGHT	1330.83	1283.64	1112.74	1064.24	1149.67	1010.66	1087.62	869.37	1161.12
Spleen (G)	1.050	0.903	0.969	1.019	0.896	0.895	0.873	0.878	1.014
% BRAIN WEIGHT	50.19	41.73	43.03	44.50	42.03	41.11	38.19	40.26	48.08
Testes with Epididymides (G)	5.783	5.057	5.432	5.123	5.090	5.532	5.172	5.344	4.550
% BRAIN WEIGHT	276.43	233.69	241.21	223.71	238.74	254.11	226.25	245.03	215.74

INDIVIDUAL ORGAN WEIGHTS

STUDY: 152
SEX: MALE

GROUP: 2-M - 0.5 mg base/kg/day
ALL FATES DAYS: 183-185 ALL BALANCES

DRAFT

ANIMAL ID:	469	470
BALANCE NO.:	2027	2027
BODY WEIGHT (G)	713	594
Adrenal Glands (G)	0.053	0.065
% BRAIN WEIGHT	2.55	2.86
Brain (G)	2.078	2.271
Heart (G)	1.781	1.378
% BRAIN WEIGHT	85.71	60.68
Kidneys (G)	4.376	3.466
% BRAIN WEIGHT	210.59	152.62
Lungs/Bronchi (G)	1.967	1.858
% BRAIN WEIGHT	94.66	81.81
Liver (G)	25.626	22.053
% BRAIN WEIGHT	1233.20	971.07
Spleen (G)	0.902	0.807
% BRAIN WEIGHT	43.41	35.54
Testes with Epididymides (G)	5.021	4.730
% BRAIN WEIGHT	241.63	208.28

INDIVIDUAL ORGAN WEIGHTS

DRAFT

STUDY: 152
SEX: MALE
GROUP: 4-M - 9.0 mg base/kg/day
ALL FATES DAYS: 183-185 ALL BALANCES

ANIMAL ID: / BALANCE NO.:	551 / 2027	552 / 2027	553 / 2027	554 / 2027	555 / 2027	556 / 2027	557 / 2027	559 / 2027	560 / 2027
BODY WEIGHT (G)	576	527	452	556	421	521	615	538	446
Adrenal Glands (G)	0.044	0.076	0.051	0.073	0.055	0.074	0.077	0.046	0.064
% BRAIN WEIGHT	1.94	3.45	2.61	3.47	2.69	3.46	3.35	2.10	2.76
Brain (G)	2.265	2.205	1.955	2.103	2.048	2.141	2.301	2.190	2.320
Heart (G)	1.619	1.446	1.381	1.444	1.227	1.493	2.016	1.456	1.423
% BRAIN WEIGHT	71.48	65.58	70.64	68.66	59.91	69.73	87.61	66.48	61.34
Kidneys (G)	5.405	4.146	4.133	4.455	3.691	4.453	6.213	5.362	3.644
% BRAIN WEIGHT	238.63	188.03	211.41	211.84	180.22	207.99	270.01	244.84	157.07
Lungs/Bronchi (G)	3.894	4.210	3.732	4.308	3.286	3.886	4.257	4.953	3.651
% BRAIN WEIGHT	171.92	190.93	190.90	204.85	160.45	181.50	185.01	226.16	157.37
Liver (G)	21.013	20.000	19.227	21.428	14.949	22.649	26.849	21.848	17.347
% BRAIN WEIGHT	927.73	907.03	983.48	1018.93	729.93	1057.87	1166.84	997.63	747.72
Spleen (G)	2.437	2.861	1.573	2.434	1.149	1.859	2.823	2.480	2.278
% BRAIN WEIGHT	107.59	129.75	80.46	115.74	56.10	86.83	122.69	113.24	98.19
Testes with Epididymides (G)	5.190	5.077	5.146	6.896	4.463	5.427	5.702	5.665	4.787
% BRAIN WEIGHT	229.14	230.25	263.22	327.91	217.92	253.48	247.81	258.68	206.34

INDIVIDUAL ORGAN WEIGHTS

DRAFT

STUDY: 152
SEX: MALE
GROUP: 4-M - 9.0 mg base/kg/day
ALL FATES DAYS: 183-185 ALL BALANCES

ANIMAL ID: / BALANCE NO.:	561 / 2027	562 / 2027	563 / 2027	564 / 2027	565 / 2027	566 / 2027	567 / 2027	568 / 2027	569 / 2027
BODY WEIGHT (G)	505	541	548	507	508	523	592	473	571
Adrenal Glands (G)	0.097	0.048	0.081	0.051	0.088	0.047	0.083	0.101	0.079
% BRAIN WEIGHT	4.47	2.15	3.76	2.30	3.94	2.29	4.32	4.37	3.56
Brain (G)	2.172	2.236	2.155	2.221	2.233	2.051	1.921	2.310	2.217
Heart (G)	1.563	1.748	1.807	1.397	2.051	1.729	1.871	1.530	1.564
% BRAIN WEIGHT	71.96	78.18	83.85	62.90	91.85	84.30	97.40	66.23	70.55
Kidneys (G)	4.693	4.881	4.668	3.686	4.755	3.803	3.773	3.706	5.978
% BRAIN WEIGHT	216.07	218.29	216.61	165.96	212.94	185.42	196.41	160.43	269.64
Lungs/Bronchi (G)	4.704	4.783	5.236	3.884	4.008	4.279	4.632	7.705	6.176
% BRAIN WEIGHT	216.57	213.91	242.97	174.88	179.49	208.63	241.12	333.55	278.57
Liver (G)	21.743	23.179	23.490	19.251	29.796	22.223	26.805	20.559	26.048
% BRAIN WEIGHT	1001.06	1036.63	1090.02	866.77	1334.35	1083.52	1395.37	890.00	1174.92
Spleen (G)	2.375	2.739	2.615	2.206	3.348	2.432	3.289	2.144	2.654
% BRAIN WEIGHT	109.35	122.50	121.35	99.32	149.93	118.58	171.21	92.81	119.71
Testes with Epididymides (G)	5.531	5.233	4.933	5.345	4.274	5.161	5.336	5.630	5.268
% BRAIN WEIGHT	254.65	234.03	228.91	240.66	191.40	251.63	277.77	243.72	237.62

INDIVIDUAL ORGAN WEIGHTS

DRAFT

STUDY: 152
SEX: MALE
GROUP: 3-M - 2.0 mg base/kg/day
ALL FATES DAYS: 183-185 ALL BALANCES

ANIMAL ID:	501	502	503	504	505	506	507	508	509
BALANCE NO.:	2027	2027	2027	2027	2027	2027	2027	2027	2027
BODY WEIGHT (G)	666	619	592	624	640	644	665	668	598
Adrenal Glands (G)	0.079	0.063	0.055	0.056	0.047	0.077	0.064	0.081	0.087
% BRAIN WEIGHT	3.78	2.54	2.41	2.70	1.99	3.47	2.96	3.60	3.32
Brain (G)	2.089	2.480	2.283	2.073	2.362	2.222	2.161	2.249	2.622
Heart (G)	1.802	1.540	1.580	1.668	1.601	1.742	1.782	1.784	1.673
% BRAIN WEIGHT	86.26	62.10	69.21	80.46	67.78	78.40	82.46	79.32	63.81
Kidneys (G)	4.348	4.097	3.701	4.060	4.817	4.361	4.604	4.810	4.548
% BRAIN WEIGHT	208.14	165.20	162.11	195.85	203.94	196.26	213.05	213.87	173.46
Lungs/Bronchi (G)	3.070	2.861	2.962	3.155	3.263	4.864	3.699	3.787	3.550
% BRAIN WEIGHT	146.96	115.36	129.74	152.19	138.15	218.90	171.17	168.39	135.39
Liver (G)	27.381	22.461	20.165	24.177	28.280	24.791	24.612	30.291	22.189
% BRAIN WEIGHT	1310.72	905.69	883.27	1166.28	1197.29	1115.71	1138.92	1346.87	846.26
Spleen (G)	1.482	1.175	1.067	1.248	1.122	1.046	1.362	1.092	1.490
% BRAIN WEIGHT	70.94	47.38	46.74	60.20	47.50	47.07	63.03	48.55	56.83
Testes with Epididymides (G)	6.009	5.683	4.941	4.877	5.089	5.597	5.928	5.900	6.834
% BRAIN WEIGHT	287.65	229.15	216.43	235.26	215.45	251.89	274.32	262.34	260.64

INDIVIDUAL ORGAN WEIGHTS

STUDY: 152
SEX: MALE

GROUP: 3-M - 2.0 mg base/kg/day
ALL FATES DAYS: 183-185 ALL BALANCES

DRAFT

ANIMAL ID:	510	511	512	513	514	515	516	517	518
BALANCE NO.:	2027	2027	2027	2027	2027	2027	2027	2027	2027
BODY WEIGHT (G)	623	682	778	677	695	781	634	641	669
Adrenal Glands (G)	0.051	0.041	0.031	0.086	0.079	0.029	0.066	0.051	0.074
% BRAIN WEIGHT	2.43	1.87	1.36	4.01	3.71	1.39	3.19	2.42	3.33
Brain (G)	2.102	2.197	2.279	2.144	2.129	2.092	2.067	2.111	2.222
Heart (G)	1.509	1.607	1.645	1.767	1.652	1.778	1.615	1.740	1.727
% BRAIN WEIGHT	71.79	73.15	72.18	82.42	77.60	84.99	78.13	82.43	77.72
Kidneys (G)	4.436	4.937	4.956	4.622	4.550	5.009	4.619	4.119	4.803
% BRAIN WEIGHT	211.04	224.72	217.46	215.58	213.72	239.44	223.46	195.12	216.16
Lungs/Bronchi (G)	2.309	3.563	3.104	3.523	3.130	4.093	3.522	2.826	3.370
% BRAIN WEIGHT	109.85	162.18	136.20	164.32	147.02	195.65	170.39	133.87	151.67
Liver (G)	24.529	27.155	27.012	25.586	25.044	28.221	24.884	24.720	21.666
% BRAIN WEIGHT	1166.94	1236.00	1185.26	1193.38	1176.33	1349.00	1203.87	1171.01	975.07
Spleen (G)	0.906	1.188	1.144	1.318	1.170	1.199	1.148	1.385	1.259
% BRAIN WEIGHT	43.10	54.07	50.20	61.47	54.96	57.31	55.54	65.61	56.66
Testes with Epididymides (G)	5.855	5.379	5.044	5.779	5.433	5.509	5.235	5.863	4.805
% BRAIN WEIGHT	278.54	244.83	221.33	269.54	255.19	263.34	253.27	277.74	216.25

INDIVIDUAL ORGAN WEIGHTS

DRAFT

STUDY: 152
SEX: MALE

GROUP: 3-M - 2.0 mg base/kg/day
ALL FATES DAYS: 183-185 ALL BALANCES

ANIMAL ID:	519	520
BALANCE NO.:		2027
BODY WEIGHT (G)	600	669
Adrenal Glands (G)	0.032	0.054
% BRAIN WEIGHT	1.50	2.48
Brain (G)	2.140	2.175
Heart (G)	1.575	1.522
% BRAIN WEIGHT	73.60	69.98
Kidneys (G)	4.290	5.018
% BRAIN WEIGHT	200.47	230.71
Lungs/Bronchi (G)	3.041	3.751
% BRAIN WEIGHT	142.10	172.46
Liver (G)	25.334	28.100
% BRAIN WEIGHT	1183.83	1291.95
Spleen (G)	1.039	1.130
% BRAIN WEIGHT	48.55	51.95
Testes with Epididymides (G)	5.172	4.559
% BRAIN WEIGHT	241.68	209.61

INDIVIDUAL ORGAN WEIGHTS

DRAFT

STUDY: 152
SEX: MALE

GROUP: 4-M - 9.0 mg base/kg/day
ALL FATES DAYS: 183-185 ALL BALANCES

ANIMAL ID:	570
BALANCE NO.:	2027
BODY WEIGHT (G)	680
Adrenal Glands (G)	0.079
% BRAIN WEIGHT	3.49
Brain (G)	2.266
Heart (G)	1.825
% BRAIN WEIGHT	80.54
Kidneys (G)	5.962
% BRAIN WEIGHT	263.11
Lungs/Bronchi (G)	4.981
% BRAIN WEIGHT	219.81
Liver (G)	31.327
% BRAIN WEIGHT	1382.48
Spleen (G)	4.372
% BRAIN WEIGHT	192.94

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 152
SEX: FEMALE

GROUP: 4-F - 9.0 mg base/kg/day
ALL FATES DAYS: 183-185 ALL BALANCES

DRAFT

ANIMAL ID:	576	577	578	579	580	581	582	583	584
BALANCE NO.:	2027	2027	2027	2027	2027	2027	2027	2027	2027
BODY WEIGHT (G)	352	305	353	317	324	294	302	331	312
Adrenal Glands (G)	0.098	0.080	0.089	0.067	0.111	0.097	0.109	0.114	0.079
% BRAIN WEIGHT	4.92	4.11	4.63	3.50	5.83	4.92	5.43	5.54	4.05
Brain (G)	1.990	1.947	1.924	1.917	1.905	1.973	2.006	2.058	1.953
Heart (G)	1.029	1.079	1.043	1.115	0.989	0.911	0.970	1.071	1.043
% BRAIN WEIGHT	51.71	55.42	54.21	58.16	51.92	46.17	48.35	52.04	53.41
Kidneys (G)	2.708	2.475	2.990	2.907	2.528	2.687	2.330	2.736	2.855
% BRAIN WEIGHT	136.08	127.12	155.41	151.64	132.70	136.19	116.15	132.94	146.19
Lungs/Bronchi (G)	2.735	3.143	3.137	3.721	2.540	3.302	2.923	4.409	4.823
% BRAIN WEIGHT	137.44	161.43	163.05	194.11	133.33	167.36	145.71	214.24	246.95
Liver (G)	13.682	12.246	14.656	13.008	13.816	10.929	11.913	13.909	12.603
% BRAIN WEIGHT	687.54	628.97	761.75	678.56	725.25	553.93	593.87	675.85	645.31
Ovaries (G)	0.148	0.108	0.118	0.141	0.139	0.110	0.050	0.147	0.103
% BRAIN WEIGHT	7.44	5.55	6.13	7.36	7.30	5.58	2.49	7.14	5.27
Spleen (G)	0.820	0.923	1.319	1.473	1.268	1.033	1.291	1.222	1.271
% BRAIN WEIGHT	41.21	47.41	68.56	76.84	66.56	52.36	64.36	59.38	65.08

INDIVIDUAL ORGAN WEIGHTS

DRAFT

STUDY: 152
SEX: FEMALE
GROUP: 4-F - 9.0 mg base/kg/day
ALL FATES DAYS: 183-185 ALL BALANCES

ANIMAL ID:	585	586	587	588	589	590	591	592	593
BALANCE NO.:	2027	2027	2027	2027	2027	2027	2027	2027	2027
BODY WEIGHT (G)	334	360	313	306	326	328	319	301	290
Adrenal Glands (G)	0.078	0.085	0.121	0.079	0.094	0.104	0.106	0.092	0.088
% BRAIN WEIGHT	4.13	4.45	6.38	3.70	4.47	4.64	5.11	4.79	4.12
Brain (G)	1.887	1.908	1.898	2.135	2.101	2.239	2.074	1.920	2.136
Heart (G)	1.000	1.106	1.023	0.911	1.200	1.066	1.074	0.918	0.914
% BRAIN WEIGHT	52.99	57.97	53.90	42.67	57.12	47.61	51.78	47.81	42.79
Kidneys (G)	2.564	3.159	2.973	2.368	3.136	2.628	2.791	2.890	2.559
% BRAIN WEIGHT	135.88	165.57	156.64	110.91	149.26	117.37	134.57	150.52	119.80
Lungs/Bronchi (G)	3.102	2.977	3.793	3.140	3.307	3.921	3.385	2.672	3.194
% BRAIN WEIGHT	164.39	156.03	199.84	147.07	157.40	175.12	163.21	139.17	149.53
Liver (G)	12.812	15.026	11.470	10.062	14.319	12.035	11.522	13.739	11.698
% BRAIN WEIGHT	678.96	787.53	604.32	471.29	681.53	537.52	555.54	715.57	547.66
Ovaries (G)	0.118	0.147	0.125	0.086	0.067	0.134	0.117	0.087	0.097
% BRAIN WEIGHT	6.25	7.70	6.59	4.03	3.19	5.98	5.64	4.53	4.54
Spleen (G)	1.227	1.404	1.606	1.510	1.829	1.502	1.209	1.167	1.291
% BRAIN WEIGHT	65.02	73.58	84.62	70.73	87.05	67.08	58.29	60.78	60.44

INDIVIDUAL ORGAN WEIGHTS

STUDY: 152
SEX: FEMALE

GROUP: 4-F - 9.0 mg base/kg/day
ALL FATES DAYS: 183-185 ALL BALANCES

DRAFT

ANIMAL ID:	594	595
BALANCE NO.:	2027	2027
BODY WEIGHT (G)	305	296
Adrenal Glands (G)	0.089	0.087
% BRAIN WEIGHT	4.61	4.50
Brain (G)	1.931	1.935
Heart (G)	0.960	0.770
% BRAIN WEIGHT	49.72	39.79
Kidneys (G)	2.408	2.290
% BRAIN WEIGHT	124.70	118.35
Lungs/Bronchi (G)	3.763	2.620
% BRAIN WEIGHT	194.87	135.40
Liver (G)	12.510	11.093
% BRAIN WEIGHT	647.85	573.28
Ovaries (G)	0.097	0.068
% BRAIN WEIGHT	5.02	3.51
Spleen (G)	1.139	0.972
% BRAIN WEIGHT	58.98	50.23

DRAFT

APPENDIX J

PATHOLOGY REPORT

DRAFT PATHOLOGY REPORT FOR SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS UIC/TRL STUDY NUMBER 152

PREPARED
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JUNE 28, 1996

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SECTION I

PATHOLOGY NARRATIVE

DRAFT PATHOLOGY REPORT

SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS

INTRODUCTION

This pathology report, submitted by Pathology Associates International (PAI) to Toxicology Research Laboratory, University of Illinois at Chicago (UIC/TRL), represents the histopathology findings for the study designated as "Six Month Oral Toxicity Study of WR238605 Succinate in Rats", UIC/TRL Study Number 152.

EXPERIMENTAL DESIGN AND METHODS

Three groups (Groups 2-4), each composed of 20 male and 20 female CD® (Virus Antibody Free) rats designated for histopathology, were given the test article once daily by oral gavage in 5 ml/kg/day of test article vehicle (aqueous 1% methylcellulose/0.2% Tween 80) for at least twenty-six weeks. The dose levels administered were 0.5, 2.0, and 9.0 mg base/kg/day for animals in the low, mid, and high dose groups, respectively. Also, one group (control), composed of 20 male and 20 female CD® (Virus Antibody Free) rats designated for histopathology, was given the test article vehicle alone once daily by oral gavage for at least twenty-six weeks. The experimental design is summarized in Table I (Summary of Experimental Design).

With the exception of one animal (high dose male, animal number 0558) found dead on Day 137, all animals were sacrificed and necropsied in random order on Study Days 183, 184, and 185. Animals were anesthetized with carbon dioxide and sacrificed by exanguination. All necropsies were performed according to UIC/TRL Standard Operating Procedures and were conducted by PAI personnel, except for the high dose male (number 0558) which was necropsied on the day of death by an approved UIC/TRL technician. Tissues required by the protocol (see Table II, Protocol-Required Tissues) were examined and placed in 10% neutral buffered formalin. Bone marrow smears were prepared from the femur of each animal at necropsy. The bone marrow smears were fixed in methanol, stained with a Wrights-Giemsa stain, and evaluated microscopically to determine the Myeloid:Erythroid (M:E) Ratio.

Tissues required for histopathologic evaluation in control (Group 1) and high dose (Group 4) groups were trimmed and processed, and slides were prepared in accordance with PAI Standard Operating Procedures. In addition, kidney sections from 3 high dose animals (0567, 0585, and 0587) were stained by the Periodic Acid Schiff method[1] and livers from 3 high dose animals

[1] "Periodic Acid Schiff (PAS) Procedure", Armed Forces Institute of Pathology: Laboratory Methods in Histotechnology, 1992; pages 151-152.

(0556, 0561, and 0566) were post-fixed with osmium tetroxide for lipid visualization[2]. These tissues were evaluated by light microscopy and the results were tabulated. Some tissues are inherently difficult to obtain in sections because of their small size (e.g. parathyroid gland). Tissues were recorded as "unsuitable for complete evaluation" when they were missing in both the original section and in recut and/or retrim attempts to obtain them. Adrenal glands, liver (males only), spleen, lung, kidneys, uterus, and sternum with bone marrow were trimmed and processed, slides were prepared, and the tissues were examined microscopically for animals in the low and mid dose groups. Also, all gross lesions were examined microscopically.

Treatment-related lesions are summarized in Table III, Summary of Treatment-Related Lesions. Microscopic findings for all groups are summarized in the Project Summary Tables (Section II). The mean group severity scores are found in the Severity Summary Tables (Section III). Where applicable, all tissue changes received a severity grade based upon the following scale: 1 = minimal, 2 = mild, 3 = moderate, and 4 = marked. Final average severity scores for each change were slightly modified by weighting factors automatically assigned by the LABCAT® histopathology data management system. Weighting factors are explained in Table IV (Severity Weighting Factors). Microscopic findings in the protocol-required tissues for individual animals are presented in the Tabulated Animal Data Tables (Section IV). The correlation of the necropsy findings and histopathology findings are reported in the Correlation of Gross and Microscopic (Micro) Findings (Section V). The codes used as entries in these tables are explained in the Report Codes Table. The results of the bone marrow evaluation are presented in the Bone Marrow Evaluation Report (Section VII).

RESULTS AND DISCUSSION

The Results and Discussion section is divided into five parts: Necropsy Findings, Diagnostic Terms, Surgical Specimen Findings, Histopathology Findings, and Bone Marrow Evaluation Findings. The Necropsy Findings portion describes lesions seen at necropsy or trimming that were test article-related. The Diagnostic Terms portion lists and clarifies diagnostic terminology that may be unclear. Terms listed in the Diagnostic Terms portion of this section includes, but is not limited to, those that were considered to be test article-related. The Surgical Specimens Findings portion reports findings from surgical specimens from the study. The Histopathology Findings portion of this section reports the results and provides discussion of the histopathologic evaluation of the tissues. The Bone Marrow Evaluation Findings portion of this section reports the results of bone marrow smear evaluations.

Necropsy Findings

Gross lesions were observed in lung from 4 of 20, 5 of 20, 18 of 20, and 20 of 20 males in control, low, mid, and high dose groups, respectively; and in 9 of 20, 7 of 20, 19 of 20, and 20 of 20 females in control, low, mid, and high dose groups, respectively. Lung lesions generally

[2] "Osmium Tetroxide Method for Fat (Paraffin Sections)", Manual of Histologic Staining Methods of the Armed Forces Institute of Pathology, third edition, 1968; pages 143-145.

consisted of pigmentation changes such as red or white foci or mottled appearance. Red lung lesions generally correlated to hemorrhage and white lung lesions generally correlated to interstitial inflammation and/or accumulation of foamy macrophages.

Enlarged spleen was observed in 0 of 20, 0 of 20, 0 of 20, and 9 of 20 males in control, low, mid, and high dose groups, respectively; and in 0 of 20, 0 of 20, 0 of 20, and 2 of 20 females in the control, low, mid, and high dose groups, respectively. Enlarged spleens correlated to splenic congestion.

All other gross lesions were interpreted as incidental findings. Gross observations are listed in the Correlation of Gross and Microscopic (Micro) Findings report in Section V. Microscopic findings were correlated with gross lesions when possible.

Diagnostic Terms

The morphologic characteristics of observations and lesions which require comment are presented in subsequent paragraphs to aid in the interpretation of the data.

Lung

Chronic interstitial inflammation was characterized by the presence of alveolar macrophages in alveolar lumens and thickened alveolar walls which stained more basophilic than normal in the affected region. Foamy macrophage accumulation was diagnosed when lumenal macrophages were very large with copious foamy cytoplasm. Hemorrhage was characterized by the presence of free erythrocytes and fibrin in the lumen of alveoli in the affected region. Chronic perivascular inflammation was characterized by focal accumulation of mature lymphocytes around or adjacent to small arteries. Hemorrhage, foamy macrophage accumulation, and chronic interstitial inflammation were generally present in the same regions. Chronic interstitial inflammation was interpreted as the end result of chronic hemorrhage with macrophage accumulation, because it tended to develop in the more extensive lesions.

Granulomatous inflammation was characterized by the presence of large multinucleated cells with an eosinophilic homogeneous central region and nuclei aligned around the outer margin. Such cells were interpreted to represent the presence of particulate material such as might occur from aspiration of food or methylcellulose dosing medium. Acute inflammation was represented by accumulation of neutrophils in alveoli of affected areas. Edema consisted of alveoli filled with eosinophilic homogeneous material. Edema was generally associated with acute inflammation when present.

Spleen

Erythropoiesis was characterized by increased number and size of erythrocyte precursor cell colonies in red pulp of spleen. Pigmentation was characterized by the presence of focal groups of macrophages that contained dark brown granular material in their cytoplasm. Some pigment is normally present in splenic macrophages. Therefore, it was only diagnosed when present in sufficient quantity to be readily recognized at 40x magnification. Hyperplasia of

reticuloendothelial cells was characterized by an increased thickness and prominence of the lightly basophilic zone of cells at the interface between red and white pulp. Congestion was characterized by increased prominence of red pulp regions due to pooling of erythrocytes in splenic sinusoids.

Sternum

Bone marrow hyperplasia was diagnosed when blood precursor cells were increased at the expense of lipid cells. Granulopoiesis was diagnosed when the number of myeloid cells was increased at the expense of lipid cells.

Liver

Apoptosis was characterized by the presence of condensed deeply eosinophilic round bodies in centrilobular regions of the liver. Fatty change was diagnosed when cells in centrilobular to midzonal regions contained discrete round vacuoles in their cytoplasm. Vacuoles in hepatocytes were generally empty, but sometimes contained lightly eosinophilic homogeneous material, and they displaced the nucleus to the outer margin of the cell. Osmium post-fixation demonstrated that at least some of the hepatocyte vacuoles in liver from animal numbers 0556 and 0566 were due to lipid content. Osmium staining was not observed in liver from animal number 0561. Vacuolated cell focus was characterized by the presence of a focal region of hepatocytes with finely vacuolated cytoplasm and a centrally located nucleus.

Pigmentation was characterized by the presence of brown granular material in the cytoplasm of centrilobular hepatocytes. Congestion was diagnosed when blood-filled sinusoids were observed in centrilobular areas that are generally occupied by hepatocytes. Chronic inflammation was characterized by focal accumulation of lymphocytes in some portal regions, adjacent to vessels, or within sinusoids.

Kidney

Pigmentation in renal cortex was characterized by the presence of brown granular pigment in the cytoplasm of some renal tubule epithelial cells. The pattern of pigmented cell distribution was most consistent with specific accumulation in proximal convoluted tubules. Periodic Acid Schiff (PAS) staining in sections from three animals confirmed that the pigment was in proximal convoluted tubule epithelium, as indicated by the presence of PAS positive brush borders on the lumen surface of the pigmented cells. Round homogeneous bodies consistent with protein globules were also present in the lumen of some pigmented proximal convoluted tubules, but there was insufficient evidence of epithelial cell necrosis to justify a diagnosis of nephrosis. Pigmentation of cortical epithelial cells was considered to be a sensitive morphologic indicator of chronic hemoglobin resorptive activity in the kidney.

Adrenal Gland

Pigmentation was characterized by the presence of cells in the zona reticularis region that contained a variable amount of brown granular pigment in their cytoplasm. Congestion was diagnosed when vessels in the adrenal cortex were dilated and filled with erythrocytes. Pigmentation in the zona reticularis region generally occurs in aging rats due to lipofuscin

deposits. However, in this study the possibility of hemosiderin deposits cannot be ruled out because of the chronic pulmonary hemorrhage observed, and thus the probable circulation of free hemoglobin in blood.

Uterus

Dilatation was diagnosed when the uterine horn lumen size was increased in cross-sectional diameter with associated thinning of the uterine wall.

The remainder of the diagnoses used in this study were considered to be self-explanatory and were not discussed in this section.

Surgical Specimen Findings

A skin mass was observed and surgically removed from the lower left abdominal region of animal number 0599 (high dose female) during the second week of the study. Histopathological evaluation of the mass revealed it to be malignant adenocarcinoma of mammary gland. A second mass was observed in the left abdominal region of this same animal during Study Week 6 and surgically removed during Study Week 8. The second mass was also a malignant adenocarcinoma of mammary gland. The second tumor probably represents growth from incomplete removal of the first one.

A skin mass was observed on the lower right abdominal region of animal number 0539 (mid dose female) during Study Week 20 and surgically removed during Study Week 21. Histopathological evaluation of the mass revealed it to be a benign adenoma of mammary gland.

Mammary gland tumors are common in aging CD® rats, but uncommon in CD® rats that are less than 6 months of age. However, they do occur in younger rats, as evidenced by the report by Oishi et al. of a spontaneously occurring mammary adenocarcinoma in a 10-week-old female Sprague Dawley rat (Toxicologic Pathology, Volume 23, No. 6, 1995, pages 696-700). Induced mammary gland neoplasia is frequently associated with focal or multifocal acinar hyperplasia. The only occurrences of acinar hyperplasia in this study were in animal number 0415 (control male) and animal number 0481 (low dose female). There was no indication of treatment-related focal or multifocal mammary gland acinar hyperplasia in this study. Therefore, the mammary gland tumors observed in this study are probably incidental findings.

Histopathology Findings

The incidence and severity of treatment-related histopathology findings are summarized in Table III, Summary of Treatment-Related Lesions. These findings are further discussed by organ in this section of the narrative report.

Lung

Hemorrhage, accumulation of foamy macrophages, and chronic interstitial inflammation were observed in all high dose males and females. Hemorrhage was less frequently observed in mid dose males (4 of 20, SEV = 0.30) and mid dose females (9 of 20, SEV = 0.25), but accumulation of foamy macrophages and chronic interstitial inflammation were present in all mid dose males and females. Treatment-related lesions were not observed in low dose females, and were essentially absent from low dose males, the exception being the presence of foamy macrophages in lung from 2 of 20 (SEV = 0.05) low dose males. The slight increase in incidence and severity of hemorrhage in low and mid dose lungs was not considered to be significantly different from the background lesions in control animals.

The pathogenesis of these lung lesions cannot be stated with certainty. However, one possible mechanism could be a primary lesion (not evident from light microscopy) to endothelium and/or type I alveolar cells that would result in hemorrhage. The presence of erythrocytes and blood protein could result in attraction of macrophages to the alveolar lumen. Macrophages may develop copious foamy cytoplasm as they attempt to digest the lipid membrane component of erythrocytes. Macrophages may release enzymes into the alveolar lumen resulting in an interstitial inflammatory response. Other potential causes of hemorrhage include high arterial blood pressure, lack of thrombocytes, or lack of one or more clotting factors.

Liver

Apoptosis, pigmentation, and fatty change were observed in centrilobular hepatocytes of several high dose males, but were not apparent in high dose females. The incidence of fatty change in liver was slightly higher in mid dose males (6 of 20, SEV = 0.30) than in control males (2 of 20, SEV = 0.10), but the incidence of fatty change in low dose males (3 of 20, SEV = 0.10) was not considered to be significantly different from control males (2 of 20, SEV = 0.10). The centrilobular lesions observed in livers from males in the high dose group were consistent with classic cases of chronic congestion, but they could also be due to the presence of circulating free hemoglobin in the blood or a direct effect of the test article. The incidence of congestion in liver was relatively low (2 of 20 and 2 of 20 in mid and high dose males, respectively), but exanguination prior to necropsy may have influenced the histologic appearance relative to its in vivo-state. If the low incidence of congestion is accepted as reflective of the in-vivo state, then a direct test article effect is more likely.

Spleen

The incidence of congestion of spleen was notably increased in high dose males (18 of 20) and females (17 of 20) and was rarely present in control, low, or mid dose males or females. Splenic congestion probably accounts for the increased splenic weight/brain weight ratios observed in males and females in the high dose group.

Pigmentation and erythropoiesis were frequently present in spleens from females in all the dose groups. The high background incidence of pigmentation and erythropoiesis in female spleen may have masked any subtle treatment effects on these changes in the female rats. In

males, there appears to be a mild dose-dependency for the incidence of both erythropoiesis and pigmentation, including a slightly increased incidence of both in the low dose males. Hyperplasia of reticuloendothelial cells was occasionally present in spleens from both males (4 of 20, SEV = 0.30) and females (1 of 20, SEV = 0.10) in the high dose group, but was not observed in control, low, or mid dose groups.

Sternum with Marrow

Bone marrow hyperplasia was present in all of the male and female dose groups except for the controls and the incidence increased in a dose-dependent fashion. Bone marrow hyperplasia is most consistent with a low grade clinical anemia. The variability of the bone marrow response within a given group (i.e. hyperplasia of marrow in some animals while others in the same group are normal) suggests the possibility of intermittent hemorrhage as the cause of the anemia and consequent bone marrow hyperplasia. A no-effect level was not observed in this study for bone marrow hyperplasia.

Granulopoiesis was observed in one early death high dose male (animal number 0558) and one high dose female (animal number 0578). Granulopoiesis in bone marrow suggests that an inflammatory response occurred somewhere in the body within 1 to 2 weeks prior to necropsy.

Kidney

Pigmentation in renal proximal convoluted tubule epithelial cells was observed in both males and females in the high and mid dose groups, but was not present in control and low dose group animals. The pigment was consistent with either hemosiderin or lipofuscin deposition. However, hemosiderin is considered to be more likely in the presence of pulmonary hemorrhage because such hemorrhage would be expected to lead to hemoglobin release and return to the blood via direct resorption or lymphatic return. Pigmentation probably resulted in the process of resorption of hemoglobin after filtration through the renal glomeruli.

Adrenal Gland

Pigmentation in the zona reticularis region of adrenal cortex was notably present in the high dose males (10 of 20, SEV = 0.60) and high dose females (18 of 20, SEV = 1.55); and to a lessor extent in the mid dose males (3 of 20, SEV = 0.15), mid dose females (2 of 20, SEV = 0.10), low dose males (1 of 20, SEV = 0.05), and low dose females (1 of 20, SEV = 0.05). Pigmentation of adrenal gland was not observed in control animals of either sex. Pigmentation of adrenal cortical cells in the zona reticularis region of adrenal cortex was interpreted as a treatment-related change. The nature of the brown pigment is uncertain. Lipofuscin deposits commonly occur in this region with advancing age, but hemosiderin deposition cannot be ruled out without iron and/or acid-fast staining.

The incidence of adrenal gland congestion was increased in the high dose females (18 of 20, SEV = 1.50) compared to the mid dose females (7 of 20, SEV = 0.40), low dose females (3 of 20, SEV = 0.15), and control females (7 of 20, SEV = 0.35). Congestion probably accounts for the increased weight of the adrenals in the high dose females. Adrenal gland congestion is

interpreted as a treatment-related finding, but it is uncertain whether the effect is primary or secondary to inflammatory events occurring elsewhere in the body (i.e., lung). However, the relative sex-specificity of the adrenal congestion suggests a primary sex-linked effect, because the lung changes occurred in both sexes.

Bone Marrow Evaluation Findings

The bone marrow evaluation findings are presented with supporting data in Section VII of this report. The M:E Ratios from high dose and control animals necropsied during Week 27 were not significantly different and were within normal limits.

CONCLUSIONS

Under the conditions of this study, daily administration of WR238605 Succinate by oral gavage to CD® rats for at least 6 months at a dose of 2.0 or 9.0 mg base/kg/day resulted in histopathologic lesions in lung (foamy macrophage accumulation and chronic interstitial inflammation) and kidney (pigmentation in cortical epithelial cells) in both males and females. The 9.0 mg base/kg/day dose level also resulted in increased congestion in spleen (males and females) and adrenal gland (females only); apoptosis, pigmentation, and fatty change (also slightly elevated at the 2.0 mg base/kg/day dose level) in centrilobular regions of liver (males only); pigmentation in adrenal gland (males and females); hemorrhage in lung (males and females); and reticuloendothelial cell hyperplasia in spleen (males and one female). Treatment-related effects on bone marrow M:E ratios were not seen. The 0.5 mg base/kg/day dose level resulted in only minimal evidence of pulmonary changes (foamy macrophage accumulation in 2 of 20 males), bone marrow changes (hyperplasia in 5 of 20 males and 4 of 20 females), and possibly some effect on splenic erythropoiesis (4 of 20 in low dose males compared to 2 of 20 control males). Therefore, although the histopathologic changes observed at the 0.5 mg base/kg/day dose are of minimal clinical significance, a no-effect level for WR238605 Succinate was not established in this study.

_____ _____

Robert L. Morrissey, DVM, Ph.D. Date
Diplomate, ACVP

TABLE I

SUMMARY OF EXPERIMENTAL DESIGN

Group Number	Dose Group	Dose Level (mg base/kg/day)	Dose Conc. (mg base/ml)	Dose Volume (ml/kg/day)	Number of Males	Number of Females
1	Control	0	0	5	20* + 5	20* + 5
2	Low	0.5	0.1	5	20* + 5	20* + 5
3	Mid	2.0	0.4	5	20* + 5	20* + 5
4	High	9.0	1.8	5	20* + 5	20* + 5

* Core toxicity study animals

TABLE II

PROTOCOL-REQUIRED TISSUES

Adrenal glands
Animal identification
Brain
Cecum
Colon
Diaphragm
Duodenum
Epididymis
Esophagus
Eyes with harderian glands
Heart
Ileum
Jejunum
Kidneys
Liver
Lung/Bronchi
Lymph node (mesenteric)
Mammary gland
Ovaries
Pancreas
Pituitary gland
Prostate
Rib with costochondral junction
Salivary gland (submaxillary)
Sciatic nerve
Skeletal muscle
Skin
Spinal cord (thoracic)
Spleen
Sternum with bone marrow
Stomach
Testes
Thymus
Thyroid gland with parathyroids
Tongue
Trachea
Urinary bladder
Uterus
Gross lesions

TABLE III
SUMMARY OF TREATMENT-RELATED LESIONS

		Dose (mg base/kg/day)			
ORGAN - lesion		0	0.5	2.0	9.0
LUNG					
- Hemorrhage	M	2/20 (0.09)*	1/20 (0.06)	4/20 (0.30)	20/20 (1.50)
	F	6/20 (0.14)	9/20 (0.30)	9/20 (0.25)	20/20 (2.10)
- Accumulation, foamy macrophage	M	0/20 (0.00)	2/20 (0.05)	20/20 (1.80)	20/20 (2.65)
	F	0/20 (0.00)	0/20 (0.00)	20/20 (1.95)	20/20 (1.85)
- Inflammation, chronic, interstitium	M	2/20 (0.03)	3/20 (0.06)	20/20 (1.20)	20/20 (2.40)
	F	3/20 (0.05)	0/20 (0.00)	20/20 (1.40)	20/20 (1.90)
LIVER					
- Apoptosis, centrilobular	M	0/20 (0.00)	0/20 (0.00)	0/20 (0.00)	11/20 (0.70)
	F	0/20 (0.00)	-	-	0/20 (0.00)
- Pigmentation, centrilobular	M	0/20 (0.00)	0/20 (0.00)	0/20 (0.00)	11/20 (0.60)
	F	0/20 (0.00)	-	-	0/20 (0.00)
- Fatty change, centrilobular	M	2/20 (0.10)	3/20 (0.10)	6/20 (0.30)	10/20 (0.50)
	F	0/20 (0.00)	-	-	0/20 (0.00)
- Congestion, centrilobular	M	0/20 (0.00)	0/20 (0.00)	2/20 (0.10)	2/20 (0.13)
	F	0/20 (0.00)	-	-	0/20 (0.00)
SPLEEN					
- Erythropoiesis	M	2/20 (0.10)	4/20 (0.20)	8/20 (0.50)	8/20 (0.55)
	F	10/20 (0.70)	11/20 (0.90)	14/20 (1.25)	8/20 (0.60)
- Pigmentation	M	1/20 (0.10)	4/20 (0.20)	8/20 (0.45)	11/20 (0.80)
	F	17/20 (1.15)	20/20 (1.90)	18/20 (1.80)	17/20 (1.20)
- Congestion	M	0/20 (0.00)	0/20 (0.00)	0/20 (0.00)	18/20 (1.90)
	F	0/20 (0.00)	1/20 (0.05)	1/20 (0.05)	17/20 (1.45)
- Hyperplasia, reticuloendothelial cell	M	0/20 (0.00)	0/20 (0.00)	0/20 (0.00)	4/20 (0.30)
	F	0/20 (0.00)	0/20 (0.00)	0/20 (0.00)	1/20 (0.10)
STERNUM WITH MARROW					
- Hyperplasia, bone marrow	M	0/20 (0.00)	5/20 (0.30)	11/20 (0.60)	19/20 (1.25)
	F	0/20 (0.00)	4/20 (0.20)	7/20 (0.40)	13/20 (0.90)
- Granulopoiesis	M	0/20 (0.00)	0/20 (0.00)	0/20 (0.00)	1/20 (0.10)
	F	0/20 (0.00)	0/20 (0.00)	0/20 (0.00)	1/20 (0.05)
KIDNEY					
- Pigmentation, cortex	M	0/20 (0.00)	0/20 (0.00)	4/20 (0.20)	16/19 (1.11)
	F	0/20 (0.00)	0/20 (0.00)	7/20 (0.35)	20/20 (1.60)
ADRENAL GLAND					
- Pigmentation, zona reticularis	M	0/20 (0.00)	1/20 (0.05)	3/20 (0.15)	10/20 (0.60)
	F	0/20 (0.00)	1/20 (0.05)	2/20 (0.10)	18/20 (1.55)
- Congestion	M	1/20 (0.05)	1/20 (0.05)	4/20 (0.25)	2/20 (0.10)
	F	7/20 (0.35)	3/20 (0.15)	7/20 (0.40)	18/20 (1.50)

* Incidence (mean group severity score) - Not examined

Lesion severity as modified by distribution is defined in Table IV.

TABLE IV

SEVERITY WEIGHTING FACTORS

The PAI pathology computer system (LABCAT®) has a built-in weighting system for calculating the average severity for each tissue observation. These weighted averages are based upon the severity and distribution as outlined in the following table.

Severity Grading	No Modifier	Focal	Multifocal	Diffuse
1	1.0	0.25	0.5	0.75
2	2.0	1.25	1.5	1.75
3	3.0	2.25	2.5	2.75
4	4.0	3.25	3.5	3.75

PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

Report Codes Table

A. Codes applying to organs

N	Tissues within normal histological limits
A	Autolysis precluding adequate evaluation
U	Tissues unsuitable for complete evaluation
S	Tissues not applicable to animal

B. Codes applying to microscopic diagnoses

1	minimal
2	mild
3	moderate
4	marked
( )	focal
[ ]	diffuse
< >	multifocal
P	Present
B	Neoplasm, benign
M	Neoplasm, malignant without metastasis
C	Neoplasm, malignant with metastasis
X	Metastatic site (+)
I	Bilateral
L	Unilateral
-	No data entered

SECTION II

PROJECT SUMMARY TABLE

DRAFT

PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

PROJECT SUMMARY

STUDY ID : SN152 STUDY NUMBER: SN152
FATE: ALL
SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		1		2		3		4	
		(1)		(2)		(3)		(4)	
NUMBER OF ANIMALS:		20		20		20		20	
		#	%	#	%	#	%	#	%
BRAIN	# EX	20		0		0		20	
Dilitation, ventricle		1	5.0	0	0.0	0	0.0	0	0.0
THYMUS	# EX	20		0		0		18	
Hemorrhage		14	70.0	0	0.0	0	0.0	14	78.0
Depletion, lymphoid		1	5.0	0	0.0	0	0.0	3	17.0
SALIVARY GLAND	# EX	20		0		0		20	
PANCREAS	# EX	20		0		0		20	
Inflammation, chronic		7	35.0	0	0.0	0	0.0	7	35.0
Atrophy, acinar		1	5.0	0	0.0	0	0.0	1	5.0
ADRENAL GLAND	# EX	20		20		20		20	
Hypertrophy, zona glomerulosa		2	10.0	1	5.0	1	5.0	4	20.0
Vacuolation, cortex		2	10.0	3	15.0	1	5.0	1	5.0
Pigmentation, zona reticularis		0	0.0	1	5.0	3	15.0	10	50.0
Congestion		1	5.0	1	5.0	4	20.0	2	10.0
Hypertrophy, zona reticularis		6	30.0	3	15.0	6	30.0	3	15.0
SPINAL CORD (THORACIC)	# EX	20		0		0		20	
DIAPHRAGM	# EX	20		0		0		20	
Inflammation, chronic		1	5.0	0	0.0	0	0.0	3	15.0
ESOPHAGUS	# EX	20		0		0		20	
Inflammation, chronic, muscle		0	0.0	0	0.0	0	0.0	1	5.0
TRACHEA	# EX	20		0		0		20	
Inflammation, chronic		5	25.0	0	0.0	0	0.0	3	15.0
Inflammation, subacute		0	0.0	0	0.0	0	0.0	1	5.0

Incidence Calculated by No. of Tissues Scored
(1) - 0 mg base/kg/day Dose Level
(2) - 0.5 mg base/kg/day Dose Level
(3) - 2.0 mg base/kg/day Dose Level
(4) - 9.0 mg base/kg/day Dose Level

DRAFT

PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

PROJECT SUMMARY

STUDY ID : SN152 STUDY NUMBER: SN152
FATE: ALL
SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		1 (1)		2 (2)		3 (3)		4 (4)	
NUMBER OF ANIMALS:		20		20		20		20	
		#	%	#	%	#	%	#	%
THYROID GLAND	# EX	20		0		0		20	
Atrophy, follicle		0	0.0	0	0.0	0	0.0	1	5.0
PARATHYROID GLAND	# EX	18		0		0		17	
TONGUE	# EX	20		0		0		20	
HEART	# EX	20		0		0		20	
Cardiomyopathy		9	45.0	0	0.0	0	0.0	5	25.0
Inflammation, chronic, serosa		0	0.0	0	0.0	0	0.0	2	10.0
Thrombosis, chronic		0	0.0	0	0.0	0	0.0	1	5.0
DUODENUM	# EX	20		0		0		19	
COLON	# EX	20		0		0		19	
STOMACH	# EX	20		0		0		19	
Dilatation, crypt glands		2	10.0	0	0.0	0	0.0	1	5.0
LIVER	# EX	20		20		20		20	
Inflammation, chronic		10	50.0	12	60.0	10	50.0	7	35.0
Necrosis		1	5.0	0	0.0	1	5.0	0	0.0
Focus, vacuolated cell		1	5.0	0	0.0	2	10.0	3	15.0
Hepatodiaphragmatic nodule		1	5.0	0	0.0	1	5.0	0	0.0
Necrosis, coagulation		0	0.0	0	0.0	0	0.0	1	5.0
Apoptosis, centrilobular		0	0.0	0	0.0	0	0.0	11	55.0
Pigmentation, centrilobular		0	0.0	0	0.0	0	0.0	11	55.0
Fatty change, centrilobular		2	10.0	3	15.0	6	30.0	10	50.0
Congestion, centrilobular		0	0.0	0	0.0	2	10.0	2	10.0
Inflammation, subacute, centrilobular		0	0.0	0	0.0	0	0.0	1	5.0
Focus, basophilic cell		0	0.0	0	0.0	0	0.0	1	5.0
Hyperplasia, bile duct		0	0.0	0	0.0	0	0.0	1	5.0

Incidence Calculated by No. of Tissues Scored
(1) - 0 mg base/kg/day Dose Level
(2) - 0.5 mg base/kg/day Dose Level
(3) - 2.0 mg base/kg/day Dose Level
(4) - 9.0 mg base/kg/day Dose Level

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PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

PROJECT SUMMARY

STUDY ID : SN152 STUDY NUMBER: SN152
FATE: ALL
SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		1		2		3		4	
		(1)		(2)		(3)		(4)	
NUMBER OF ANIMALS:		20		20		20		20	
		#	%	#	%	#	%	#	%
SPLEEN	# EX	20		20		20		20	
Erythropoiesis		2	10.0	4	20.0	8	40.0	8	40.0
Pigmentation		1	5.0	4	20.0	8	40.0	11	55.0
Congestion		0	0.0	0	0.0	0	0.0	18	90.0
Hyperplasia, reticuloendothelial cell		0	0.0	0	0.0	0	0.0	4	20.0
Cyst, serosa		0	0.0	1	5.0	0	0.0	0	0.0
JEJUNUM	# EX	20		0		0		19	
LUNG	# EX	20		20		20		20	
Inflammation, chronic, interstitium		2	10.0	3	15.0	20	100.0	20	100.0
Hemorrhage		2	10.0	1	5.0	4	20.0	20	100.0
Inflammation, granulomatous		1	5.0	2	10.0	0	0.0	3	15.0
Congestion		1	5.0	1	5.0	1	5.0	0	0.0
Hyperplasia, lymphoid, peribronchial		0	0.0	0	0.0	2	10.0	0	0.0
Inflammation, acute		0	0.0	0	0.0	0	0.0	2	10.0
Inflammation, chronic, serosa		1	5.0	0	0.0	0	0.0	1	5.0
Inflammation, granulomatous, serosa		0	0.0	1	5.0	0	0.0	0	0.0
Inflammation, chronic, perivascular		13	65.0	18	90.0	20	100.0	17	85.0
Accumulation, foamy macrophage		0	0.0	2	10.0	20	100.0	20	100.0
Edema		0	0.0	0	0.0	0	0.0	1	5.0
KIDNEY	# EX	20		20		20		19	
Inflammation, chronic		16	80.0	17	85.0	19	95.0	14	74.0
Nephropathy		14	70.0	16	80.0	15	75.0	9	47.0
Hydronephrosis		0	0.0	0	0.0	0	0.0	1	5.0
Pigmentation, cortex		0	0.0	0	0.0	4	20.0	16	84.0
Hemorrhage, pelvis		0	0.0	1	5.0	0	0.0	0	0.0
Cyst		0	0.0	0	0.0	0	0.0	1	5.0
URINARY BLADDER	# EX	20		3		0		20	
Inflammation, chronic		1	5.0	0	0.0	0	0.0	0	0.0

Incidence Calculated by No. of Tissues Scored
(1) - 0 mg base/kg/day Dose Level
(2) - 0.5 mg base/kg/day Dose Level
(3) - 2.0 mg base/kg/day Dose Level
(4) - 9.0 mg base/kg/day Dose Level

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PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

PROJECT SUMMARY

STUDY ID : SN152 STUDY NUMBER: SN152
FATE: ALL

SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		1		2		3		4	
		(1)		(2)		(3)		(4)	
NUMBER OF ANIMALS:		20		20		20		20	
		#	%	#	%	#	%	#	%
URINARY BLADDER	# EX	20		3		0		20	
Inflammation, chronic, urethra		1	5.0	0	0.0	0	0.0	0	0.0
Semen plug		0	0.0	3	100.0	0	0.0	0	0.0
PROSTATE	# EX	20		0		0		20	
Inflammation, chronic		1	5.0	0	0.0	0	0.0	0	0.0
SKIN	# EX	20		0		0		20	
MAMMARY GLAND	# EX	20		0		0		18	
Hyperplasia, acinar		1	5.0	0	0.0	0	0.0	0	0.0
Metaplasia, squamous		1	5.0	0	0.0	0	0.0	0	0.0
Inflammation, chronic		1	5.0	0	0.0	0	0.0	0	0.0
ILEUM	# EX	20		0		0		19	
CECUM	# EX	20		0		0		19	
LYMPH NODE, MESENTERIC	# EX	20		0		0		19	
Hemorrhage		0	0.0	0	0.0	0	0.0	1	5.0
Inflammation, granulomatous		0	0.0	0	0.0	0	0.0	1	5.0
SKELETAL MUSCLE	# EX	20		0		0		20	
SCIATIC NERVE	# EX	20		0		0		20	
TESTES	# EX	20		0		0		20	
Arrested spermatogenesis		1	5.0	0	0.0	0	0.0	0	0.0
Degeneration		1	5.0	0	0.0	0	0.0	1	5.0
EPIDIDYMIS	# EX	20		0		0		20	
Inflammation, chronic		1	5.0	0	0.0	0	0.0	0	0.0

Incidence Calculated by No. of Tissues Scored
(1) - 0 mg base/kg/day Dose Level
(2) - 0.5 mg base/kg/day Dose Level
(3) - 2.0 mg base/kg/day Dose Level
(4) - 9.0 mg base/kg/day Dose Level

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PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

PROJECT SUMMARY

STUDY ID : SN152 STUDY NUMBER: SN152
FATE: ALL
SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		1 (1)		2 (2)		3 (3)		4 (4)	
NUMBER OF ANIMALS:		20		20		20		20	
		#	%	#	%	#	%	#	%
EPIDIDYMIS	# EX	20		0		0		20	
Oligospermia		1	5.0	0	0.0	0	0.0	0	0.0
PITUITARY GLAND	# EX	20		0		0		20	
Vacuolation		9	45.0	0	0.0	0	0.0	10	50.0
Cyst		0	0.0	0	0.0	0	0.0	4	20.0
EYE	# EX	20		0		0		19	
Mineralization, cornea		1	5.0	0	0.0	0	0.0	0	0.0
HARDERIAN GLAND	# EX	20		0		0		20	
Inflammation, chronic		2	10.0	0	0.0	0	0.0	1	5.0
Inflammation, subacute		0	0.0	0	0.0	0	0.0	1	5.0
RIB	# EX	20		0		0		20	
Granulopoiesis		0	0.0	0	0.0	0	0.0	1	5.0
STERNUM (WITH MARROW)	# EX	20		20		20		20	
Hyperplasia, bone marrow		0	0.0	5	25.0	11	55.0	19	95.0
Granulopoiesis		0	0.0	0	0.0	0	0.0	1	5.0
LYMPH NODE, MANDIBULAR	# EX	1		1		0		0	
Hyperplasia, lymphoid		1	100.0	1	100.0	0	0.0	0	0.0
Accumulation, plasma cell		1	100.0	1	100.0	0	0.0	0	0.0
MESENTERY	# EX	1		0		1		0	
Necrosis, fat		1	100.0	0	0.0	1	100.0	0	0.0

Incidence Calculated by No. of Tissues Scored
(1) - 0 mg base/kg/day Dose Level
(2) - 0.5 mg base/kg/day Dose Level
(3) - 2.0 mg base/kg/day Dose Level
(4) - 9.0 mg base/kg/day Dose Level

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PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

PROJECT SUMMARY

STUDY ID : SN152 STUDY NUMBER: SN152
FATE: ALL
SEX: FEMALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		1 (1)		2 (2)		3 (3)		4 (4)	
NUMBER OF ANIMALS:		20		20		20		20	
		#	%	#	%	#	%	#	%
BRAIN	# EX	20		0		1		20	
THYMUS	# EX	20		0		0		20	
Hemorrhage		8	40.0	0	0.0	0	0.0	9	45.0
Depletion, lymphoid		3	15.0	0	0.0	0	0.0	2	10.0
SALIVARY GLAND	# EX	20		0		0		20	
PANCREAS	# EX	20		0		0		20	
Inflammation, chronic		7	35.0	0	0.0	0	0.0	6	30.0
Atrophy, acinar		1	5.0	0	0.0	0	0.0	3	15.0
ADRENAL GLAND	# EX	20		20		20		20	
Hypertrophy, zona glomerulosa		1	5.0	1	5.0	3	15.0	0	0.0
Vacuolation, cortex		1	5.0	0	0.0	0	0.0	0	0.0
Pigmentation, zona reticularis		0	0.0	1	5.0	2	10.0	18	90.0
Congestion		7	35.0	3	15.0	7	35.0	18	90.0
Hypertrophy, zona reticularis		8	40.0	5	25.0	5	25.0	1	5.0
Cyst, blood		0	0.0	1	5.0	0	0.0	0	0.0
SPINAL CORD (THORACIC)	# EX	20		0		0		20	
DIAPHRAGM	# EX	20		0		0		20	
Inflammation, chronic		2	10.0	0	0.0	0	0.0	1	5.0
Adhesion, liver		0	0.0	0	0.0	0	0.0	1	5.0
ESOPHAGUS	# EX	20		0		0		20	
Inflammation, chronic, muscle		0	0.0	0	0.0	0	0.0	1	5.0
TRACHEA	# EX	20		0		0		20	
Inflammation, chronic		2	10.0	0	0.0	0	0.0	3	15.0

Incidence Calculated by No. of Tissues Scored
(1) - 0 mg base/kg/day Dose Level
(2) - 0.5 mg base/kg/day Dose Level
(3) - 2.0 mg base/kg/day Dose Level
(4) - 9.0 mg base/kg/day Dose Level

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PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

PROJECT SUMMARY

STUDY ID : SN152 STUDY NUMBER: SN152
FATE: ALL
SEX: FEMALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		1		2		3		4	
		(1)		(2)		(3)		(4)	
NUMBER OF ANIMALS:		20		20		20		20	
		#	%	#	%	#	%	#	%
THYROID GLAND	# EX	20		0		0		20	
Inflammation, subacute		1	5.0	0	0.0	0	0.0	0	0.0
PARATHYROID GLAND	# EX	17		0		0		20	
TONGUE	# EX	20		0		0		20	
HEART	# EX	20		0		0		20	
Cardiomyopathy		1	5.0	0	0.0	0	0.0	1	5.0
Inflammation, chronic, artery		1	5.0	0	0.0	0	0.0	0	0.0
DUODENUM	# EX	20		0		0		20	
COLON	# EX	20		0		0		20	
Metazoan parasite, lumen		0	0.0	0	0.0	0	0.0	2	10.0
STOMACH	# EX	20		0		0		20	
Dilatation, crypt glands		3	15.0	0	0.0	0	0.0	1	5.0
LIVER	# EX	20		0		1		20	
Inflammation, chronic		11	55.0	0	0.0	0	0.0	9	45.0
Focus, vacuolated cell		0	0.0	0	0.0	0	0.0	1	5.0
Hepatodiaphragmatic nodule		0	0.0	0	0.0	1	100.0	0	0.0
SPLEEN	# EX	20		20		20		20	
Erythropoiesis		10	50.0	11	55.0	14	70.0	8	40.0
Adhesion		1	5.0	0	0.0	0	0.0	0	0.0
Pigmentation		17	85.0	20	100.0	18	90.0	17	85.0
Congestion		0	0.0	1	5.0	1	5.0	17	85.0
Hyperplasia, reticuloendothelial cell		0	0.0	0	0.0	0	0.0	1	5.0
Cyst, serosa		0	0.0	1	5.0	0	0.0	0	0.0

Incidence Calculated by No. of Tissues Scored
(1) - 0 mg base/kg/day Dose Level
(2) - 0.5 mg base/kg/day Dose Level
(3) - 2.0 mg base/kg/day Dose Level
(4) - 9.0 mg base/kg/day Dose Level

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PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

PROJECT SUMMARY

STUDY ID : SN152 STUDY NUMBER: SN152
FATE: ALL
SEX: FEMALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		1		2		3		4	
		(1)		(2)		(3)		(4)	
NUMBER OF ANIMALS:		20		20		20		20	
		#	%	#	%	#	%	#	%
JEJUNUM	# EX	20		0		0		20	
LUNG	# EX	20		20		20		20	
Inflammation, chronic, interstitium		3	15.0	0	0.0	20	100.0	20	100.0
Hemorrhage		6	30.0	9	45.0	9	45.0	20	100.0
Congestion		0	0.0	0	0.0	1	5.0	0	0.0
Hyperplasia, lymphoid, peribronchial		1	5.0	0	0.0	0	0.0	0	0.0
Inflammation, chronic, serosa		1	5.0	0	0.0	0	0.0	0	0.0
Inflammation, chronic, perivascular		13	65.0	17	85.0	20	100.0	18	90.0
Accumulation, foamy macrophage		0	0.0	0	0.0	20	100.0	20	100.0
KIDNEY	# EX	20		20		20		20	
Mineralization		9	45.0	9	45.0	10	50.0	5	25.0
Inflammation, chronic		11	55.0	18	90.0	17	85.0	13	65.0
Nephropathy		6	30.0	8	40.0	11	55.0	6	30.0
Hydronephrosis		2	10.0	0	0.0	1	5.0	1	5.0
Pyelonephritis		1	5.0	0	0.0	1	5.0	0	0.0
Hyperplasia, pelvic epithelium		1	5.0	0	0.0	1	5.0	0	0.0
Pigmentation, cortex		0	0.0	0	0.0	7	35.0	20	100.0
Cyst		0	0.0	1	5.0	0	0.0	1	5.0
URINARY BLADDER	# EX	20		0		0		20	
Inflammation, chronic		2	10.0	0	0.0	0	0.0	0	0.0
Hyperplasia, epithelium		1	5.0	0	0.0	0	0.0	0	0.0
SKIN	# EX	20		0		0		20	
MAMMARY GLAND	# EX	20		2		0		20	
Cyst, milk		3	15.0	2	100.0	0	0.0	0	0.0
Inflammation, xanthogranulomatous		2	10.0	0	0.0	0	0.0	0	0.0
Hyperplasia, acinar		0	0.0	1	50.0	0	0.0	0	0.0

Incidence Calculated by No. of Tissues Scored
(1) - 0 mg base/kg/day Dose Level
(2) - 0.5 mg base/kg/day Dose Level
(3) - 2.0 mg base/kg/day Dose Level
(4) - 9.0 mg base/kg/day Dose Level

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PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

PROJECT SUMMARY

STUDY ID : SN152 STUDY NUMBER: SN152
FATE: ALL
SEX: FEMALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		1		2		3		4	
		(1)		(2)		(3)		(4)	
NUMBER OF ANIMALS:		20		20		20		20	
		#	%	#	%	#	%	#	%
ILEUM	# EX	20		0		0		20	
CECUM	# EX	20		0		0		20	
LYMPH NODE, MESENTERIC	# EX	20		0		0		20	
SKELETAL MUSCLE	# EX	20		0		0		20	
SCIATIC NERVE	# EX	20		0		0		20	
OVARY	# EX	20		1		0		20	
Necrosis, corpus luteum		1	5.0	0	0.0	0	0.0	0	0.0
Cyst		3	15.0	0	0.0	0	0.0	0	0.0
Atrophy		0	0.0	1	100.0	0	0.0	0	0.0
UTERUS	# EX	20		20		20		20	
Dilatation		3	15.0	8	40.0	6	30.0	8	40.0
PITUITARY GLAND	# EX	20		2		1		20	
EYE	# EX	19		0		0		20	
Inflammation, granulomatous, optic nerve		2	11.0	0	0.0	0	0.0	0	0.0
HARDERIAN GLAND	# EX	20		0		0		20	
Inflammation, chronic		1	5.0	0	0.0	0	0.0	4	20.0
RIB	# EX	20		0		0		20	
STERNUM (WITH MARROW)	# EX	20		20		20		20	
Hyperplasia, bone marrow		0	0.0	4	20.0	7	35.0	13	65.0
Granulopoiesis		0	0.0	0	0.0	0	0.0	1	5.0

Incidence Calculated by No. of Tissues Scored
(1) - 0 mg base/kg/day Dose Level
(2) - 0.5 mg base/kg/day Dose Level
(3) - 2.0 mg base/kg/day Dose Level
(4) - 9.0 mg base/kg/day Dose Level

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PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

PROJECT SUMMARY

STUDY ID : SN152 STUDY NUMBER: SN152
FATE: ALL
SEX: FEMALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		1		2		3		4	
		(1)		(2)		(3)		(4)	
NUMBER OF ANIMALS:		20		20		20		20	
		#	%	#	%	#	%	#	%
MESENTERY	# EX	1		0		0		0	
Necrosis, fat		1	100.0	0	0.0	0	0.0	0	0.0
BONE	# EX	0		1		0		0	
Fracture, healed		0	0.0	1	100.0	0	0.0	0	0.0

Incidence Calculated by No. of Tissues Scored
(1) - 0 mg base/kg/day Dose Level
(2) - 0.5 mg base/kg/day Dose Level
(3) - 2.0 mg base/kg/day Dose Level
(4) - 9.0 mg base/kg/day Dose Level

SECTION III

SEVERITY SUMMARY TABLE

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PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

SEVERITY SUMMARY

STUDY ID : SN152 STUDY NUMBER: SN152
FATE: ALL
SEX: MALE

GROUP:		1	2	3	4
		(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:		20	20	20	20
		# SEV	# SEV	# SEV	# SEV
BRAIN	# EX	20	0	0	20
Dilitation, ventricle		1 0.10	0 0.00	0 0.00	0 0.00
THYMUS	# EX	20	0	0	18
Hemorrhage		14 0.64	0 0.00	0 0.00	14 0.60
Depletion, lymphoid		1 0.05	0 0.00	0 0.00	3 0.33
SALIVARY GLAND	# EX	20	0	0	20
PANCREAS	# EX	20	0	0	20
Inflammation, chronic		7 0.13	0 0.00	0 0.00	7 0.20
Atrophy, acinar		1 0.06	0 0.00	0 0.00	1 0.08
ADRENAL GLAND	# EX	20	20	20	20
Hypertrophy, zona glomerulosa		2 0.09	1 0.01	1 0.03	4 0.11
Vacuolation, cortex		2 0.06	3 0.25	1 0.05	1 0.01
Pigmentation, zona reticularis		0 0.00	1 0.05	3 0.15	10 0.60
Congestion		1 0.05	1 0.05	4 0.25	2 0.10
Hypertrophy, zona reticularis		6 0.15	3 0.06	6 0.18	3 0.08
SPINAL CORD (THORACIC)	# EX	20	0	0	20
DIAPHRAGM	# EX	20	0	0	20
Inflammation, chronic		1 0.01	0 0.00	0 0.00	3 0.25
ESOPHAGUS	# EX	20	0	0	20
Inflammation, chronic, muscle		0 0.00	0 0.00	0 0.00	1 0.06
TRACHEA	# EX	20	0	0	20
Inflammation, chronic		5 0.13	0 0.00	0 0.00	3 0.05
Inflammation, subacute		0 0.00	0 0.00	0 0.00	1 0.10

Severity Calculated by No. of Tissues Scored
(1) - 0 mg base/kg/day Dose Level
(2) - 0.5 mg base/kg/day Dose Level
(3) - 2.0 mg base/kg/day Dose Level
(4) - 9.0 mg base/kg/day Dose Level

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PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

SEVERITY SUMMARY

STUDY ID : SN152 STUDY NUMBER: SN152
FATE: ALL
SEX: MALE

GROUP:		1 (1)	2 (2)	3 (3)	4 (4)
NUMBER OF ANIMALS:		20	20	20	20
		# SEV	# SEV	# SEV	# SEV
THYROID GLAND	# EX	20	0	0	20
Atrophy, follicle		0 0.00	0 0.00	0 0.00	1 0.10
PARATHYROID GLAND	# EX	18	0	0	17
TONGUE	# EX	20	0	0	20
HEART	# EX	20	0	0	20
Cardiomyopathy		9 0.35	0 0.00	0 0.00	5 0.14
Inflammation, chronic, serosa		0 0.00	0 0.00	0 0.00	2 0.21
Thrombosis, chronic		0 0.00	0 0.00	0 0.00	1 0.11
DUODENUM	# EX	20	0	0	19
COLON	# EX	20	0	0	19
STOMACH	# EX	20	0	0	19
Dilatation, crypt glands		2 0.05	0 0.00	0 0.00	1 0.03
LIVER	# EX	20	20	20	20
Inflammation, chronic		10 0.23	12 0.29	10 0.20	7 0.20
Necrosis		1 0.08	0 0.00	1 0.08	0 0.00
Focus, vacuolated cell		1 0.01	0 0.00	2 0.13	3 0.11
Necrosis, coagulation		0 0.00	0 0.00	0 0.00	1 0.08
Apoptosis, centrilobular		0 0.00	0 0.00	0 0.00	11 0.70
Pigmentation, centrilobular		0 0.00	0 0.00	0 0.00	11 0.60
Fatty change, centrilobular		2 0.10	3 0.10	6 0.30	10 0.50
Congestion, centrilobular		0 0.00	0 0.00	2 0.10	2 0.13
Inflammation, subacute, centrilobular		0 0.00	0 0.00	0 0.00	1 0.03
Focus, basophilic cell		0 0.00	0 0.00	0 0.00	1 0.03
Hyperplasia, bile duct		0 0.00	0 0.00	0 0.00	1 0.03

Severity Calculated by No. of Tissues Scored
(1) - 0 mg base/kg/day Dose Level
(2) - 0.5 mg base/kg/day Dose Level
(3) - 2.0 mg base/kg/day Dose Level
(4) - 9.0 mg base/kg/day Dose Level

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TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

SEVERITY SUMMARY

STUDY ID : SN152 STUDY NUMBER: SN152
FATE: ALL
SEX: MALE

GROUP:		1	2	3	4
		(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:		20	20	20	20
		# SEV	# SEV	# SEV	# SEV
SPLEEN	# EX	20	20	20	20
Erythropoiesis		2 0.10	4 0.20	8 0.50	8 0.55
Pigmentation		1 0.10	4 0.20	8 0.45	11 0.80
Congestion		0 0.00	0 0.00	0 0.00	18 1.90
Hyperplasia, reticuloendothelial cell		0 0.00	0 0.00	0 0.00	4 0.30
Cyst, serosa		0 0.00	1 0.01	0 0.00	0 0.00
JEJUNUM	# EX	20	0	0	19
LUNG	# EX	20	20	20	20
Inflammation, chronic, interstitium		2 0.03	3 0.06	20 1.20	20 2.40
Hemorrhage		2 0.09	1 0.06	4 0.30	20 1.50
Inflammation, granulomatous		1 0.01	2 0.14	0 0.00	3 0.11
Congestion		1 0.03	1 0.03	1 0.08	0 0.00
Hyperplasia, lymphoid, peribronchial		0 0.00	0 0.00	2 0.10	0 0.00
Inflammation, acute		0 0.00	0 0.00	0 0.00	2 0.23
Inflammation, chronic, serosa		1 0.03	0 0.00	0 0.00	1 0.10
Inflammation, granulomatous, serosa		0 0.00	1 0.08	0 0.00	0 0.00
Inflammation, chronic, perivascular		13 0.40	18 0.55	20 1.05	17 0.78
Accumulation, foamy macrophage		0 0.00	2 0.05	20 1.80	20 2.65
Edema		0 0.00	0 0.00	0 0.00	1 0.13
KIDNEY	# EX	20	20	20	19
Inflammation, chronic		16 0.54	17 0.45	19 0.46	14 0.36
Nephropathy		14 0.43	16 0.56	15 0.45	9 0.26
Hydronephrosis		0 0.00	0 0.00	0 0.00	1 0.05
Pigmentation, cortex		0 0.00	0 0.00	4 0.20	16 1.11
Hemorrhage, pelvis		0 0.00	1 0.06	0 0.00	0 0.00
Cyst		0 0.00	0 0.00	0 0.00	1 0.01
URINARY BLADDER	# EX	20	3	0	20
Inflammation, chronic		1 0.01	0 0.00	0 0.00	0 0.00
Inflammation, chronic, urethra		1 0.06	0 0.00	0 0.00	0 0.00

Severity Calculated by No. of Tissues Scored
(1) - 0 mg base/kg/day Dose Level
(2) - 0.5 mg base/kg/day Dose Level
(3) - 2.0 mg base/kg/day Dose Level
(4) - 9.0 mg base/kg/day Dose Level

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PATHOLOGY ASSOCIATES INTERNATIONAL
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TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

SEVERITY SUMMARY

STUDY ID : SN152 STUDY NUMBER: SN152
FATE: ALL
SEX: MALE

GROUP:		1	2	3	4
		(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:		20	20	20	20
		# SEV	# SEV	# SEV	# SEV
PROSTATE	# EX	20	0	0	20
Inflammation, chronic		1 0.03	0 0.00	0 0.00	0 0.00
SKIN	# EX	20	0	0	20
MAMMARY GLAND	# EX	20	0	0	18
Hyperplasia, acinar		1 0.11	0 0.00	0 0.00	0 0.00
Metaplasia, squamous		1 0.08	0 0.00	0 0.00	0 0.00
Inflammation, chronic		1 0.03	0 0.00	0 0.00	0 0.00
ILEUM	# EX	20	0	0	19
CECUM	# EX	20	0	0	19
LYMPH NODE, MESENTERIC	# EX	20	0	0	19
Hemorrhage		0 0.00	0 0.00	0 0.00	1 0.11
Inflammation, granulomatous		0 0.00	0 0.00	0 0.00	1 0.13
SKELETAL MUSCLE	# EX	20	0	0	20
SCIATIC NERVE	# EX	20	0	0	20
TESTES	# EX	20	0	0	20
Arrested spermatogenesis		1 0.20	0 0.00	0 0.00	0 0.00
Degeneration		1 0.08	0 0.00	0 0.00	1 0.13
EPIDIDYMIS	# EX	20	0	0	20
Inflammation, chronic		1 0.01	0 0.00	0 0.00	0 0.00
Oligospermia		1 0.20	0 0.00	0 0.00	0 0.00
PITUITARY GLAND	# EX	20	0	0	20
Vacuolation		9 0.35	0 0.00	0 0.00	10 0.55
Cyst		0 0.00	0 0.00	0 0.00	4 0.16

Severity Calculated by No. of Tissues Scored
(1) - 0 mg base/kg/day Dose Level
(2) - 0.5 mg base/kg/day Dose Level
(3) - 2.0 mg base/kg/day Dose Level
(4) - 9.0 mg base/kg/day Dose Level

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TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

SEVERITY SUMMARY

STUDY ID : SN152 STUDY NUMBER: SN152
FATE: ALL
SEX: MALE

GROUP:		1 (1)	2 (2)	3 (3)	4 (4)
NUMBER OF ANIMALS:		20	20	20	20
		# SEV	# SEV	# SEV	# SEV
EYE	# EX	20	0	0	19
Mineralization, cornea		1 0.06	0 0.00	0 0.00	0 0.00
HARDERIAN GLAND	# EX	20	0	0	20
Inflammation, chronic		2 0.08	0 0.00	0 0.00	1 0.01
Inflammation, subacute		0 0.00	0 0.00	0 0.00	1 0.14
RIB	# EX	20	0	0	20
Granulopoiesis		0 0.00	0 0.00	0 0.00	1 0.05
STERNUM (WITH MARROW)	# EX	20	20	20	20
Hyperplasia, bone marrow		0 0.00	5 0.30	11 0.60	19 1.25
Granulopoiesis		0 0.00	0 0.00	0 0.00	1 0.10
LYMPH NODE, MANDIBULAR	# EX	1	1	0	0
Hyperplasia, lymphoid		1 2.00	1 2.00	0 0.00	0 0.00
Accumulation, plasma cell		1 2.00	1 3.00	0 0.00	0 0.00
MESENTERY	# EX	1	0	1	0
Necrosis, fat		1 2.25	0 0.00	1 2.25	0 0.00

Severity Calculated by No. of Tissues Scored
(1) - 0 mg base/kg/day Dose Level
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(3) - 2.0 mg base/kg/day Dose Level
(4) - 9.0 mg base/kg/day Dose Level

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SEVERITY SUMMARY

STUDY ID : SN152 STUDY NUMBER: SN152
FATE: ALL
SEX: FEMALE

GROUP:		1 (1)	2 (2)	3 (3)	4 (4)
NUMBER OF ANIMALS:		20	20	20	20
		# SEV	# SEV	# SEV	# SEV
BRAIN	# EX	20	0	1	20
THYMUS	# EX	20	0	0	20
Hemorrhage		8 0.23	0 0.00	0 0.00	9 0.38
Depletion, lymphoid		3 0.21	0 0.00	0 0.00	2 0.20
SALIVARY GLAND	# EX	20	0	0	20
PANCREAS	# EX	20	0	0	20
Inflammation, chronic		7 0.09	0 0.00	0 0.00	6 0.11
Atrophy, acinar		1 0.01	0 0.00	0 0.00	3 0.06
ADRENAL GLAND	# EX	20	20	20	20
Hypertrophy, zona glomerulosa		1 0.03	1 0.01	3 0.08	0 0.00
Vacuolation, cortex		1 0.08	0 0.00	0 0.00	0 0.00
Pigmentation, zona reticularis		0 0.00	1 0.05	2 0.10	18 1.55
Congestion		7 0.35	3 0.15	7 0.40	18 1.50
Hypertrophy, zona reticularis		8 0.24	5 0.11	5 0.14	1 0.01
Cyst, blood		0 0.00	1 0.06	0 0.00	0 0.00
SPINAL CORD (THORACIC)	# EX	20	0	0	20
DIAPHRAGM	# EX	20	0	0	20
Inflammation, chronic		2 0.04	0 0.00	0 0.00	1 0.01
Adhesion, liver		0 0.00	0 0.00	0 0.00	1 0.06
ESOPHAGUS	# EX	20	0	0	20
Inflammation, chronic, muscle		0 0.00	0 0.00	0 0.00	1 0.01
TRACHEA	# EX	20	0	0	20
Inflammation, chronic		2 0.03	0 0.00	0 0.00	3 0.04

Severity Calculated by No. of Tissues Scored
(1) - 0 mg base/kg/day Dose Level
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(4) - 9.0 mg base/kg/day Dose Level

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SEVERITY SUMMARY

STUDY ID : SN152 STUDY NUMBER: SN152
FATE: ALL
SEX: FEMALE

GROUP:		1 (1)	2 (2)	3 (3)	4 (4)
NUMBER OF ANIMALS:		20	20	20	20
		# SEV	# SEV	# SEV	# SEV
THYROID GLAND	# EX	20	0	0	20
Inflammation, subacute		1 0.06	0 0.00	0 0.00	0 0.00
PARATHYROID GLAND	# EX	17	0	0	20
TONGUE	# EX	20	0	0	20
HEART	# EX	20	0	0	20
Cardiomyopathy		1 0.01	0 0.00	0 0.00	1 0.05
Inflammation, chronic, artery		1 0.08	0 0.00	0 0.00	0 0.00
DUODENUM	# EX	20	0	0	20
COLON	# EX	20	0	0	20
STOMACH	# EX	20	0	0	20
Dilatation, crypt glands		3 0.08	0 0.00	0 0.00	1 0.03
LIVER	# EX	20	0	1	20
Inflammation, chronic		11 0.21	0 0.00	0 0.00	9 0.20
Focus, vacuolated cell		0 0.00	0 0.00	0 0.00	1 0.01
SPLEEN	# EX	20	20	20	20
Erythropoiesis		10 0.70	11 0.90	14 1.25	8 0.60
Adhesion		1 0.06	0 0.00	0 0.00	0 0.00
Pigmentation		17 1.15	20 1.90	18 1.80	17 1.20
Congestion		0 0.00	1 0.05	1 0.05	17 1.45
Hyperplasia, reticuloendothelial cell		0 0.00	0 0.00	0 0.00	1 0.10
Cyst, serosa		0 0.00	1 0.08	0 0.00	0 0.00
JEJUNUM	# EX	20	0	0	20

Severity Calculated by No. of Tissues Scored
(1) - 0 mg base/kg/day Dose Level
(2) - 0.5 mg base/kg/day Dose Level
(3) - 2.0 mg base/kg/day Dose Level
(4) - 9.0 mg base/kg/day Dose Level

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FATE: ALL
SEX: FEMALE

GROUP:		1 (1)	2 (2)	3 (3)	4 (4)
NUMBER OF ANIMALS:		20	20	20	20
		# SEV	# SEV	# SEV	# SEV
LUNG	# EX	20	20	20	20
Inflammation, chronic, interstitium		3 0.05	0 0.00	20 1.40	20 1.90
Hemorrhage		6 0.14	9 0.30	9 0.25	20 2.10
Congestion		0 0.00	0 0.00	1 0.05	0 0.00
Hyperplasia, lymphoid, peribronchial		1 0.15	0 0.00	0 0.00	0 0.00
Inflammation, chronic, serosa		1 0.03	0 0.00	0 0.00	0 0.00
Inflammation, chronic, perivascular		13 0.29	17 0.41	20 0.64	18 0.55
Accumulation, foamy macrophage		0 0.00	0 0.00	20 1.95	20 1.85
KIDNEY	# EX	20	20	20	20
Mineralization		9 0.16	9 0.20	10 0.29	5 0.14
Inflammation, chronic		11 0.20	18 0.44	17 0.40	13 0.29
Nephropathy		6 0.16	8 0.21	11 0.28	6 0.18
Hydronephrosis		2 0.30	0 0.00	1 0.15	1 0.10
Pyelonephritis		1 0.15	0 0.00	1 0.05	0 0.00
Hyperplasia, pelvic epithelium		1 0.14	0 0.00	1 0.09	0 0.00
Pigmentation, cortex		0 0.00	0 0.00	7 0.35	20 1.60
Cyst		0 0.00	1 0.08	0 0.00	1 0.06
URINARY BLADDER	# EX	20	0	0	20
Inflammation, chronic		2 0.03	0 0.00	0 0.00	0 0.00
Hyperplasia, epithelium		1 0.09	0 0.00	0 0.00	0 0.00
SKIN	# EX	20	0	0	20
MAMMARY GLAND	# EX	20	2	0	20
Cyst, milk		3 0.41	2 3.00	0 0.00	0 0.00
Inflammation, xanthogranulomatous		2 0.09	0 0.00	0 0.00	0 0.00
Hyperplasia, acinar		0 0.00	1 0.63	0 0.00	0 0.00
ILEUM	# EX	20	0	0	20

Severity Calculated by No. of Tissues Scored
(1) - 0 mg base/kg/day Dose Level
(2) - 0.5 mg base/kg/day Dose Level
(3) - 2.0 mg base/kg/day Dose Level
(4) - 9.0 mg base/kg/day Dose Level

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TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

SEVERITY SUMMARY

STUDY ID : SN152 STUDY NUMBER: SN152
FATE: ALL
SEX: FEMALE

GROUP:		1	2	3	4
		(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:		20	20	20	20
		# SEV	# SEV	# SEV	# SEV
CECUM	# EX	20	0	0	20
LYMPH NODE, MESENTERIC	# EX	20	0	0	20
SKELETAL MUSCLE	# EX	20	0	0	20
SCIATIC NERVE	# EX	20	0	0	20
OVARY	# EX	20	1	0	20
Necrosis, corpus luteum		1 0.08	0 0.00	0 0.00	0 0.00
Cyst		3 0.25	0 0.00	0 0.00	0 0.00
Atrophy		0 0.00	1 4.00	0 0.00	0 0.00
UTERUS	# EX	20	20	20	20
Dilatation		3 0.20	8 0.70	6 0.55	8 0.85
PITUITARY GLAND	# EX	20	2	1	20
EYE	# EX	19	0	0	20
Inflammation, granulomatous, optic nerve		2 0.18	0 0.00	0 0.00	0 0.00
HARDERIAN GLAND	# EX	20	0	0	20
Inflammation, chronic		1 0.01	0 0.00	0 0.00	4 0.18
RIB	# EX	20	0	0	20
STERNUM (WITH MARROW)	# EX	20	20	20	20
Hyperplasia, bone marrow		0 0.00	4 0.20	7 0.40	13 0.90
Granulopoiesis		0 0.00	0 0.00	0 0.00	1 0.05
MESENTERY	# EX	1	0	0	0
Necrosis, fat		1 2.25	0 0.00	0 0.00	0 0.00

Severity Calculated by No. of Tissues Scored
(1) - 0 mg base/kg/day Dose Level
(2) - 0.5 mg base/kg/day Dose Level
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(4) - 9.0 mg base/kg/day Dose Level

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SEVERITY SUMMARY

STUDY ID : SN152 STUDY NUMBER: SN152
FATE: ALL
SEX: FEMALE

GROUP:		1	2	3	4
		(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:		20	20	20	20
		# SEV	# SEV	# SEV	# SEV
BONE	# EX	0	1	0	0

Severity Calculated by No. of Tissues Scored
(1) - 0 mg base/kg/day Dose Level
(2) - 0.5 mg base/kg/day Dose Level
(3) - 2.0 mg base/kg/day Dose Level
(4) - 9.0 mg base/kg/day Dose Level

SECTION IV

TABULATED ANIMAL DATA

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TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152
FATE: ALL

STUDY NUMBER: SN152
GROUP: 1: 0 mg base/kg/day Dose Level
SEX: MALE

ANIMAL ID:	0401	0402	0403	0404	0405	0406	0407	0408	0409	0410
BRAIN	N	N	N	N	N	N	N	N	N	N
THYMUS				N					N	
Hemorrhage	<2>	(1)	(1)	-	(1)	<2>	(1)	<2>	-	<1>
SALIVARY GLAND	N	N	N	N	N	N	N	N	N	N
PANCREAS		N	N	N	N		N	N		N
Inflammation, chronic	<1>	-	-	-	-	(1)	-	-	<1>	-
ADRENAL GLAND	N	N	N	N	N		N			
Hypertrophy, zona glomerulosa	-	-	-	-	-	-	-	(2)	-	-
Vacuolation, cortex	-	-	-	-	-	-	-	-	-	(1)
Hypertrophy, zona reticularis	-	-	-	-	-	<1>	-	<1>	<1>	-
SPINAL CORD (THORACIC)	N	N	N	N	N	N	N	N	N	N
DIAPHRAGM	N	N	N	N	N	N	N	N		N
Inflammation, chronic	-	-	-	-	-	-	-	-	(1)	-
ESOPHAGUS	N	N	N	N	N	N	N	N	N	N
TRACHEA	N	N		N	N	N			N	N
Inflammation, chronic	-	-	(1)	-	-	-	<2>	(1)	-	-
THYROID GLAND	N	N	N	N	N	N	N	N	N	N
PARATHYROID GLAND	N	N	N	N	N	N	N	U	N	N
TONGUE	N	N	N	N	N	N	N	N	N	N
HEART	N	N	N	N	N					
Cardiomyopathy	-	-	-	-	-	<1>	<2>	<2>	(1)	<2>

See Reports Code Table for Symbol Definitions

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TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 1: 0 mg base/kg/day Dose Level
SEX: MALE

ANIMAL ID:	0401	0402	0403	0404	0405	0406	0407	0408	0409	0410
DUODENUM	N	N	N	N	N	N	N	N	N	N
COLON	N	N	N	N	N	N	N	N	N	N
STOMACH	N	N	N	N	N	N	N	N	N	N
LIVER								N	N	N
Inflammation, chronic	<1>	-	<1>	<1>	-	<1>	-	-	-	-
Necrosis	-	-	-	-	<2>	-	-	-	-	-
Focus, vacuolated cell	-	-	-	-	-	-	(1)	-	-	-
Hepatodiaphragmatic nodule	-	-	-	-	-	-	P	-	-	-
Fatty change, centrilobular	1	1	-	-	-	-	-	-	-	-
SPLEEN	N	N	N	N	N	N	N	N		
Erythropoiesis	-	-	-	-	-	-	-	-	1	1
JEJUNUM	N	N	N	N	N	N	N	N	N	N
LUNG						N	N	N		N
Inflammation, chronic, interstitium	-	-	-	-	-	-	-	-	(1)	-
Inflammation, granulomatous	-	-	-	(1)	-	-	-	-	-	-
Inflammation, chronic, serosa	-	-	-	<1>	-	-	-	-	-	-
Inflammation, chronic, perivascular	<1>	<1>	<1>	-	(1)	-	-	-	(1)	-
KIDNEY										
Inflammation, chronic	-	<1>	<2>	<1>	<2>	<1>	(1)	<1>	<2>	-
Nephropathy	(1)	<1>	<2>	-	<1>	-	<1>	<1>	<1>	(1)
URINARY BLADDER	N	N	N	N	N		N	N	N	N
Inflammation, chronic	-	-	-	-	-	(1)	-	-	-	-
PROSTATE	N	N	N	N		N	N	N	N	N
Inflammation, chronic	-	-	-	-	<1>	-	-	-	-	-
SKIN	N	N	N	N	N	N	N	N	N	N

See Reports Code Table for Symbol Definitions

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PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152
FATE: ALL

STUDY NUMBER: SN152
GROUP: 1: 0 mg base/kg/day Dose Level
SEX: MALE

ANIMAL ID:	0401	0402	0403	0404	0405	0406	0407	0408	0409	0410
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N
ILEUM	N	N	N	N	N	N	N	N	N	N
CECUM	N	N	N	N	N	N	N	N	N	N
LYMPH NODE, MESENTERIC	N	N	N	N	N	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
SCIATIC NERVE	N	N	N	N	N	N	N	N	N	N
TESTES	N	N	N	N	N	N	N	N	N	N
EPIDIDYMIS	N		N	N	N	N	N	N	N	N
Inflammation, chronic	-	(1)	-	-	-	-	-	-	-	-
PITUITARY GLAND		N	N	N	N			N		
Vacuolation	<1>	-	-	-	-	<1>	<1>	-	1	<1>
EYE	N	N	N	N	N	N		N	N	N
Mineralization, cornea	-	-	-	-	-	-	(2)	-	-	-
HARDERIAN GLAND	N	N	N	N	N		N		N	N
Inflammation, chronic	-	-	-	-	-	(1)	-	(2)	-	-
RIB	N	N	N	N	N	N	N	N	N	N
STERNUM (WITH MARROW)	N	N	N	N	N	N	N	N	N	N
LYMPH NODE, MANDIBULAR										
Hyperplasia, lymphoid	-	2	-	-	-	-	-	-	-	-
Accumulation, plasma cell	-	2	-	-	-	-	-	-	-	-
MESENTERY										
Necrosis, fat	-	-	-	-	-	-	-	-	-	(3)

See Reports Code Table for Symbol Definitions

LABCAT HP4.11

24-JUN-1996

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TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 1: 0 mg base/kg/day Dose Level
SEX: MALE

ANIMAL ID:	0411	0412	0413	0414	0415	0416	0417	0418	0419	0420
BRAIN	N	N	N	N	N	N	N	N		N
Dilitation, ventricle	-	-	-	-	-	-	-	-	2	-
THYMUS			N			N			N	N
Hemorrhage	<2>	<1>	-	<1>	<3>	-	<2>	(1)	-	-
Depletion, lymphoid	-	-	-	-	-	-	-	1	-	-
SALIVARY GLAND	N	N	N	N	N	N	N	N	N	N
PANCREAS			N			N	N	N	N	N
Inflammation, chronic	(1)	(1)	-	<1>	(1)	-	-	-	-	-
Atrophy, acinar	-	-	-	-	(2)	-	-	-	-	-
ADRENAL GLAND					N	N	N	N	N	
Hypertrophy, zona glomerulosa	<1>	-	-	-	-	-	-	-	-	-
Vacuolation, cortex	-	-	-	-	-	-	-	-	-	1
Congestion	-	-	-	1	-	-	-	-	-	-
Hypertrophy, zona reticularis	-	<1>	<1>	-	-	-	-	-	-	<1>
SPINAL CORD (THORACIC)	N	N	N	N	N	N	N	N	N	N
DIAPHRAGM	N	N	N	N	N	N	N	N	N	N
ESOPHAGUS	N	N	N	N	N	N	N	N	N	N
TRACHEA	N		N		N	N	N	N	N	N
Inflammation, chronic	-	(1)	-	(1)	-	-	-	-	-	-
THYROID GLAND	N	N	N	N	N	N	N	N	N	N
PARATHYROID GLAND	N	N	N	N	N	U	N	N	N	N
TONGUE	N	N	N	N	N	N	N	N	N	N
HEART	N		N	N	N			N	N	
Cardiomyopathy	-	(1)	-	-	-	<1>	<1>	-	-	<1>

See Reports Code Table for Symbol Definitions

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 1: 0 mg base/kg/day Dose Level
SEX: MALE

ANIMAL ID:	0411	0412	0413	0414	0415	0416	0417	0418	0419	0420
DUODENUM	N	N	N	N	N	N	N	N	N	N
COLON	N	N	N	N	N	N	N	N	N	N
STOMACH	N	N	N		N		N	N	N	N
Dilatation, crypt glands	-	-	-	<1>	-	<1>	-	-	-	-
LIVER			N		N	N				N
Inflammation, chronic	(1)	(1)	-	<1>	-	-	<1>	<1>	<1>	-
SPLEEN	N	N		N	N	N	N	N	N	N
Pigmentation	-	-	2	-	-	-	-	-	-	-
JEJUNUM	N	N	N	N	N	N	N	N	N	N
LUNG						N				
Inflammation, chronic, interstitium	-	-	-	-	(1)	-	-	-	-	-
Hemorrhage	-	-	-	<1>	-	-	-	(2)	-	-
Congestion	-	-	-	-	-	-	-	-	<1>	-
Inflammation, chronic, perivascular	<2>	<1>	<1>	<2>	<1>	-	<1>	-	<1>	<1>
KIDNEY							N			
Inflammation, chronic	<1>	<1>	<1>	<1>	<1>	<1>	-	-	<1>	<1>
Nephropathy	<1>	<1>	-	<2>	-	<1>	-	<1>	-	<1>
URINARY BLADDER	N	N	N	N	N		N	N	N	N
Inflammation, chronic, urethra	-	-	-	-	-	(2)	-	-	-	-
PROSTATE	N	N	N	N	N	N	N	N	N	N
SKIN	N	N	N	N	N	N	N	N	N	N
MAMMARY GLAND	N	N	N	N		N	N	N	N	N
Hyperplasia, acinar	-	-	-	-	(3)	-	-	-	-	-
Metaplasia, squamous	-	-	-	-	<2>	-	-	-	-	-
Inflammation, chronic	-	-	-	-	<1>	-	-	-	-	-

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 1: 0 mg base/kg/day Dose Level
SEX: MALE

ANIMAL ID:	0411	0412	0413	0414	0415	0416	0417	0418	0419	0420
ILEUM	N	N	N	N	N	N	N	N	N	N
CECUM	N	N	N	N	N	N	N	N	N	N
LYMPH NODE, MESENTERIC	N	N	N	N	N	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
SCIATIC NERVE	N	N	N	N	N	N	N	N	N	N
TESTES	N	N	N	N	N	N			N	N
Arrested spermatogenesis	-	-	-	-	-	-	4L	-	-	-
Degeneration	-	-	-	-	-	-	-	<2>	-	-
EPIDIDYMIS	N	N	N	N	N	N		N	N	N
Oligospermia	-	-	-	-	-	-	4L	-	-	-
PITUITARY GLAND	N	N			N		N	N	N	
Vacuolation	-	-	<2>	<1>	-	<1>	-	-	-	<2>
EYE	N	N	N	N	N	N	N	N	N	N
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N
RIB	N	N	N	N	N	N	N	N	N	N
STERNUM (WITH MARROW)	N	N	N	N	N	N	N	N	N	N

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 2: 0.5 mg base/kg/day Dose Level
SEX: MALE

ANIMAL ID:	0451	0452	0453	0454	0455	0456	0457	0458	0459	0460
ADRENAL GLAND	N		N		N	N	N	N		N
Vacuolation, cortex	-	-	-	2	-	-	-	-	-	-
Hypertrophy, zona reticularis	-	<1>	-	-	-	-	-	-	<1>	-
LIVER	N					N	N		N	
Inflammation, chronic	-	<1>	(1)	<1>	<1>	-	-	<1>	-	<1>
Fatty change, centrilobular	-	-	-	<1>	-	-	-	<1>	-	-
SPLEEN			N		N			N	N	N
Erythropoiesis	1	1	-	1	-	-	1	-	-	-
Pigmentation	-	1	-	1	-	1	-	-	-	-
LUNG										
Inflammation, chronic, interstitium	-	-	-	-	<1>	-	-	-	-	-
Hemorrhage	-	-	(2)	-	-	-	-	-	-	-
Inflammation, granulomatous	-	-	<3>	-	-	-	-	-	-	-
Inflammation, granulomatous, serosa	<2>	-	-	-	-	-	-	-	-	-
Inflammation, chronic, perivascular	<1>	<1>	<1>	<1>	<1>	<2>	<1>	<1>	<1>	<2>
Accumulation, foamy macrophage	-	-	-	-	-	[1]	-	-	-	(1)
KIDNEY									N	
Inflammation, chronic	<1>	<1>	<1>	<1>	(1)	<1>	<1>	<1>	-	<1>
Nephropathy	(1)	-	<1>	<1>	<1>	<1>	<2>	<2>	-	<1>
Hemorrhage, pelvis	-	-	-	-	-	-	(2)	-	-	-
URINARY BLADDER										
Semen plug	-	-	-	-	-	-	P	-	P	-
STERNUM (WITH MARROW)	N	N	N			N	N	N	N	
Hyperplasia, bone marrow	-	-	-	1	1	-	-	-	-	2
LYMPH NODE, MANDIBULAR										
Hyperplasia, lymphoid	-	2	-	-	-	-	-	-	-	-
Accumulation, plasma cell	-	3	-	-	-	-	-	-	-	-

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TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 2: 0.5 mg base/kg/day Dose Level
SEX: MALE

ANIMAL ID:	0461	0462	0463	0464	0465	0466	0467	0468	0469	0470
ADRENAL GLAND	N	N	N				N	N	N	
Hypertrophy, zona glomerulosa	-	-	-	-	-	(1)	-	-	-	-
Vacuolation, cortex	-	-	-	-	2	-	-	-	-	1
Pigmentation, zona reticularis	-	-	-	1	-	-	-	-	-	-
Congestion	-	-	-	1	-	-	-	-	-	-
Hypertrophy, zona reticularis	-	-	-	-	(1)	-	-	-	-	-
LIVER	N		N		N			N		
Inflammation, chronic	-	<1>	-	<1>	-	<1>	<1>	-	<1>	<1>
Fatty change, centrilobular	-	-	-	-	-	-	-	-	1	-
SPLEEN	N	N		N	N		N	N	N	N
Pigmentation	-	-	-	-	-	1	-	-	-	-
Cyst, serosa	-	-	(1)	-	-	-	-	-	-	-
LUNG		N				N				
Inflammation, chronic, interstitium	-	-	-	-	-	-	<1>	-	(1)	-
Inflammation, granulomatous	-	-	-	-	-	-	(1)	-	-	-
Congestion	<1>	-	-	-	-	-	-	-	-	-
Inflammation, chronic, perivascular	<1>	-	<1>	<1>	<1>	-	<1>	<1>	<1>	<1>
KIDNEY					N					
Inflammation, chronic	<1>	<2>	-	<1>	-	<1>	(1)	<1>	<1>	<1>
Nephropathy	<2>	<2>	<1>	<1>	-	(1)	(1)	-	<1>	<1>
URINARY BLADDER										
Semen plug	-	-	-	-	-	P	-	-	-	-
STERNUM (WITH MARROW)		N		N	N	N	N	N	N	N
Hyperplasia, bone marrow	1	-	1	-	-	-	-	-	-	-

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TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 3: 2.0 mg base/kg/day Dose Level
SEX: MALE

ANIMAL ID:	0501	0502	0503	0504	0505	0506	0507	0508	0509	0510
ADRENAL GLAND	N	N	N	N		N		N	N	
Hypertrophy, zona glomerulosa	-	-	-	-	-	-	-	-	-	<1>
Vacuolation, cortex	-	-	-	-	1	-	-	-	-	-
Hypertrophy, zona reticularis	-	-	-	-	-	-	<1>	-	-	-
LIVER		N						N	N	
Inflammation, chronic	-	-	<1>	-	<1>	<1>	<1>	-	-	-
Focus, vacuolated cell	(2)	-	-	-	-	(2)	-	-	-	-
Hepatodiaphragmatic nodule	-	-	-	-	-	-	-	-	-	P
Fatty change, centrilobular	-	-	-	1	-	-	1	-	-	1
SPLEEN										
Erythropoiesis	1	1	1	2	-	1	-	1	1	2
Pigmentation	-	-	-	-	1	1	1	1	1	2
LUNG										
Inflammation, chronic, interstitium	<1>	<1>	<2>	<1>	<2>	<2>	<3>	<2>	<1>	<2>
Hemorrhage	-	-	-	-	-	<2>	-	<2>	-	-
Congestion	-	-	-	-	-	-	<2>	-	-	-
Inflammation, chronic, perivascular	<1>	<1>	<2>	<1>	<2>	<2>	<2>	<2>	<2>	<1>
Accumulation, foamy macrophage	<3>	<2>	<2>	<2>	<2>	<2>	<3>	<3>	<2>	<3>
KIDNEY										
Inflammation, chronic	<1>	<1>	<1>	<1>	(1)	<1>	<1>	<1>	<1>	<1>
Nephropathy	(1)	<1>	(1)	<1>	-	<1>	<1>	-	<1>	<2>
Pigmentation, cortex	1	-	1	1	-	-	-	-	-	-
STERNUM (WITH MARROW)	N			N		N				N
Hyperplasia, bone marrow	-	1	1	-	1	-	1	1	1	-
MESENTERY										
Necrosis, fat	(3)	-	-	-	-	-	-	-	-	-

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 3: 2.0 mg base/kg/day Dose Level
SEX: MALE

ANIMAL ID:	0511	0512	0513	0514	0515	0516	0517	0518	0519	0520
ADRENAL GLAND				N				N	N	N
Pigmentation, zona reticularis	-	1	-	-	1	1	-	-	-	-
Congestion	1	2	-	-	1	1	-	-	-	-
Hypertrophy, zona reticularis	1	<1>	<1>	-	-	<1>	<1>	-	-	-
LIVER			N	N						
Inflammation, chronic	-	<1>	-	-	-	(1)	(1)	(1)	<1>	(1)
Necrosis	-	<2>	-	-	-	-	-	-	-	-
Fatty change, centrilobular	-	-	-	-	1	-	1	-	1	-
Congestion, centrilobular	1	-	-	-	1	-	-	-	-	-
SPLEEN		N	N	N	N	N	N		N	N
Pigmentation	1	-	-	-	-	-	-	1	-	-
LUNG										
Inflammation, chronic, interstitium	<1>	<2>	<1>	<2>	<3>	<3>	<1>	<1>	<1>	<2>
Hemorrhage	-	-	-	<2>	<2>	-	-	-	-	-
Hyperplasia, lymphoid, peribronchial	-	-	1	-	-	1	-	-	-	-
Inflammation, chronic, perivascular	<2>	<1>	<1>	<2>	<2>	<2>	<2>	<1>	<1>	<1>
Accumulation, foamy macrophage	<2>	<2>	<1>	<3>	<3>	<3>	<2>	<2>	<2>	<2>
KIDNEY	N									
Inflammation, chronic	-	<1>	<1>	<1>	<1>	<1>	<1>	<1>	<1>	<1>
Nephropathy	-	<1>	<1>	-	<1>	<2>	<1>	-	<1>	<1>
Pigmentation, cortex	-	-	-	1	-	-	-	-	-	-
STERNUM (WITH MARROW)	N	N						N	N	N
Hyperplasia, bone marrow	-	-	1	1	1	1	2	-	-	-

See Reports Code Table for Symbol Definitions

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 4: 9.0 mg base/kg/day Dose Level
SEX: MALE

ANIMAL ID:	0551	0552	0553	0554	0555	0556	0557	0558	0559	0560
BRAIN	N	N	N	N	N	N	N	N	N	N
THYMUS								U		
Hemorrhage	<1>	<1>	-	<1>	<1>	<1>	<1>	-	<1>	<2>
Depletion, lymphoid	-	-	2	2	-	-	-	-	-	-
SALIVARY GLAND	N	N	N	N	N	N	N	N	N	N
PANCREAS	N	N	N		N	N		N	N	N
Inflammation, chronic	-	-	-	<1>	-	-	(3)	-	-	-
Atrophy, acinar	-	-	-	<2>	-	-	-	-	-	-
ADRENAL GLAND				N	N	N				N
Hypertrophy, zona glomerulosa	(1)	-	<1>	-	-	-	-	-	-	-
Pigmentation, zona reticularis	-	2	1	-	-	-	1	-	1	-
Hypertrophy, zona reticularis	-	<1>	-	-	-	-	-	<1>	-	-
SPINAL CORD (THORACIC)	N	N	N	N	N	N	N	N	N	N
DIAPHRAGM	N	N	N	N	N	N			N	N
Inflammation, chronic	-	-	-	-	-	-	(1)	2	-	-
ESOPHAGUS	N	N	N	N	N	N	N	N	N	N
TRACHEA	N	N	N	N	N	N	N		N	N
Inflammation, subacute	-	-	-	-	-	-	-	2	-	-
THYROID GLAND	N	N	N	N		N	N	N	N	N
Atrophy, follicle	-	-	-	-	2	-	-	-	-	-
PARATHYROID GLAND	N	N	N	N	N	N	N	N	N	N
TONGUE	N	N	N	N	N	N	N	N	N	N

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TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 4: 9.0 mg base/kg/day Dose Level
SEX: MALE

ANIMAL ID:	0551	0552	0553	0554	0555	0556	0557	0558	0559	0560
HEART	N	N	N				N		N	N
Cardiomyopathy	-	-	-	(1)	<1>	<1>	-	-	-	-
Inflammation, chronic, serosa	-	-	-	-	-	-	-	<2>	-	-
DUODENUM	N	N	N	N	N	N	N	A	N	N
COLON	N	N	N	N	N	N	N	A	N	N
STOMACH	N	N	N	N		N	N	A	N	N
Dilatation, crypt glands	-	-	-	-	<1>	-	-	-	-	-
LIVER		N								
Inflammation, chronic	<2>	-	(1)	-	<1>	-	(1)	-	-	-
Necrosis, coagulation	<2>	-	-	-	-	-	-	-	-	-
Apoptosis, centrilobular	2	-	-	1	1	1	-	1	-	1
Pigmentation, centrilobular	1	-	-	-	1	1	-	1	-	1
Fatty change, centrilobular	-	-	1	1	-	1	-	-	1	1
Congestion, centrilobular	-	-	-	-	-	<1>	-	2	-	-
Inflammation, subacute, centrilobular	-	-	-	-	-	-	-	-	-	<1>
Hyperplasia, bile duct	-	-	-	-	-	-	<1>	-	-	-
SPLEEN										
Erythropoiesis	2	-	-	2	2	1	1	-	-	-
Pigmentation	-	-	-	-	2	-	-	1	1	1
Congestion	1	2	2	2	1	-	3	-	3	2
Hyperplasia, reticuloendothelial cell	-	2	-	-	-	-	-	-	1	-
JEJUNUM	N	N	N	N	N	N	N	A	N	N
LUNG										
Inflammation, chronic, interstitium	<3>	<3>	<3>	<3>	<3>	<3>	<3>	<3>	<2>	<3>
Hemorrhage	<1>	<2>	<2>	<1>	<2>	<2>	<2>	<3>	<1>	<3>
Inflammation, granulomatous	-	-	-	(2)	-	-	-	-	-	-
Inflammation, acute	-	-	-	-	-	-	-	<4>	-	-
Inflammation, chronic, perivascular	-	<1>	<1>	<2>	<2>	<2>	<1>	-	<1>	<2>
Accumulation, foamy macrophage	<4>	<3>	<3>	<4>	<4>	<3>	<3>	<3>	<3>	<3>

See Reports Code Table for Symbol Definitions

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PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 4: 9.0 mg base/kg/day Dose Level
SEX: MALE

ANIMAL ID:	0551	0552	0553	0554	0555	0556	0557	0558	0559	0560
LUNG										
Edema	-	-	-	-	-	-	-	<3>	-	-
KIDNEY					N	N		A		
Inflammation, chronic	<1>	<1>	<1>	-	-	-	<1>	-	(1)	-
Nephropathy	-	<1>	<1>	-	-	-	-	-	-	-
Pigmentation, cortex	1	2	-	1	-	-	1	-	1	1
URINARY BLADDER	N	N	N	N	N	N	N	N	N	N
PROSTATE	N	N	N	N	N	N	N	N	N	N
SKIN	N	N	N	N	N	N	N	N	N	N
MAMMARY GLAND	N	U	N	N	N	N	U	N	N	N
ILEUM	N	N	N	N	N	N	N	A	N	N
CECUM	N	N	N	N	N	N	N	A	N	N
LYMPH NODE, MESENTERIC	N	N	N	N	N	N	N	U	N	N
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
SCIATIC NERVE	N	N	N	N	N	N	N	N	N	N
TESTES	N	N	N	N	N	N	N	N	N	N
EPIDIDYMIS	N	N	N	N	N	N	N	N	N	N
PITUITARY GLAND							N	N		N
Vacuolation	<1>	<1>	1	1	2	1	-	-	1	-
Cyst	(2)	-	-	-	(1)	<2>	-	-	-	-
EYE	N	N	N	N	N	N	N	A	N	N

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 4: 9.0 mg base/kg/day Dose Level
SEX: MALE

ANIMAL ID:	0551	0552	0553	0554	0555	0556	0557	0558	0559	0560
HARDERIAN GLAND	N	N	N	N	N	N		N	N	N
Inflammation, chronic	-	-	-	-	-	-	(1)	-	-	-
RIB	N	N	N	N	N	N	N		N	N
Granulopoiesis	-	-	-	-	-	-	-	1	-	-
STERNUM (WITH MARROW)										
Hyperplasia, bone marrow	1	1	1	1	2	1	2	2	1	2
Granulopoiesis	-	-	-	-	-	-	-	2	-	-

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PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 4: 9.0 mg base/kg/day Dose Level
SEX: MALE

ANIMAL ID:	0561	0562	0563	0564	0565	0566	0567	0568	0569	0570
BRAIN	N	N	N	N	N	N	N	N	N	N
THYMUS	N	N		U	N					
Hemorrhage	-	-	<3>	-	-	(1)	<1>	<2>	<1>	<1>
Depletion, lymphoid	-	-	-	-	-	2	-	-	-	-
SALIVARY GLAND	N	N	N	N	N	N	N	N	N	N
PANCREAS	N	N			N		N		N	
Inflammation, chronic	-	-	(1)	(1)	-	(1)	-	(1)	-	(1)
ADRENAL GLAND			N	N						
Hypertrophy, zona glomerulosa	(1)	-	-	-	-	-	(2)	-	-	-
Vacuolation, cortex	(1)	-	-	-	-	-	-	-	-	-
Pigmentation, zona reticularis	-	1	-	-	1	1	2	1	-	1
Congestion	-	-	-	-	-	-	1	1	-	-
Hypertrophy, zona reticularis	-	-	-	-	-	-	-	-	<1>	-
SPINAL CORD (THORACIC)	N	N	N	N	N	N	N	N	N	N
DIAPHRAGM	N	N	N	N		N	N	N	N	N
Inflammation, chronic	-	-	-	-	[3]	-	-	-	-	-
ESOPHAGUS	N	N	N	N		N	N	N	N	N
Inflammation, chronic, muscle	-	-	-	-	(2)	-	-	-	-	-
TRACHEA	N	N	N			N		N	N	N
Inflammation, chronic	-	-	-	(1)	(1)	-	<1>	-	-	-
THYROID GLAND	N	N	N	N	N	N	N	N	N	N
PARATHYROID GLAND	U	N	N	N	N	U	U	N	N	N
TONGUE	N	N	N	N	N	N	N	N	N	N
HEART	N		N	N		N	N		N	N

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PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152 STUDY NUMBER: SN152
FATE: ALL GROUP: 4: 9.0 mg base/kg/day Dose Level
SEX: MALE

ANIMAL ID:	0561	0562	0563	0564	0565	0566	0567	0568	0569	0570
HEART	N		N	N		N	N		N	N
Cardiomyopathy	-	<1>	-	-	1	-	-	-	-	-
Inflammation, chronic, serosa	-	-	-	-	[3]	-	-	-	-	-
Thrombosis, chronic	-	-	-	-	-	-	-	(3)	-	-
DUODENUM	N	N	N	N	N	N	N	N	N	N
COLON	N	N	N	N	N	N	N	N	N	N
STOMACH	N	N	N	N	N	N	N	N	N	N
LIVER					N		N			N
Inflammation, chronic	<1>	-	-	<1>	-	-	-	-	<1>	-
Focus, vacuolated cell	<2>	-	-	<1>	-	(1)	-	-	-	-
Apoptosis, centrilobular	2	-	1	1	-	1	-	-	2	-
Pigmentation, centrilobular	1	-	1	1	-	1	-	2	1	-
Fatty change, centrilobular	1	1	-	-	-	1	-	1	1	-
Focus, basophilic cell	-	-	-	-	-	-	-	<1>	-	-
SPLEEN										
Erythropoiesis	-	-	-	-	1	-	1	-	-	1
Pigmentation	1	1	-	2	-	1	1	3	2	-
Congestion	2	3	2	2	3	2	2	2	2	2
Hyperplasia, reticuloendothelial cell	-	2	1	-	-	-	-	-	-	-
JEJUNUM	N	N	N	N	N	N	N	N	N	N
LUNG										
Inflammation, chronic, interstitium	<2>	<3>	<3>	<3>	<3>	<3>	<3>	<3>	<3>	<3>
Hemorrhage	<4>	<3>	<1>	<2>	<1>	<1>	<2>	<3>	<2>	<2>
Inflammation, granulomatous	-	-	<1>	-	<1>	-	-	-	-	-
Inflammation, acute	-	-	1	-	-	-	-	-	-	-
Inflammation, chronic, serosa	-	-	-	-	2	-	-	-	-	-
Inflammation, chronic, perivascular	<2>	<1>	<1>	<2>	-	<1>	<1>	<1>	<1>	<2>
Accumulation, foamy macrophage	<3>	<3>	<3>	<4>	<2>	<3>	<2>	<4>	<3>	<3>

See Reports Code Table for Symbol Definitions

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PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 4: 9.0 mg base/kg/day Dose Level
SEX: MALE

ANIMAL ID:	0561	0562	0563	0564	0565	0566	0567	0568	0569	0570
KIDNEY										
Inflammation, chronic	<1>	<1>	<1>	<1>	<1>	-	<1>	<1>	<1>	<1>
Nephropathy	-	<1>	<1>	(1)	<1>	-	<1>	-	(1)	<2>
Hydronephrosis	-	-	-	-	-	-	-	-	1L	-
Pigmentation, cortex	1	2	1	2	1	1	2	1	1	2
Cyst	-	-	-	-	-	-	-	-	(1)	-
URINARY BLADDER	N	N	N	N	N	N	N	N	N	N
PROSTATE	N	N	N	N	N	N	N	N	N	N
SKIN	N	N	N	N	N	N	N	N	N	N
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N
ILEUM	N	N	N	N	N	N	N	N	N	N
CECUM	N	N	N	N	N	N	N	N	N	N
LYMPH NODE, MESENTERIC			N	N	N	N	N	N	N	N
Hemorrhage	2	-	-	-	-	-	-	-	-	-
Inflammation, granulomatous	-	<3>	-	-	-	-	-	-	-	-
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
SCIATIC NERVE	N	N	N	N	N	N	N	N	N	N
TESTES	N	N	N	N	N	N	N	N	N	
Degeneration	-	-	-	-	-	-	-	-	-	<3>I
EPIDIDYMIS	N	N	N	N	N	N	N	N	N	N
PITUITARY GLAND		N	N	N	N	N	N	N		
Vacuolation	1	-	-	-	-	-	-	-	2	1
Cyst	(1)	-	-	-	-	-	-	-	-	-

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PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152
FATE: ALL

STUDY NUMBER: SN152
GROUP: 1: 0 mg base/kg/day Dose Level
SEX: FEMALE

ANIMAL ID:	0426	0427	0428	0429	0430	0431	0432	0433	0434	0435
BRAIN	N	N	N	N	N	N	N	N	N	N
THYMUS	N	N	N			N	N			N
Hemorrhage	-	-	-	<1>	-	-	-	<1>	<1>	-
Depletion, lymphoid	-	-	-	-	1	-	-	-	-	-
SALIVARY GLAND	N	N	N	N	N	N	N	N	N	N
PANCREAS		N	N	N		N	N			N
Inflammation, chronic	(1)	-	-	-	(1)	-	-	(1)	(1)	-
Atrophy, acinar	(1)	-	-	-	-	-	-	-	-	-
ADRENAL GLAND		N		N		N	N			N
Hypertrophy, zona glomerulosa	-	-	-	-	<1>	-	-	-	-	-
Congestion	1	-	1	-	-	-	-	1	-	-
Hypertrophy, zona reticularis	-	-	-	-	(1)	-	-	<1>	<1>	-
SPINAL CORD (THORACIC)	N	N	N	N	N	N	N	N	N	N
DIAPHRAGM		N	N	N	N	N	N	N	N	N
Inflammation, chronic	(1)	-	-	-	-	-	-	-	-	-
ESOPHAGUS	N	N	N	N	N	N	N	N	N	N
TRACHEA	N	N	N	N	N	N	N		N	N
Inflammation, chronic	-	-	-	-	-	-	-	(1)	-	-
THYROID GLAND	N	N	N	N	N	N	N	N	N	N
PARATHYROID GLAND	N	N	N	U	U	U	N	N	N	N
TONGUE	N	N	N	N	N	N	N	N	N	N
HEART		N	N	N	N	N	N	N	N	N

See Reports Code Table for Symbol Definitions

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PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 1: 0 mg base/kg/day Dose Level
SEX: FEMALE

ANIMAL ID:	0426	0427	0428	0429	0430	0431	0432	0433	0434	0435
HEART		N	N	N	N	N	N	N	N	N
Cardiomyopathy	(1)	-	-	-	-	-	-	-	-	-
DUODENUM	N	N	N	N	N	N	N	N	N	N
COLON	N	N	N	N	N	N	N	N	N	N
STOMACH	N			N	N	N	N	N	N	N
Dilatation, crypt glands	-	<1>	<1>	-	-	-	-	-	-	-
LIVER	N			N			N		N	N
Inflammation, chronic	-	(1)	<1>	-	(1)	<1>	-	(1)	-	-
SPLEEN	N									
Erythropoiesis	-	1	2	2	1	1	2	1	2	1
Pigmentation	-	1	1	1	2	-	-	1	1	1
JEJUNUM	N	N	N	N	N	N	N	N	N	N
LUNG		N			N					
Inflammation, chronic, interstitium	-	-	-	(1)	-	-	-	-	-	-
Hemorrhage	-	-	(1)	<1>	-	-	-	-	-	-
Inflammation, chronic, serosa	-	-	-	-	-	-	<1>	-	-	-
Inflammation, chronic, perivascular	<1>	-	<1>	-	-	(1)	-	<1>	(1)	<1>
KIDNEY	N				N					
Mineralization	-	<1>	-	(1)	-	-	-	(1)	<1>	-
Inflammation, chronic	-	<1>	-	(1)	-	(1)	(1)	(1)	-	<1>
Nephropathy	-	(1)	-	(1)	-	-	-	-	(1)	-
Hydronephrosis	-	-	3L	-	-	-	-	-	-	-
Pyelonephritis	-	-	3I	-	-	-	-	-	-	-
Hyperplasia, pelvic epithelium	-	-	[3]I	-	-	-	-	-	-	-
URINARY BLADDER	N	N		N	N	N	N	N	N	
Inflammation, chronic	-	-	-	-	-	-	-	-	-	(1)
Hyperplasia, epithelium	-	-	[2]	-	-	-	-	-	-	-

See Reports Code Table for Symbol Definitions

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PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 1: 0 mg base/kg/day Dose Level
SEX: FEMALE

ANIMAL ID:	0426	0427	0428	0429	0430	0431	0432	0433	0434	0435
SKIN	N	N	N	N	N	N	N	N	N	N
MAMMARY GLAND	N	N.	N	N	N	N	N		N	N
Cyst, milk	-	-	-	-	-	-	-	(3)	-	-
ILEUM	N	N	N	N	N	N	N	N	N	N
CECUM	N	N	N	N	N	N	N	N	N	N
LYMPH NODE, MESENTERIC	N	N	N	N	N	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
SCIATIC NERVE	N	N	N	N	N	N	N	N	N	N
OVARY	N	N		N	N	N	N	N	N	N
Cyst	-	-	2	-	-	-	-	-	-	-
UTERUS	N	N	N	N	N	N	N	N	N	N
PITUITARY GLAND	N	N	N	N	N	N	N	N	N	N
EYE	N		N	U	N	N	N	N	N	
Inflammation, granulomatous, optic nerve	-	(3)	-	-	-	-	-	-	-	(2)
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N
RIB	N	N	N	N	N	N	N	N	N	N
STERNUM (WITH MARROW)	N	N	N	N	N	N	N	N	N	N
MESENTERY										
Necrosis, fat	-	-	-	-	-	-	-	-	-	(3)

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PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 1: 0 mg base/kg/day Dose Level
SEX: FEMALE

ANIMAL ID:	0436	0437	0438	0439	0440	0441	0442	0443	0444	0445
BRAIN	N	N	N	N	N	N	N	N	N	N
THYMUS			N		N			N		
Hemorrhage	<1>	<1>	-	(1)	-	-	<2>	-	-	(1)
Depletion, lymphoid	-	-	-	-	-	(2)	-	-	2	-
SALIVARY GLAND	N	N	N	N	N	N	N	N	N	N
PANCREAS	N			N	N		N	N	N	N
Inflammation, chronic	-	(1)	(1)	-	-	(1)	-	-	-	-
ADRENAL GLAND				N			N		N	
Vacuolation, cortex	<2>	-	-	-	-	-	-	-	-	-
Congestion	-	1	-	-	1	-	-	1	-	1
Hypertrophy, zona reticularis	<1>	-	<1>	-	-	<1>	-	<1>	-	<2>
SPINAL CORD (THORACIC)	N	N	N	N	N	N	N	N	N	N
DIAPHRAGM	N	N	N	N	N	N	N	N		N
Inflammation, chronic	-	-	-	-	-	-	-	-	<1>	-
ESOPHAGUS	N	N	N	N	N	N	N	N	N	N
TRACHEA	N	N	N	N	N	N	N	N	N	
Inflammation, chronic	-	-	-	-	-	-	-	-	-	(1)
THYROID GLAND		N	N	N	N	N	N	N	N	N
Inflammation, subacute	(2)	-	-	-	-	-	-	-	-	-
PARATHYROID GLAND	N	N	N	N	N	N	N	N	N	N
TONGUE	N	N	N	N	N	N	N	N	N	N
HEART	N	N	N	N	N	N	N	N		N
Inflammation, chronic, artery	-	-	-	-	-	-	-	-	<2>	-

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152 STUDY NUMBER: SN152
FATE: ALL GROUP: 1: 0 mg base/kg/day Dose Level
SEX: FEMALE

ANIMAL ID:	0436	0437	0438	0439	0440	0441	0442	0443	0444	0445
DUODENUM	N	N	N	N	N	N	N	N	N	N
COLON	N	N	N	N	N	N	N	N	N	N
STOMACH	N	N	N	N	N	N	N	N	N	
Dilatation, crypt glands	-	-	-	-	-	-	-	-	-	<1>
LIVER				N	N			N		N
Inflammation, chronic	(1)	(1)	<1>	-	-	<1>	<1>	-	<1>	-
SPLEEN										
Erythropoiesis	-	-	1	-	-	-	-	-	-	-
Adhesion	-	-	-	-	-	-	-	-	(2)	-
Pigmentation	1	1	2	1	1	1	2	1	3	2
JEJUNUM	N	N	N	N	N	N	N	N	N	N
LUNG	N		N							
Inflammation, chronic, interstitium	-	-	-	(1)	-	-	-	-	<1>	-
Hemorrhage	-	-	-	-	-	<1>	<1>	<1>	<1>	-
Hyperplasia, lymphoid, peribronchial	-	-	-	-	-	-	-	-	3	-
Inflammation, chronic, perivascular	-	<1>	-	<1>	<1>	<1>	<1>	-	<1>	(1)
KIDNEY										
Mineralization	-	-	-	(1)	<1>	(1)	-	<1>	(1)	-
Inflammation, chronic	<1>	-	<1>	-	-	<1>	(1)	-	-	(1)
Nephropathy	<1>	<1>	<2>	-	-	-	-	-	-	-
Hydronephrosis	-	-	-	-	-	-	-	-	3	-
URINARY BLADDER	N	N	N	N	N		N	N	N	N
Inflammation, chronic	-	-	-	-	-	(1)	-	-	-	-
SKIN	N	N	N	N	N	N	N	N	N	N
MAMMARY GLAND	N	N		N	N		N	N	N	N
Cyst, milk	-	-	<3>	-	-	<4>	-	-	-	-

See Reports Code Table for Symbol Definitions

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PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152
FATE: ALL

STUDY NUMBER: SN152
GROUP: 1: 0 mg base/kg/day Dose Level
SEX: FEMALE

ANIMAL ID:	0436	0437	0438	0439	0440	0441	0442	0443	0444	0445
MAMMARY GLAND	N	N		N	N		N	N	N	N
Inflammation, xanthogranulomatous	-	-	(1)	-	-	<2>	-	-	-	-
ILEUM	N	N	N	N	N	N	N	N	N	N
CECUM	N	N	N	N	N	N	N	N	N	N
LYMPH NODE, MESENTERIC	N	N	N	N	N	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
SCIATIC NERVE	N	N	N	N	N	N	N	N	N	N
OVARY	N			N	N		N	N	N	N
Necrosis, corpus luteum	-	<2>	-	-	-	-	-	-	-	-
Cyst	-	-	1	-	-	2	-	-	-	-
UTERUS			N	N	N		N	N	N	N
Dilatation	1	2	-	-	-	1	-	-	-	-
PITUITARY GLAND	N	N	N	N	N	N	N	N	N	N
EYE	N	N	N	N	N	N	N	N	N	N
HARDERIAN GLAND	N	N		N	N	N	N	N	N	N
Inflammation, chronic	-	-	(1)	-	-	-	-	-	-	-
RIB	N	N	N	N	N	N	N	N	N	N
STERNUM (WITH MARROW)	N	N	N	N	N	N	N	N	N	N

See Reports Code Table for Symbol Definitions

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PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 2: 0.5 mg base/kg/day Dose Level
SEX: FEMALE

ANIMAL ID:	0476	0477	0478	0479	0480	0481	0482	0483	0484	0485
ADRENAL GLAND		N	N		N	N	N	N		N
Hypertrophy, zona glomerulosa	-	-	-	(1)	-	-	-	-	-	-
Hypertrophy, zona reticularis	<1>	-	-	-	-	-	-	-	(1)	-
SPLEEN										
Erythropoiesis	1	2	2	2	1	2	2	1	2	2
Pigmentation	1	2	1	2	2	2	2	3	2	2
LUNG							N			
Hemorrhage	-	-	<1>	-	-	<1>	-	-	-	(2)
Inflammation, chronic, perivascular	<1>	<1>	-	<1>	<1>	<1>	-	<1>	<1>	<1>
KIDNEY										
Mineralization	-	(1)	<1>	-	-	-	<1>	<1>	<1>	(1)
Inflammation, chronic	<1>	<1>	<1>	<1>	<1>	<1>	<1>	(1)	<1>	<1>
Nephropathy	(1)	<1>	-	-	<1>	<1>	-	-	-	-
MAMMARY GLAND										
Cyst, milk	-	-	-	-	-	<3>	-	-	-	-
Hyperplasia, acinar	-	-	-	-	-	(2)	-	-	-	-
UTERUS	N	N	N	N				N		
Dilatation	-	-	-	-	1I	3I	2I	-	1I	2I
STERNUM (WITH MARROW)	N	N	N	N	N	N			N	N
Hyperplasia, bone marrow	-	-	-	-	-	-	1	1	-	-
BONE										
Fracture, healed	-	-	-	-	-	-	P	-	-	-

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152 STUDY NUMBER: SN152
FATE: ALL GROUP: 2: 0.5 mg base/kg/day Dose Level
SEX: FEMALE

ANIMAL ID:	0486	0487	0488	0489	0490	0491	0492	0493	0494	0495
ADRENAL GLAND	N					N		N	N	
Pigmentation, zona reticularis	-	-	1	-	-	-	-	-	-	-
Congestion	-	-	1	-	1	-	-	-	-	1
Hypertrophy, zona reticularis	-	<1>	-	<1>	<1>	-	-	-	-	-
Cyst, blood	-	-	-	-	-	-	(2)L	-	-	-
SPLEEN										
Erythropoiesis	-	-	-	-	1	-	-	-	-	-
Pigmentation	2	2	1	2	2	2	2	1	2	3
Congestion	-	-	-	-	1	-	-	-	-	-
Cyst, serosa	-	-	-	-	-	-	<2>	-	-	-
LUNG						N				
Hemorrhage	<1>	<1>	<1>	-	<2>	-	<1>	(1)	-	-
Inflammation, chronic, perivascular	<1>	<1>	<1>	<1>	<1>	-	(1)	<1>	<1>	<1>
KIDNEY										
Mineralization	-	-	<1>	<1>	-	-	-	<1>	-	-
Inflammation, chronic	<1>	<1>	<1>	-	<1>	<1>	<1>	-	<1>	<1>
Nephropathy	-	(1)	-	-	-	<1>	-	-	(1)	<2>
Cyst	-	-	-	-	-	<2>	-	-	-	-
MAMMARY GLAND										
Cyst, milk	-	-	-	-	<4>	-	-	-	-	-
OVARY										
Atrophy	-	-	-	-	-	4L	-	-	-	-
UTERUS	N		N		N		N	N	N	N
Dilatation	-	1I	-	2I	-	2I	-	-	-	-
PITUITARY GLAND		N			N					
STERNUM (WITH MARROW)	N	N	N			N	N	N	N	N
Hyperplasia, bone marrow	-	-	-	1	1	-	-	-	-	-

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PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 3: 2.0 mg base/kg/day Dose Level
SEX: FEMALE

ANIMAL ID:	0526	0527	0528	0529	0530	0531	0532	0533	0534	0535
ADRENAL GLAND	N	N	N	N	N				N	
Pigmentation, zona reticularis	-	-	-	-	-	-	1	1	-	-
Congestion	-	-	-	-	-	1	2	1	-	-
Hypertrophy, zona reticularis	-	-	-	-	-	<1>	-	-	-	<1>
LIVER										
Hepatodiaphragmatic nodule	-	-	-	-	-	P	-	-	-	-
SPLEEN										
Erythropoiesis	2	3	3	2	1	2	1	2	2	3
Pigmentation	2	2	-	1	2	2	2	-	2	2
Congestion	-	-	-	-	-	-	1	-	-	-
LUNG										
Inflammation, chronic, interstitium	<2>	<3>	<2>	<2>	<2>	<2>	<2>	<2>	<2>	<2>
Hemorrhage	<1>	-	<1>	-	<1>	<1>	<1>	(1)	-	-
Inflammation, chronic, perivascular	<2>	<1>	<2>	<1>	<1>	<1>	<1>	<1>	<1>	<1>
Accumulation, foamy macrophage	<3>	<3>	<3>	<3>	<2>	<2>	<3>	<2>	<3>	<3>
KIDNEY									N	
Mineralization	<1>	<2>	(1)	(1)	(1)	-	-	<2>	-	-
Inflammation, chronic	<1>	-	-	(1)	<1>	<1>	<1>	<1>	-	<1>
Nephropathy	<1>	-	(1)	-	-	<2>	<1>	(1)	-	-
Pigmentation, cortex	1	1	-	1	-	-	-	1	-	-
UTERUS		N	N	N	N	N	N		N	N
Dilatation	1I	-	-	-	-	-	-	2I	-	-
STERNUM (WITH MARROW)	N			N		N	N	N	N	
Hyperplasia, bone marrow	-	2	1	-	1	-	-	-	-	1

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TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 3: 2.0 mg base/kg/day Dose Level
SEX: FEMALE

ANIMAL ID:	0536	0537	0538	0539	0540	0541	0542	0543	0544	0545
BRAIN				N						
ADRENAL GLAND				N		N				N
Hypertrophy, zona glomerulosa	-	-	<1>	-	-	-	<1>	<1>	-	-
Congestion	-	1	-	-	1	-	-	1	1	-
Hypertrophy, zona reticularis	(1)	1	-	-	-	-	-	<1>	-	-
SPLEEN										
Erythropoiesis	-	-	1	1	-	-	-	1	-	1
Pigmentation	2	3	2	2	2	2	2	3	1	2
LUNG										
Inflammation, chronic, interstitium	<1>	<1>	<2>	<2>	<2>	<2>	<1>	<2>	<2>	<2>
Hemorrhage	(2)	-	<1>	-	-	-	-	<1>	-	-
Congestion	-	-	-	-	-	-	-	-	-	1
Inflammation, chronic, perivascular	(1)	<1>	<1>	<1>	<1>	<1>	<1>	<1>	<1>	<2>
Accumulation, foamy macrophage	<2>	<2>	<1>	<3>	<2>	<2>	<2>	<3>	<2>	<3>
KIDNEY										
Mineralization	-	<1>	(1)	-	-	<1>	-	-	-	(1)
Inflammation, chronic	<1>	<1>	<1>	<1>	<1>	<1>	<1>	<1>	<1>	(1)
Nephropathy	(1)	-	(1)	-	<1>	-	<1>	<1>	-	<1>
Hydronephrosis	-	-	-	3I	-	-	-	-	-	-
Pyelonephritis	-	-	-	1I	-	-	-	-	-	-
Hyperplasia, pelvic epithelium	-	-	-	[2]	-	-	-	-	-	-
Pigmentation, cortex	-	1	-	-	-	-	-	1	-	1
UTERUS	N		N				N	N	N	N
Dilatation	-	2I	-	2I	1I	3I	-	-	-	-
PITUITARY GLAND				N						
STERNUM (WITH MARROW)	N	N	N		N	N	N		N	
Hyperplasia, bone marrow	-	-	-	1	-	-	-	1	-	1

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 4: 9.0 mg base/kg/day Dose Level
SEX: FEMALE

ANIMAL ID:	0576	0577	0578	0579	0580	0581	0582	0583	0584	0585
BRAIN	N	N	N	N	N	N	N	N	N	N
THYMUS		N	N		N				N	N
Hemorrhage	<1>	-	-	<1>	-	-	<1>	<>	-	-
Depletion, lymphoid	-	-	-	2	-	2	-	-	-	-
SALIVARY GLAND	N	N	N	N	N	N	N	N	N	N
PANCREAS	N	N	N					N	N	
Inflammation, chronic	-	-	-	(1)	-	(1)	<1>	-	-	<1>
Atrophy, acinar	-	-	-	-	<1>	-	-	-	-	-
ADRENAL GLAND							N			
Pigmentation, zona reticularis	1	-	2	2	3	2	-	1	1	2
Congestion	-	1	3	1	2	1	-	2	1	3
Hypertrophy, zona reticularis	-	-	-	-	-	(1)	-	-	-	-
SPINAL CORD (THORACIC)	N	N	N	N	N	N	N	N	N	N
DIAPHRAGM	N	N	N		N	N	N	N	N	N
Inflammation, chronic	-	-	-	(1)	-	-	-	-	-	-
ESOPHAGUS	N	N	N	N	N		N	N	N	N
Inflammation, chronic, muscle	-	-	-	-	-	(1)	-	-	-	-
TRACHEA	N	N	N	N	N	N	N	N	N	N
THYROID GLAND	N	N	N	N	N	N	N	N	N	N
PARATHYROID GLAND	N	N	N	N	N	N	N	N	N	N
TONGUE	N	N	N	N	N	N	N	N	N	N
HEART	N	N	N		N	N	N	N	N	N

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 4: 9.0 mg base/kg/day Dose Level
SEX: FEMALE

ANIMAL ID:	0576	0577	0578	0579	0580	0581	0582	0583	0584	0585
HEART	N	N	N		N	N	N	N	N	N
Cardiomyopathy	-	-	-	1	-	-	-	-	-	-
DUODENUM	N	N	N	N	N	N	N	N	N	N
COLON	N	N	N	N	N		N	N		N
Metazoan parasite, lumen	-	-	-	-	-	P	-	-	P	-
STOMACH	N	N	N		N	N	N	N	N	N
Dilatation, crypt glands	-	-	-	<1>	-	-	-	-	-	-
LIVER	N		N	N				N		N
Inflammation, chronic	-	<1>	-	-	(1)	<1>	<1>	-	<1>	-
SPLEEN										
Erythropoiesis	2	2	-	-	1	2	1	-	2	1
Pigmentation	3	2	1	-	1	2	1	1	1	1
Congestion	-	-	-	2	1	1	1	1	2	2
JEJUNUM	N	N	N	N	N	N	N	N	N	N
LUNG										
Inflammation, chronic, interstitium	<3>	<2>	<2>	<2>	<3>	<3>	<2>	<2>	<2>	<3>
Hemorrhage	<3>	<3>	<3>	<3>	<2>	<2>	<2>	<3>	<4>	<3>
Inflammation, chronic, perivascular	<1>	<2>	<1>	<1>	<1>	<1>	<1>	<1>	<1>	<1>
Accumulation, foamy macrophage	<3>	<3>	<4>	<2>	<3>	<3>	<2>	<2>	<2>	<2>
KIDNEY										
Mineralization	(1)	-	-	-	<2>	-	-	-	-	<1>
Inflammation, chronic	(1)	-	<1>	-	-	<1>	-	<1>	<1>	<1>
Nephropathy	-	(1)	-	<1>	-	(1)	<1>	-	-	-
Hydronephrosis	-	-	2L	-	-	-	-	-	-	-
Pigmentation, cortex	2	1	1	2	2	1	1	2	1	2
URINARY BLADDER	N	N	N	N	N	N	N	N	N	N

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 4: 9.0 mg base/kg/day Dose Level
SEX: FEMALE

ANIMAL ID:	0576	0577	0578	0579	0580	0581	0582	0583	0584	0585
SKIN	N	N	N	N	N	N	N	N	N	N
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N
ILEUM	N	N	N	N	N	N	N	N	N	N
CECUM	N	N	N	N	N	N	N	N	N	N
LYMPH NODE, MESENTERIC	N	N	N	N	N	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
SCIATIC NERVE	N	N	N	N	N	N	N	N	N	N
OVARY	N	N	N	N	N	N	N	N	N	N
UTERUS	N		N	N	N	N	N		N	N
Dilatation	-	1I	-	-	-	-	-	2I	-	-
PITUITARY GLAND	N	N	N	N	N	N	N	N	N	N
EYE	N	N	N	N	N	N	N	N	N	N
HARDERIAN GLAND	N		N	N		N			N	N
Inflammation, chronic	-	<2>	-	-	(1)	-	(1)	<2>	-	-
RIB	N	N	N	N	N	N	N	N	N	N
STERNUM (WITH MARROW)						N				
Hyperplasia, bone marrow	2	1	2	2	2	-	1	1	2	1
Granulopoiesis	-	-	1	-	-	-	-	-	-	-

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PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 4: 9.0 mg base/kg/day Dose Level
SEX: FEMALE

ANIMAL ID:	0586	0587	0588	0589	0590	0591	0592	0593	0594	0595
BRAIN	N	N	N	N	N	N	N	N	N	N
THYMUS	N	N		N	N	N				
Hemorrhage	-	-	<1>	-	-	-	<1>	<2>	<1>	<2>
SALIVARY GLAND	N	N	N	N	N	N	N	N	N	N
PANCREAS	N	N	N	N	N			N		N
Inflammation, chronic	-	-	-	-	-	-	(1)	-	<1>	-
Atrophy, acinar	-	-	-	-	-	<1>	-	-	(1)	-
ADRENAL GLAND										
Pigmentation, zona reticularis	3	1	1	3	2	1	1	1	1	3
Congestion	3	1	1	2	1	2	2	1	1	2
SPINAL CORD (THORACIC)	N	N	N	N	N	N	N	N	N	N
DIAPHRAGM	N	N	N	N	N		N	N	N	N
Adhesion, liver	-	-	-	-	-	(2)	-	-	-	-
ESOPHAGUS	N	N	N	N	N	N	N	N	N	N
TRACHEA	N	N	N		N	N		N	N	
Inflammation, chronic	-	-	-	(1)	-	-	(1)	-	-	(1)
THYROID GLAND	N	N	N	N	N	N	N	N	N	N
PARATHYROID GLAND	N	N	N	N	N	N	N	N	N	N
TONGUE	N	N	N	N	N	N	N	N	N	N
HEART	N	N	N	N	N	N	N	N	N	N
DUODENUM	N	N	N	N	N	N	N	N	N	N
COLON	N	N	N	N	N	N	N	N	N	N

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TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152
FATE: ALL

STUDY NUMBER: SN152
GROUP: 4: 9.0 mg base/kg/day Dose Level
SEX: FEMALE

ANIMAL ID:	0586	0587	0588	0589	0590	0591	0592	0593	0594	0595
STOMACH	N	N	N	N	N	N	N	N	N	N
LIVER	N						N	N	N	N
Inflammation, chronic	-	(1)	<1>	<1>	-	<1>	-	-	-	-
Focus, vacuolated cell	-	-	-	-	(1)	-	-	-	-	-
SPLEEN										
Erythropoiesis	-	-	-	1	-	-	-	-	-	-
Pigmentation	2	2	1	1	-	1	1	1	-	2
Congestion	2	3	3	2	2	2	2	1	1	1
Hyperplasia, reticuloendothelial cell	-	-	-	-	-	-	-	-	2	-
JEJUNUM	N	N	N	N	N	N	N	N	N	N
LUNG										
Inflammation, chronic, interstitium	<3>	<3>	<2>	<3>	<2>	<2>	<2>	<2>	<2>	<3>
Hemorrhage	<2>	<3>	<2>	<2>	<3>	<3>	<2>	<3>	<3>	<1>
Inflammation, chronic, perivascular	<1>	<2>	-	<1>	<1>	-	<1>	<1>	<1>	<1>
Accumulation, foamy macrophage	<2>	<2>	<2>	<3>	<2>	<2>	<2>	<2>	<2>	<2>
KIDNEY										
Mineralization	-	(1)	-	-	-	-	-	(1)	-	-
Inflammation, chronic	-	(1)	<1>	<1>	<1>	-	<1>	(1)	-	<1>
Nephropathy	<2>	-	-	<1>	-	-	-	-	-	-
Pigmentation, cortex	2	2	2	2	2	2	2	1	1	1
Cyst	-	-	-	-	-	-	(2)	-	-	-
URINARY BLADDER	N	N	N	N	N	N	N	N	N	N
SKIN	N	N	N	N	N	N	N	N	N	N
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N
ILEUM	N	N	N	N	N	N	N	N	N	N
CECUM	N	N	N	N	N	N	N	N	N	N

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

TABULATED ANIMAL DATA

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 4: 9.0 mg base/kg/day Dose Level
SEX: FEMALE

ANIMAL ID:	0586	0587	0588	0589	0590	0591	0592	0593	0594	0595
LYMPH NODE, MESENTERIC	N	N	N	N	N	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
SCIATIC NERVE	N	N	N	N	N	N	N	N	N	N
OVARY	N	N	N	N	N	N	N	N	N	N
UTERUS	N	N	N					N		
Dilatation	-	-	-	3I	1	3I	2I	-	4I	1I
PITUITARY GLAND	N	N	N	N	N	N	N	N	N	N
EYE	N	N	N	N	N	N	N	N	N	N
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N
RIB	N	N	N	N	N	N	N	N	N	N
STERNUM (WITH MARROW)	N	N			N	N		N		N
Hyperplasia, bone marrow	-	-	1	1	-	-	1	-	1	-

See Reports Code Table for Symbol Definitions

SECTION V

CORRELATION OF GROSS AND MICROSCOPIC (MICRO) FINDINGS

PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152 | STUDY NUMBER: SN152
FATE: ALL | GROUP: 1: 0 mg base/kg/day Dose Level
SEX: MALE

Animal ID: 0402
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LYMPH NODE, MANDIBULAR - ENLARGED, 10 MM X 6 MM, SINGLE, DARK	LYMPH NODE, MANDIBULAR - Hyperplasia, lymphoid; LYMPH NODE, MANDIBULAR - Accumulation, plasma cell

Animal ID: 0407
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LIVER - MEDIAN LOBE, NODULE, 10 X 12 X 4 MM	LIVER - Hepatodiaphragmatic nodule

Animal ID: 0410
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
MESENTERY - NODULE, 6 X 4 X 3 MM, YELLOW	MESENTERY - Necrosis, fat
LIVER - BILATERAL, PIGMENTATION, PALE	LIVER - No corresponding lesion

Animal ID: 0412
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, FOCUS, 1 X 1 MM, RED, MULTIPLE	LUNG - No corresponding lesion

Animal ID: 0417
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
TESTES - RIGHT, PIGMENTATION, PURPLE	TESTES - Arrested spermatogenesis
URINARY BLADDER - LACERATION, 10 X 4 MM	URINARY BLADDER - No corresponding lesion

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PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 1: 0 mg base/kg/day Dose Level
SEX: MALE

Animal ID: 0417
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
EPIDIDYMIS - RIGHT, PIGMENTATION, OPAQUE	EPIDIDYMIS - Oligospermia
KIDNEY - LEFT, PIGMENTATION, MOTTLED	KIDNEY - No corresponding lesion
KIDNEY - RIGHT, PIGMENTATION, MOTTLED	KIDNEY - No corresponding lesion
LUNG - BILATERAL, PIGMENTATION, PURPLE, RED	LUNG - No corresponding lesion
LUNG - LEFT, NODULE, 2 X 2 MM, MULTIPLE, WHITE	LUNG - No corresponding lesion

Animal ID: 0419
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, PURPLE, PALE, RED, PINK	LUNG - Congestion

Animal ID: 0420
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTAION, PURPLE, RED	LUNG - No corresponding lesion

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PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 2: 0.5 mg base/kg/day Dose Level
SEX: MALE

Animal ID: 0452
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LYMPH NODE, MANDIBULAR - ENLARGED, MULTIPLE	LYMPH NODE, MANDIBULAR - Hyperplasia, lymphoid; LYMPH NODE, MANDIBULAR - Accumulation, plasma cell

Animal ID: 0455
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, MOTTLED	LUNG - Inflammation, chronic, interstitium

Animal ID: 0457
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
URINARY BLADDER - LACERATION, 4 X 10 MM	URINARY BLADDER - No corresponding lesion
LIVER - PIGMENTATION, MOTTLED	LIVER - No corresponding lesion
KIDNEY - BILATERAL, PIGMENTATION, MOTTLED	KIDNEY - Nephropathy
LUNG - BILATERAL, PIGMENTATION, MOTTLED	LUNG - No corresponding lesion

Animal ID: 0459
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
URINARY BLADDER - LACERATION, 4 X 10 MM	URINARY BLADDER - No corresponding lesion
LIVER - PIGMENTATION, PALE	LIVER - No corresponding lesion
LUNG - BILATERAL, PIGMENTATION, PALE	LUNG - No corresponding lesion

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152
FATE: ALL

STUDY NUMBER: SN152
GROUP: 2: 0.5 mg base/kg/day Dose Level
SEX: MALE

Animal ID: 0461
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, RED, PURPLE	LUNG - Congestion

Animal ID: 0463
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
SPLEEN - CYST, 4 X 2 X 2 MM, CLEAR	SPLEEN - Cyst, serosa
LUNG - BILATERAL, PIGMENTATION, MOTTLED, RED, DARK RED	LUNG - No corresponding lesion

Animal ID: 0466
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
URINARY BLADDER - MASS, 2 X 1 X 4 MM, WHITE	URINARY BLADDER - Semen plug

Animal ID: 0467
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
SPLEEN - SMALL, 40 MM X 10 MM	SPLEEN - No corresponding lesion

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PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152
FATE: ALL

STUDY NUMBER: SN152
GROUP: 3: 2.0 mg base/kg/day Dose Level
SEX: MALE

Animal ID: 0501
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
MESENTERY - NODULE, 10 X 5 X 3 MM, YELLOW, SINGLE	MESENTERY - Necrosis, fat
LUNG - NODULE, 4 X 2 X 2 MM, WHITE	LUNG - Accumulation, foamy macrophage

Animal ID: 0502
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, FOCUS, MULTIPLE, WHITE	LUNG - Accumulation, foamy macrophage

Animal ID: 0503
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - FOCUS, 2 X 2 MM, MULTIPLE	LUNG - Accumulation, foamy macrophage

Animal ID: 0504
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, MOTTLED, RED, WHITE	LUNG - Accumulation, foamy macrophage

Animal ID: 0505
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, FOCUS, 1 X 1 MM, MULTIPLE, WHITE	LUNG - Accumulation, foamy macrophage

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152
FATE: ALL

STUDY NUMBER: SN152
GROUP: 3: 2.0 mg base/kg/day Dose Level
SEX: MALE

Animal ID: 0506
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
ADRENAL GLAND - BILATERAL, PIGMENTATION, PALE	ADRENAL GLAND - No corresponding lesion
LUNG - BILATERAL, FOCUS, 1 X 1 MM, RED, MULTIPLE	LUNG - Accumulation, foamy macrophage; LUNG - Hemorrhage
LUNG - BILATERAL, PIGMENTATION, PALE, RED, TAN	LUNG - Hemorrhage
LUNG - LEFT, NODULE, 2 X 3 MM, TAN	LUNG - Inflammation, chronic, interstitium

Animal ID: 0507
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, MOTTLED, RED, WHITE	LUNG - Accumulation, foamy macrophage; LUNG - Congestion

Animal ID: 0508
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, MOTTLED, RED, WHITE	LUNG - Hemorrhage; LUNG - Accumulation, foamy macrophage

Animal ID: 0510
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, FOCUS, MULTIPLE, WHITE	LUNG - Accumulation, foamy macrophage
LIVER - MEDIAN LOBE, NODULE, 30 X 17 X 20 MM, RED	LIVER - Hepatodiaphragmatic nodule

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 3: 2.0 mg base/kg/day Dose Level
SEX: MALE

Animal ID: 0511
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LIVER - PIGMENTATION, MOTTLED	LIVER - Congestion, centrilobular
LUNG - BILATERAL, FOCUS, 5 X 5 MM, MULTIPLE, WHITE	LUNG - Accumulation, foamy macrophage

Animal ID: 0512
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, NODULE, 3 X 3 X 3 MM, MULTIPLE, WHITE	LUNG - Accumulation, foamy macrophage

Animal ID: 0513
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, FOCUS, 1 X 1 MM, WHITE, MULTIPLE	LUNG - Accumulation, foamy macrophage; LUNG - Inflammation, chronic, interstitium
LUNG - BILATERAL, PIGMENTATION, TAN, RED, PURPLE, PINK	LUNG - Inflammation, chronic, interstitium

Animal ID: 0514
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, NODULE, 5 X 3 X 10 MM, MULTIPLE, WHITE	LUNG - Accumulation, foamy macrophage

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152
FATE: ALL

STUDY NUMBER: SN152
GROUP: 3: 2.0 mg base/kg/day Dose Level
SEX: MALE

Animal ID: 0515
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:
LUNG - BILATERAL, PIGMENTATION, MOTTLED, WHITE, RED

Related Histopathology:
LUNG - Accumulation, foamy macrophage; LUNG - Hemorrhage

Animal ID: 0516
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:
LUNG - BILATERAL, FOCUS, MULTIPLE, WHITE

Related Histopathology:
LUNG - Accumulation, foamy macrophage

Animal ID: 0518
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:
LUNG - BILATERAL, PIGMENTATION, MOTTLED, RED, WHITE

Related Histopathology:
LUNG - Accumulation, foamy macrophage

Animal ID: 0519
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:
LUNG - BILATERAL, FOCUS, 2 X 2 MM, WHITE, MULTIPLE

Related Histopathology:
LUNG - Accumulation, foamy macrophage

Animal ID: 0520
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:
LUNG - BILATERAL, PIGMENTATION, MOTTLED

Related Histopathology:
LUNG - Accumulation, foamy macrophage

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 4: 9.0 mg base/kg/day Dose Level
SEX: MALE

Animal ID: 0551
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LIVER - LESION, MOTTLED	LIVER - Necrosis, coagulation; LIVER - Apoptosis, centrilobular
LUNG - BILATERAL, FOCUS, WHITE, MULTIPLE	LUNG - Inflammation, chronic, interstitium; LUNG - Accumulation, foamy macrophage
LUNG - BILATERAL, PIGMENTATION, PURPLE, RED	LUNG - Hemorrhage

Animal ID: 0552
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
SPLEEN - ENLARGED	SPLEEN - Congestion; SPLEEN - Hyperplasia, Reticuloendothelial cell
LUNG - BILATERAL, PIGMENTATION, MOTTLED, RED, WHITE	LUNG - Inflammation, chronic, interstitium; LUNG - Accumulation, foamy macrophage

Animal ID: 0553
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, FOCUS, TAN, MULTIPLE	LUNG - Inflammation, chronic, interstitium
LUNG - BILATERAL, PIGMENTATION, PURPLE	LUNG - No corresponding lesion

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TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152
FATE: ALL

STUDY NUMBER: SN152
GROUP: 4: 9.0 mg base/kg/day Dose Level
SEX: MALE

Animal ID: 0554
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, MOTTLED	LUNG - Inflammation, chronic, interstitium; LUNG - Accumulation, foamy macrophage

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Animal ID: 0555
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, MOTTLED, RED, WHITE	LUNG - Inflammation, chronic, interstitium; LUNG - Accumulation, foamy macrophage

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Animal ID: 0556
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, FOCUS, MULTIPLE, WHITE	LUNG - Inflammation, chronic, interstitium; LUNG - Accumulation, foamy macrophage

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Animal ID: 0557
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
SPLEEN - ENLARGED	SPLEEN - Congestion
LUNG - BILATERAL, PIGMENTATION, MOTTLED, WHITE, RED	LUNG - Inflammation, chronic, interstitium; LUNG - Hemorrhage; LUNG - Accumulation, foamy macrophage

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 4: 9.0 mg base/kg/day Dose Level
SEX: MALE

Animal ID: 0558
Animal Fate: Found dead

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, FOCUS, WHITE, MULTIPLE	LUNG - Inflammation, chronic, interstitium

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Animal ID: 0559
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, TAN, PURPLE, RED	LUNG - Hemorrhage; LUNG - Accumulation, foamy macrophage
LUNG - BILATERAL, FOCUS, 10 X 12 MM, TAN, MULTIPLE	LUNG - Inflammation, chronic, interstitium
SPLEEN - ENLARGED, 50 X 15 X 5 MM	SPLEEN - Congestion

Animal ID: 0560
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, FOCUS, 10 X 5 MM, WHITE, MULTIPLE	LUNG - Inflammation, chronic, interstitium; LUNG - Accumulation, foamy macrophage

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Animal ID: 0561
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
URINARY BLADDER - LACERATION, 4 X 10 MM	URINARY BLADDER - No corresponding lesion
LUNG - BILATERAL, PIGMENTATION, PURPLE, RED, TAN	LUNG - Hemorrhage; LUNG - Accumulation, foamy macrophage
SPLEEN - ENLARGED, 45 X 10 X 5 MM	SPLEEN - Congestion

PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152
FATE: ALL

STUDY NUMBER: SN152
GROUP: 4: 9.0 mg base/kg/day Dose Level
SEX: MALE

Animal ID: 0562
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, FOCUS, MULTIPLE, WHITE	LUNG - Inflammation, chronic, interstitium; LUNG - Accumulation, foamy macrophage
SPLEEN - ENLARGED	SPLEEN - Congestion
LIVER - LEFT LATERAL LOBE, ENLARGED	LIVER - No corresponding lesion
KIDNEY - RIGHT, ENLARGED	KIDNEY - No corresponding lesion

Animal ID: 0563
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, FOCUS, 5 X 8 MM - 10 X 10 MM, TAN, MULTIPLE	LUNG - Hemorrhage; LUNG - Accumulation, foamy macrophage
LUNG - BILATERAL, NODULE, 1 X 2 MM - 3 X 5 MM, MULTIPLE	LUNG - Inflammation, chronic, interstitium

Animal ID: 0564
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
KIDNEY - BILATERAL, PIGMENTATION, MOTTLED	KIDNEY - No corresponding lesion
LUNG - BILATERAL, PIGMENTATION, MOTTLED	LUNG - Inflammation, chronic, interstitium; LUNG - Hemorrhage; LUNG - Accumulation, foamy macrophage
SPLEEN - ENLARGED, 50 X 15 X 5 MM	SPLEEN - Congestion

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152
FATE: ALL

STUDY NUMBER: SN152
GROUP: 4: 9.0 mg base/kg/day Dose Level
SEX: MALE

Animal ID: 0565
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
SPLEEN - ENLARGED	SPLEEN - Congestion
LUNG - BILATERAL, PIGMENTATION, MOTTLED, RED, WHITE	LUNG - Inflammation, chronic, interstitium; LUNG - Accumulation, foamy macrophage

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Animal ID: 0566
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
SPLEEN - ENLARGED	SPLEEN - Congestion
THYMUS - SMALL	THYMUS - Depletion, lymphoid
LUNG - BILATERAL, PIGMENTATION, MOTTLED, RED, WHITE	LUNG - Inflammation, chronic, interstitium; LUNG - Hemorrhage; LUNG - Accumulation, foamy macrophage

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Animal ID: 0567
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, MOTTLED	LUNG - Inflammation, chronic, interstitium

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Animal ID: 0568
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, FOCUS, 15 X 10 X 5 MM, MULTIPLE, WHITE	LUNG - Inflammation, chronic, interstitium; LUNG - Accumulation, foamy macrophage

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TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152
FATE: ALL

STUDY NUMBER: SN152
GROUP: 4: 9.0 mg base/kg/day Dose Level
SEX: MALE

Animal ID: 0569
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
KIDNEY - BILATERAL, PIGMENTATION, MOTTLED	KIDNEY - No corresponding lesion
LIVER - DEFORMITY, MOTTLED	LIVER - Apoptosis, centrilobular; LIVER - Fatty change, centrilobular
LUNG - BILATERAL, PIGMENTATION, PURPLE, PALE	LUNG - Inflammation, chronic, interstitium; LUNG - Hemorrhage; LUNG - Accumulation, foamy macrophage

Animal ID: 0570
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, FOCUS, 1 X 1 MM, MULTIPLE, WHITE	LUNG - Inflammation, chronic, interstitium; LUNG - Accumulation, foamy macrophage
LUNG - BILATERAL, NODULE, 3 X 5 MM, TAN	LUNG - Inflammation, chronic, interstitium
LUNG - BILATERAL, PIGMENTATION, PALE	LUNG - No corresponding lesion
SPLEEN - ENLARGED	SPLEEN - Congestion

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152
FATE: ALL

STUDY NUMBER: SN152
GROUP: 1: 0 mg base/kg/day Dose Level
SEX: FEMALE

Animal ID: 0426
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, MOTTLED, RED, PURPLE	LUNG - No corresponding lesion

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Animal ID: 0427
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, MOTTLED, PURPLE, RED	LUNG - No corresponding lesion

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Animal ID: 0428
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, FOCUS, 1 X 1 MM, RED	LUNG - Hemorrhage
KIDNEY - RIGHT PELVIS, DILATATION	KIDNEY - Hydronephrosis
PITUITARY GLAND - ENLARGED, 5 X 5 MM	PITUITARY GLAND - No corresponding lesion

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Animal ID: 0429
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, MOTTLED, PURPLE, RED	LUNG - Hemorrhage

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152
FATE: ALL

STUDY NUMBER: SN152
GROUP: 1: 0 mg base/kg/day Dose Level
SEX: FEMALE

Animal ID: 0433
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
MAMMARY GLAND - INGUINAL, NODULE, 10 X 7 MM, WHITE, MULTIPLE	MAMMARY GLAND - Cyst, milk

Animal ID: 0434
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, MOTTLED, PURPLE, RED	LUNG - No corresponding lesion

Animal ID: 0435
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
MESENTERY - NODULE, 10 X 7 X 3 MM, YELLOW	MESENTERY - Necrosis, fat

Animal ID: 0437
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
OVARY - BILATERAL, PIGMENTATION, RED, MULTIPLE	OVARY - Necrosis, corpus luteum

Animal ID: 0438
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
MAMMARY GLAND - ABDOMINAL, NODULE, 10 X 10 MM, WHITE, MULTIPLE	MAMMARY GLAND - Cyst, milk
MAMMARY GLAND - CERVICAL, NODULE, 5 X 5 MM, WHITE, MULTIPLE	MAMMARY GLAND - Cyst, milk

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TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152
FATE: ALL

STUDY NUMBER: SN152
GROUP: 1: 0 mg base/kg/day Dose Level
SEX: FEMALE

Animal ID: 0438
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, PURPLE, RED	LUNG - No corresponding lesion

Animal ID: 0439
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
PITUITARY GLAND - ENLARGED, 5 X 3 X 4 MM	PITUITARY GLAND - No corresponding lesion

Animal ID: 0440
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
KIDNEY - BILATERAL, PIGMENTATION, MOTTLED	KIDNEY - No corresponding lesion
LUNG - BILATERAL, PIGMENTATION, MOTTLED	LUNG - No corresponding lesion

Animal ID: 0441
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
MAMMARY GLAND - INGUINAL, NODULE, 8 X 10 MM, WHITE, MULTIPLE	MAMMARY GLAND - Cyst, milk
MAMMARY GLAND - CERVICAL, NODULE, 10 X 10 X 10 MM, CLEAR, SINGLE	MAMMARY GLAND - Cyst, milk
MAMMARY GLAND - CERVICAL, NODULE, 8 X 10 MM, WHITE, MULTIPLE	MAMMARY GLAND - Cyst, milk
PITUITARY GLAND - ENLARGED, 5 X 7 X 5 MM	PITUITARY GLAND - No corresponding lesion
LUNG - BILATERAL, PIGMENTATION, MOTTLED	LUNG - Hemorrhage

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PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152
FATE: ALL

STUDY NUMBER: SN152
GROUP: 1: 0 mg base/kg/day Dose Level
SEX: FEMALE

Animal ID: 0442
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, TAN, PINK, PURPLE	LUNG - Hemorrhage

Animal ID: 0444
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
SPLEEN - LESION, WHITE	SPLEEN - Adhesion
KIDNEY - BILATERAL, PELVIS, DILATATION	KIDNEY - Hydronephrosis

Animal ID: 0445
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
OVARY - LEFT, SMALL, 0.5 MM X 0.5 MM	OVARY - No corresponding lesion

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 2: 0.5 mg base/kg/day Dose Level
SEX: FEMALE

Animal ID: 0478
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, MOTTLED	LUNG - Hemorrhage

Animal ID: 0479
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, FOCUS, 1 X 1 MM, RED, MULTIPLE	LUNG - No corresponding lesion
LUNG - BILATERAL, PIGMENTATION, MOTTLED	LUNG - No corresponding lesion

---

Animal ID: 0481
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
MAMMARY GLAND - INGUINAL, NODULE, 12 X 12 X 12 MM, WHITE, MULTIPLE	MAMMARY GLAND - Cyst, milk
KIDNEY - BILATERAL, PIGMENTATION, MOTTLED	KIDNEY - Nephropathy
LUNG - BILATERAL, PIGMENTATION, MOTTLED	LUNG - Hemorrhage

Animal ID: 0482
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
BONE - TIBIA, FRACTURE	BONE - Fracture, healed

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152 — STUDY NUMBER: SN152
FATE: ALL — GROUP: 2: 0.5 mg base/kg/day Dose Level
SEX: FEMALE

Animal ID: 0485
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, PURPLE, RED	LUNG - Hemorrhage

Animal ID: 0486
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, FOCUS, 1 X 1 MM, RED, MULTIPLE	LUNG - Hemorrhage
LUNG - BILATERAL, PIGMENTATION, MOTTLED	LUNG - Hemorrhage

Animal ID: 0487
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
PITUITARY GLAND - ENLARGED, 6 X 5 X 2 MM	PITUITARY GLAND - No corresponding lesion

Animal ID: 0490
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
MAMMARY GLAND - THORACIC, NODULE, 5 X 7 X 2 MM, MULTIPLE, WHITE	MAMMARY GLAND - Cyst, milk
LUNG - BILATERAL, PIGMENTATION, PURPLE, RED	LUNG - Hemorrhage
PITUITARY GLAND - ENLARGED, 7 X 8 X 3 MM	PITUITARY GLAND - No corresponding lesion

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152 | STUDY NUMBER: SN152
FATE: ALL | GROUP: 2: 0.5 mg base/kg/day Dose Level
SEX: FEMALE

Animal ID: 0491
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
OVARY - UNILATERAL, SMALL	OVARY - Atrophy

Animal ID: 0492
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
SPLEEN - CYST, 5 X 2 MM, CLEAR, MULTIPLE	SPLEEN - Cyst, serosa
LUNG - BILATERAL, PIGMENTATION, MOTTLED, PURPLE, RED	LUNG - Hemorrhage

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152
FATE: ALL

STUDY NUMBER: SN152
GROUP: 3: 2.0 mg base/kg/day Dose Level
SEX: FEMALE

Animal ID: 0526
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:
LUNG - BILATERAL, NODULE, 3 X 3 X 3 MM, MULTIPLE, WHITE

Related Histopathology:
LUNG - Accumulation, foamy macrophage

Animal ID: 0527
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:
LUNG - BILATERAL, PIGMENTATION, MOTTLED, RED, WHITE

Related Histopathology:
LUNG - Accumulation, foamy macrophage

Animal ID: 0528
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:
LUNG - BILATERAL, PIGMENTATION, MOTTLED, RED, WHITE

Related Histopathology:
LUNG - Hemorrhage; LUNG - Accumulation, foamy macrophage

Animal ID: 0529
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:
LUNG - BILATERAL, NODULE, 5 X 5 MM, TAN, MULTIPLE

Related Histopathology:
LUNG - Accumulation, foamy macrophage; LUNG - Inflammation, chronic, interstitium

---

Animal ID: 0530
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:
LUNG - BILATERAL, PIGMENTATION, PALE, PURPLE, PINK

Related Histopathology:
LUNG - Accumulation, foamy macrophage; LUNG - Inflammation, chronic, interstitium; LUNG - Hemorrhage

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152
FATE: ALL

STUDY NUMBER: SN152
GROUP: 3: 2.0 mg base/kg/day Dose Level
SEX: FEMALE

Animal ID: 0530
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, NODULE, 2 X 3 MM, TAN, MULTIPLE	LUNG - Inflammation, chronic, interstitium; LUNG - Accumulation, foamy macrophage

Animal ID: 0531
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, NODULE, 2 X 2 MM, TAN, MULTIPLE	LUNG - Inflammation, chronic, interstitium
LUNG - BILATERAL, PIGMENTATION, MOTTLED	LUNG - Inflammation, chronic, interstitium; LUNG - Hemorrhage
LIVER - HERNIA, 15 X 25 X 10 MM, MOTTLED	LIVER - Hepatodiaphragmatic nodule

Animal ID: 0532
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, NODULE, 3 X 3 X 3 MM, MULTIPLE, WHITE	LUNG - Accumulation, foamy macrophage; LUNG - Inflammation, chronic, interstitium

Animal ID: 0533
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, MOTTLED	LUNG - Accumulation, foamy macrophage; LUNG - Inflammation, chronic, interstitium
LUNG - BILATERAL, NODULE, 10 X 10 MM, TAN, MULTIPLE	LUNG - Inflammation, chronic, interstitium; LUNG - Accumulation, foamy macrophage

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PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152
FATE: ALL

STUDY NUMBER: SN152
GROUP: 3: 2.0 mg base/kg/day Dose Level
SEX: FEMALE

Animal ID: 0534
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, MOTTLED, PURPLE, WHITE	LUNG - Inflammation, chronic, interstitium; LUNG - Accumulation, foamy macrophage

---

Animal ID: 0535
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, MOTTLED	LUNG - Accumulation, foamy macrophage; LUNG - Inflammation, chronic, interstitium
LUNG - BILATERAL, NODULE, 2 X 2 MM, WHITE, MULTIPLE	LUNG - Inflammation, chronic, interstitium; LUNG - Accumulation, foamy macrophage

---

Animal ID: 0537
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, PURPLE, RED, WHITE	LUNG - Accumulation, foamy macrophage; LUNG - Inflammation, chronic, interstitium

---

Animal ID: 0538
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, NODULE, 2 X 2 X 2 MM, WHITE, MULTIPLE	LUNG - Accumulation, foamy macrophage; LUNG - Inflammation, chronic, interstitium

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152
FATE: ALL

STUDY NUMBER: SN152
GROUP: 3: 2.0 mg base/kg/day Dose Level
SEX: FEMALE

Animal ID: 0539
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
KIDNEY - BILATERAL, PELVIS, DILATATION	KIDNEY - Hydronephrosis
BRAIN - LEFT, ADHESION, 5 X 6 MM	BRAIN - No corresponding lesion
PITUITARY GLAND - ENLARGED, 5 X 4 MM	PITUITARY GLAND - No corresponding lesion
LUNG - BILATERAL, PIGMENTATION, MULTIPLE, WHITE	LUNG - Accumulation, foamy macrophage; LUNG - Inflammation, chronic, interstitium

---

Animal ID: 0540
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, DARK RED, WHITE	LUNG - Accumulation, foamy macrophage; LUNG - Inflammation, chronic, interstitium

---

Animal ID: 0541
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, NODULE, 3 X 3 MM, TAN, MULTIPLE	LUNG - Accumulation, foamy macrophage; LUNG - Inflammation, chronic, interstitium
LUNG - BILATERAL, PIGMENTATION, MOTTLED	LUNG - Inflammation, chronic, interstitium; LUNG - Accumulation, foamy macrophage

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152
FATE: ALL

STUDY NUMBER: SN152
GROUP: 3: 2.0 mg base/kg/day Dose Level
SEX: FEMALE

Animal ID: 0542
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, FOCUS, 2 X 2 X 2 MM, MULTIPLE, WHITE	LUNG - Accumulation, foamy macrophage; LUNG - Inflammation, chronic, interstitium

---

Animal ID: 0543
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, NODULE, 3 MM X 4 MM X 3 MM, WHITE, MULTIPLE	LUNG - Accumulation, foamy macrophage; LUNG - Inflammation, chronic, interstitium

---

Animal ID: 0544
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, PURPLE, TAN	LUNG - Accumulation, foamy macrophage; LUNG - Inflammation, chronic, interstitium
LUNG - BILATERAL, NODULE, 2 X 3 MM, TAN, MULTIPLE	LUNG - Inflammation, chronic, interstitium; LUNG - Accumulation, foamy macrophage

---

Animal ID: 0545
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, DARK RED	LUNG - Congestion

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152
FATE: ALL

STUDY NUMBER: SN152
GROUP: 4: 9.0 mg base/kg/day Dose Level
SEX: FEMALE

Animal ID: 0576
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, MOTTLED	LUNG - Inflammation, chronic, interstitium; LUNG - Hemorrhage; LUNG - Accumulation, foamy macrophage

---

Animal ID: 0577
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, MOTTLED, RED, WHITE	LUNG - Inflammation, chronic, interstitium; LUNG - Hemorrhage; LUNG - Accumulation, foamy macrophage

---

Animal ID: 0578
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
KIDNEY - RIGHT, DILATATION	KIDNEY - Hydronephrosis
LUNG - BILATERAL, NODULE, 1 X 5 MM, WHITE, MULTIPLE	LUNG - Inflammation, chronic, interstitium; LUNG - Hemorrhage; LUNG - Accumulation, foamy macrophage

---

Animal ID: 0579
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
SPLEEN - ENLARGED	SPLEEN - Congestion
THYMUS - SMALL	THYMUS - Depletion, lymphoid
LUNG - BILATERAL, PIGMENTATION, MOTTLED, RED, WHITE	LUNG - Inflammation, chronic, interstitium; LUNG - Hemorrhage; LUNG - Accumulation, foamy macrophage

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152 | STUDY NUMBER: SN152
FATE: ALL | GROUP: 4: 9.0 mg base/kg/day Dose Level
SEX: FEMALE

Animal ID: 0580
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, MOTTLED	LUNG - Inflammation, chronic, interstitium; LUNG - Hemorrhage; LUNG - Accumulation, foamy macrophage

Animal ID: 0581
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
THYMUS - SMALL	THYMUS - Depletion, lymphoid
LUNG - BILATERAL, PIGMENTATION, MOTTLED, PURPLE, RED	LUNG - Inflammation, chronic, interstitium; LUNG - Hemorrhage; LUNG - Accumulation, foamy macrophage

Animal ID: 0582
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, NODULE, 5 X 5 X 5 MM, MULTIPLE, TAN	LUNG - Inflammation, chronic, interstitium; LUNG - Accumulation, foamy macrophage

Animal ID: 0583
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, MOTTLED	LUNG - Hemorrhage; LUNG - Accumulation, foamy macrophage
LUNG - BILATERAL, NODULE, 10 X 10 MM, TAN, MULTIPLE	LUNG - Inflammation, chronic, interstitium

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152
FATE: ALL

STUDY NUMBER: SN152
GROUP: 4: 9.0 mg base/kg/day Dose Level
SEX: FEMALE

Animal ID: 0584
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, PURPLE	LUNG - Hemorrhage
LUNG - BILATERAL, FOCUS, 10 X 12 MM, TAN	LUNG - Inflammation, chronic, interstitium

Animal ID: 0585
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, MOTTLED	LUNG - Inflammation, chronic, interstitium; LUNG - Hemorrhage; LUNG - Accumulation, foamy macrophage

Animal ID: 0586
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, MOTTLED	LUNG - Inflammation, chronic, interstitium; LUNG - Hemorrhage; LUNG - Accumulation, foamy macrophage

Animal ID: 0587
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
SPLEEN - ENLARGED	SPLEEN - Congestion
LUNG - BILATERAL, PIGMENTATION, MOTTLED, RED, WHITE	LUNG - Inflammation, chronic, interstitium; LUNG - Hemorrhage; LUNG - Accumulation, foamy macrophage

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152
FATE: ALL

STUDY NUMBER: SN152
GROUP: 4: 9.0 mg base/kg/day Dose Level
SEX: FEMALE

Animal ID: 0588
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, MOTTLED, WHITE	LUNG - Inflammation, chronic, interstitium; LUNG - Hemorrhage; LUNG - Accumulation, foamy macrophage

Animal ID: 0589
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, PURPLE, TAN	LUNG - Inflammation, chronic, interstitium; LUNG - Hemorrhage; LUNG - Accumulation, foamy macrophage

Animal ID: 0590
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, MOTTLED	LUNG - Inflammation, chronic, interstitium; LUNG - Hemorrhage; LUNG - Accumulation, foamy macrophage

Animal ID: 0591
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, NODULE, 5 X 5 MM, TAN, MULTIPLE	LUNG - Inflammation, chronic, interstitium; LUNG - Accumulation, foamy macrophage
LUNG - BILATERAL, PIGMENTATION, MOTTLED	LUNG - Hemorrhage

PATHOLOGY ASSOCIATES INTERNATIONAL
SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS
TOXICOLOGY RESEARCH LABORATORY STUDY NUMBER 152

CORRELATION OF GROSS & MICRO

STUDY ID : SN152
FATE: ALL

STUDY NUMBER: SN152
GROUP: 4: 9.0 mg base/kg/day Dose Level
SEX: FEMALE

Animal ID: 0592
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, MOTTLED	LUNG - Inflammation, chronic, interstitium; LUNG - Hemorrhage; LUNG - Accumulation, foamy macrophage

Animal ID: 0593
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, PIGMENTATION, MOTTLED	LUNG - Inflammation, chronic, interstitium; LUNG - Hemorrhage; LUNG - Accumulation, foamy macrophage

Animal ID: 0594
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
UTERUS - BILATERAL, DILATATION	UTERUS - Dilatation
LUNG - BILATERAL, PIGMENTATION, MOTTLED	LUNG - Hemorrhage; LUNG - Accumulation, foamy macrophage
LUNG - BILATERAL, NODULE, 8 X 10 MM, TAN, MULTIPLE	LUNG - Inflammation, chronic, interstitium

Animal ID: 0595
Animal Fate: Scheduled sacrifice

Reference to Necropsy Record:	Related Histopathology:
LUNG - BILATERAL, FOCUS, WHITE	LUNG - Inflammation, chronic, interstitium; LUNG - Accumulation, foamy macrophage

SECTION VI

QUALITY ASSURANCE STATEMENT

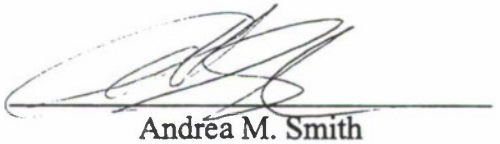
QUALITY ASSURANCE STATEMENT

This histopathology project was inspected and audited by the PAI Quality Assurance Unit (QAU) as required by the Good Laboratory Practice (GLP) standards promulgated by the U.S. Food and Drug Administration. The pathology narrative report is an accurate reflection of the recorded data. The following table is a record of the inspections/audits performed and reported by the QAU:

	Date of Inspection	Phase Inspected	Date Findings Reported to Management and Study Pathologist
*	11/08/95	Tissue Trimming	11/08/95
*	01/05/96	Processing/Embedding	01/05/96
*	03/27/96	Microtomy	03/28/96
*	12/29/95	Staining	12/29/95
*	12/29/95	Coverslipping	12/29/95
*	05/13/96	Labeling	05/13/96
*	11/16/95	Quality Control/Checkout	11/16/95
**	06/26/96	Individual Animal Data	06/26/96
**	06/26/96	Draft Pathology Report	06/26/96
**	06/28/96	Revised Draft Pathology Report	06/28/96

* General quarterly phase inspection
** Inspection specific for this study

In accordance with the PAI Quality Assurance Division's Standard Operating Procedures, all critical phase inspections are conducted on a random basis quarterly or more frequently. Those general phase inspections listed are the most recent conducted during the period each task associated with this project was performed.



Andrea M. Smith
Quality Assurance Unit
PAI Illinois Division

06/28/96
Date

SECTION VII

BONE MARROW EVALUATION REPORT

BONE MARROW EVALUATION REPORT FOR

SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS

TRL STUDY NUMBER 152

PREPARED FOR
TOXICOLOGY RESEARCH LABORATORY

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I. Bone Marrow Evaluation Narrative

BONE MARROW EVALUATION REPORT

SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS

INTRODUCTION

This report prepared by Pathology Associates International (PAI) for Toxicology Research Laboratory (UIC/TRL), University of Illinois at Chicago, Department of Pharmacology, 1940 West Taylor Street, Chicago, IL, 60612, presents the results of bone marrow evaluation from CD® rats given WR238605 succinate once daily by gavage for at least twenty-six weeks.

EXPERIMENTAL DESIGN AND METHODS

One hundred male and one hundred female CD® rats were randomized into one of four groups as described below.

Treatment Group	Dose Level (mg base/kg/day)	Dose Conc. (mg base/ml)	Dose Volume (ml/kg/day)	Number of Males	Number of Females
1	0	0	5	20 + 5*	20 + 5*
2	0.5	0.1	5	20 + 5*	20 + 5*
3	2.0	0.4	5	20 + 5*	20 + 5*
4	9.0	1.8	5	20 + 5*	20 + 5*

*Five satellite rats/sex/dose were utilized for the collection of blood samples for plasma drug level analysis. No pathology evaluations were done on these animals.

Bone marrow smears were prepared from the femur of each animal at the scheduled necropsy during Week 27. The smears were fixed in methanol, stained with a Wrights-Giemsa stain, and evaluated microscopically to determine the Myeloid:Erythroid (M:E) Ratio. The M:E Ratio was determined on a cell count of 500 cells.

Statistical analysis of the data was performed by UIC/TRL and provided to PAI for inclusion in this report.

RESULTS

M:E Ratio Group Summary tables are presented in Section II (generated by UIC/TRL from PAI data sheets). Individual animal M:E Ratio data are presented by dose group and sex in Section III (generated by UIC/TRL from PAI data sheets).

The M:E Ratios from high dose and control animals necropsied during Week 27 were not significantly different and within normal limits.

CONCLUSION

Under the conditions of this study, WR238605 did not result in any treatment-related changes in the M:E Ratio of the femoral bone marrow of male and female treated rats during Week 27.

Lynda L. Lanning, D.V.M., D.A.B.T.
May 17, 1996

II. M:E Ratio Summary Tables

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY REPORT
TEST: M:E RATIO

STUDY ID: UIC-15B
STUDY NO: 1528M
ABBR: M:E RATIO

SEX: MALE

UNITS: -

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

GROUP(s):	1-M	2-M	3-M	4-M
Period: Week 27				
MEAN	1.53	NA	NA	1.56
SD	0.094	NA	NA	0.106
N	20	0	0	19

NA-Not Applicable

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY REPORT
TEST: M:E RATIO

STUDY ID: UIC-15B
STUDY NO: 1529M
ABBR: M:E RATIO

SEX: FEMALE

UNITS: -

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

GROUP(s):	1-F	2-F	3-F	4-F
Period: Week 27				
MEAN	1.57	NA	NA	1.57
SD	0.073	NA	NA	0.096
N	20	0	0	20

NA-Not Applicable

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY-REPORT
TEST: M:E RATIO

STUDY ID: UIC-15B
STUDY NO: 152BM
ABBR: M:E RATIO

SEX: MALE

UNITS: -

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 27

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	20	30.67	1.53	0.094				TREATMENTS	1	0.007	0.007
2-M	NA	0.00	0.00	NA				ERROR	37	0.370	0.010
3-M	NA	0.00	0.00	NA							
4-M	19	29.63	1.56	0.106				TOTAL	38	0.377	

F Ratio = 0.66 'F' table values F.01 = 7.39 F.05 = 4.11
Coeff. Var. % = 6.469 Dunnett's 'T' table values P.01 = 2.70 P.05 = 2.02

Error-within groups
NA-Not Applicable

Source-Source of Variation
Treatments-between groups

SUMMARY REPORT
TEST: M:E RATIO

STUDY ID: UIC-158
STUDY NO: 152BM
ABBR: M:E RATIO

SEX: FEMALE

UNITS: -

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 27

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI
1-F	20	31.36	1.57	0.073			
2-F	NA	0.00	0.00	NA			
3-F	NA	0.00	0.00	NA			
4-F	20	31.41	1.57	0.096			

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	1	0.000	0.000
ERROR	38	0.277	0.007
TOTAL	39	0.277	

F Ratio = 0.01 'F' table values F.01 = 7.35 F.05 = 4.10
Coeff. Var. % = 5.441 Dunnett's 'T' table values P.01 = 2.70 P.05 = 2.02

Error-within groups
NA-Not Applicable

Source-Source of Variation
Treatments-between groups

III. Individual Animal M:E Ratio Tables

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: M:E RATIO

STUDY ID: UIC-15B
STUDY NO: 1528M
ABBR: M:E RATIO

SEX: MALE

UNITS: -

Animal ID	Week 27
GROUP: 1-M:0 mg base/kg/day	
401	1.43
402	1.51
403	1.37
404	1.50
405	1.59
406	1.56
407	1.72
408	1.43
409	1.49
410	1.54
411	1.62
412	1.49
413	1.50
414	1.39
415	1.55
416	1.70
417	1.63
418	1.48
419	1.58
420	1.59
MEAN	1.53
SD	0.094
N	20

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: M:E RATIO

STUDY ID: UIC-15B
STUDY NO: 152BM
ABBR: M:E RATIO

SEX: MALE

UNITS: -

Animal ID	Week 27
GROUP: 4-M:9.0 mg base/kg/day	
551	1.63
552	1.54
553	1.73
554	1.53
555	1.59
556	1.55
557	1.28
558	--
559	1.62
560	1.45
561	1.50
562	1.69
563	1.63
564	1.40
565	1.58
566	1.51
567	1.56
568	1.65
569	1.53
570	1.66
MEAN	1.56
SD	0.106
N	19

(--) - Data Unavailable

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: M:E RATIO

STUDY ID: UIC-15B
STUDY NO: 152BM
ABBR: M:E RATIO

SEX: FEMALE

UNITS: -

Animal ID	Week 27
GROUP: 1-F:0 mg base/kg/day	
426	1.63
427	1.51
428	1.58
429	1.72
430	1.54
431	1.51
432	1.56
433	1.50
434	1.60
435	1.46
436	1.62
437	1.65
438	1.55
439	1.56
440	1.49
441	1.44
442	1.54
443	1.67
444	1.63
445	1.60
MEAN	1.57
SD	0.073
N	20

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: M:E RATIO

STUDY ID: UIC-158
STUDY NO: 152BM
ABBR: M:E RATIO

SEX: FEMALE

UNITS: -

Animal ID	Week 27
GROUP: 4-F:9.0 mg base/kg/day	
576	1.67
577	1.50
578	1.60
579	1.55
580	1.59
581	1.49
582	1.51
583	1.40
584	1.65
585	1.63
586	1.73
587	1.48
588	1.53
589	1.62
590	1.65
591	1.70
592	1.58
593	1.51
594	1.37
595	1.65
MEAN	1.57
SD	0.096
N	20

IV. Quality Assurance Statement

Bone Marrow Evaluation Report

Six Month Oral Toxicity Study of WR238605 Succinate in Rats

TRL Study Number: 152

QUALITY ASSURANCE STATEMENT

This bone marrow evaluation project has been inspected and audited by the PAI Quality Assurance Unit (QAU) as required by the Good Laboratory Practice (GLP) regulations promulgated by the U.S. Food and Drug Administration or U.S. Environmental Protection Agency. The bone marrow evaluation report is an accurate reflection of the recorded data. The following table is a record of the inspections/audits performed and reported by the QAU.

Date of Inspection	Phase Inspected	Date Findings Reported to Management/ Study Pathologist
04/15/96	Individual Animal Data	04/15/96
04/15/96	Draft Bone Marrow Evaluation Report	04/15/96

Sharon E. Abel
Quality Assurance Auditor

May 29, 1996
Date

15 Worman's Mill Court, Suite I • Frederick, Maryland 21701 • (301) 663-1644 • (301) 663-8994 FAX

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APPENDIX K

PRE-TEST CLINICAL PATHOLOGY DATA

INDIVIDUAL CLINICAL CHEMISTRY DATA BY GROUP
PERIOD: BASELINE

STUDY ID: 152 QURANTINE/PRETEST
STUDY NO: 152BL

DRAFT

SEX: MALE

Animal ID	ALT IU/L	SDH IU/L	TP g/dL	ALB g/dL	GLOB g/dL	A/G -	TBA umol/L	ALKP IU/L	LDH IU/L
GROUP: 1-M									
119	78	17.8	6.0	3.2	2.8	1.14	108.9	418	263
120	62	16.5	6.8	3.8	3.0	1.27	134.9	459	87
121	46	23.0	6.4	3.7	2.7	1.37	28.0	294	218
122	--	--	--	--	--	--	--	--	--
123	68	14.1	5.7	3.4	2.3	1.48	134.5	470	366
124	--	--	--	--	--	--	--	--	--
125	51	7.0	6.1	3.7	2.4	1.54	96.1	661	670
MEAN	61	15.7	6.2	3.6	2.6	1.36	100.5	460	321
SD	12.9	5.84	0.42	0.25	0.29	0.161	43.83	132.1	219.4
N	5	5	5	5	5	5	5	5	5

(--) - Data Unavailable

INDIVIDUAL CLINICAL CHEMISTRY DATA BY GROUP
PERIOD: BASELINE

STUDY ID: 152 QURANTINE/PRETEST
STUDY NO: 152BL
SEX: MALE

Animal ID	CK IU/L	BUN mg/dL	CREAT mg/dL	NA mEq/L	K mEq/L	CL mEq/L	CA mg/dL	IP mg/dL	GLU mg/dL
GROUP: 1-M									
119	611	14.1	0.50	142	6.77	106	12.0	12.4	195
120	192	12.6	0.44	143	6.29	103	11.4	13.4	157
121	231	12.9	0.43	143	6.60	99	12.5	15.4	157
122	--	--	--	--	--	--	--	--	--
123	505	13.2	0.45	142	6.62	103	12.0	11.9	145
124	--	--	--	--	--	--	--	--	--
125	493	17.6	0.51	143	6.39	103	12.8	10.9	181
MEAN	406	14.1	0.47	143	6.53	103	12.1	12.8	167
SD	184.3	2.05	0.036	0.5	0.192	2.5	0.54	1.71	20.4
N	5	5	5	5	5	5	5	5	5

(--) - Data Unavailable

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

INDIVIDUAL CLINICAL CHEMISTRY DATA BY GROUP
PERIOD: BASELINE

STUDY ID: 152 QURANTINE/PRETEST
STUDY NO: 152BL

DRAFT

SEX: FEMALE

Animal ID	ALT IU/L	SDH IU/L	TP g/dL	ALB g/dL	GLOB g/dL	A/G -	TBA umol/L	ALKP IU/L	LDH IU/L
GROUP: 1-F									
247	49	13.5	6.6	3.9	2.7	1.44	30.9	287	353
248	58	16.0	7.0	3.9	3.1	1.26	67.3	407	210
249	62	17.4	6.4	3.8	2.6	1.46	54.3	192	147
250	63	14.9	6.5	4.0	2.5	1.60	120.9	315	367
251	31	14.6	6.6	3.8	2.8	1.36	22.8	283	559
MEAN	53	15.3	6.6	3.9	2.7	1.42	59.2	297	327
SD	13.3	1.48	0.23	0.08	0.23	0.126	38.80	77.0	159.8
N	5	5	5	5	5	5	5	5	5

INDIVIDUAL CLINICAL CHEMISTRY DATA BY GROUP
PERIOD: BASELINE

STUDY IO: 152 QURANTINE/PRETEST
STUDY NO: 152BL

DRAFT

SEX: FEMALE

Animal IO	CK IU/L	BUN mg/dL	CREAT mg/dL	NA mEq/L	K mEq/L	CL mEq/L	CA mg/dL	IP mg/dL	GLU mg/dL
GROUP: 1-F									
247	430	16.8	0.48	142	6.53	102	12.3	10.8	163
248	445	17.8	0.46	143	6.68	103	12.9	11.4	140
249	269	13.8	0.43	142	5.95	102	12.2	11.3	164
250	532	13.3	0.48	143	6.39	104	12.5	11.9	171
251	345	15.5	0.46	143	6.44	103	12.1	10.8	156
MEAN	404	15.4	0.46	143	6.40	103	12.4	11.2	159
SD	100.6	1.92	0.020	0.5	0.274	0.8	0.32	0.46	11.8
N	5	5	5	5	5	5	5	5	5

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
PERIOD: BASELINE

STUDY ID: 152 QURANTINE
STUDY NO: 152Q

DRAFT

SEX: MALE

Animal ID	RBC 10^6/mm^3	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RETICS % RBCs	HEINZ BOD. % RBCs	% METHGB % HGB
GROUP: 1-M									
119	6.37	14.0	42.4	66.6	22.0	33.0	1.3	0.0	0.1
120	6.32	14.0	42.6	67.4	22.2	32.9	0.9	0.0	0.4
121	5.49	12.5	37.3	67.9	22.8	33.5	2.8	0.0	0.7
123	5.66	12.5	37.8	66.8	22.1	33.1	1.4	0.0	0.4
125	5.54	12.7	38.3	69.1	22.9	33.2	1.8	0.0	0.8
MEAN	5.88	13.1	39.7	67.6	22.4	33.1	1.6	0.0	0.5
SD	0.433	0.79	2.60	1.00	0.42	0.23	0.72	0.00	0.28
N	5	5	5	5	5	5	5	5	5

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
PERIOD: BASELINE

STUDY ID: 152 QURANTINE
STUDY NO: 152Q

DRAFT

SEX: MALE

Animal ID	WBC 10^3/mm^3	M. Neutrop 10^3/mm^3	I. Neutrop 10^3/mm^3	Lymphocyte 10^3/mm^3	Monocytes 10^3/mm^3	Eosinophil 10^3/mm^3	Basophils 10^3/mm^3	PLT 10^3/mm^3
GROUP: 1-M								
119	17.3	3.6	0.0	13.3	0.2	0.2	0.0	1026
120	16.3	3.7	0.0	11.7	0.8	0.0	0.0	1037
121	10.9	1.2	0.0	9.2	0.5	0.0	0.0	889
123	18.5	3.7	0.0	13.5	1.3	0.0	0.0	1087
125	18.1	1.8	0.0	14.5	1.6	0.2	0.0	911
MEAN	16.2	2.8	0.0	12.4	0.9	0.1	0.0	990
SD	3.09	1.21	0.00	2.07	0.57	0.11	0.00	85.7
N	5	5	5	5	5	5	5	5

WBC corrected for NRBC = or > 10

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

WHITE DIFFERENTIAL DATA

STUDY ID: 152 QURANTINE
STUDY NO: 152Q

GROUP: 1-M

DRAFT

SEX: MALE

Animal ID		BASELINE REL	BASELINE ABS
119	Nucleated Red Cells	0	
	M. Neutrophils	21.0	3.6
	I. Neutrophils	0.0	0.0
	Lymphocytes	77.0	13.3
	Monocytes	1.0	0.2
	Eosinophils	1.0	0.2
	Basophils	0.0	0.0
	Atypical Lymphocytes	0.0	0.0
	WBC		17.3
120	Nucleated Red Cells	1	
	M. Neutrophils	23.0	3.7
	I. Neutrophils	0.0	0.0
	Lymphocytes	72.0	11.7
	Monocytes	5.0	0.8
	Eosinophils	0.0	0.0
	Basophils	0.0	0.0
	Atypical Lymphocytes	0.0	0.0
	WBC		16.3
121	Nucleated Red Cells	0	
	M. Neutrophils	11.0	1.2
	I. Neutrophils	0.0	0.0
	Lymphocytes	84.0	9.2
	Monocytes	5.0	0.5
	Eosinophils	0.0	0.0
	Basophils	0.0	0.0
	Atypical Lymphocytes	0.0	0.0
	WBC		10.9
123	Nucleated Red Cells	0	
	M. Neutrophils	20.0	3.7
	I. Neutrophils	0.0	0.0
	Lymphocytes	73.0	13.5
	Monocytes	7.0	1.3
	Eosinophils	0.0	0.0
	Basophils	0.0	0.0
	Atypical Lymphocytes	0.0	0.0
	WBC		18.5

WBC corrected for NRBC = or > 10

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

WHITE DIFFERENTIAL DATA

STUDY ID: 152 QURANTINE
STUDY NO: 152Q

GROUP: 1-M

DRAFT

SEX: MALE

Animal ID		BASELINE REL	BASELINE ABS
125	Nucleated Red Cells	1	
	M. Neutrophils	10.0	1.8
	I. Neutrophils	0.0	0.0
	Lymphocytes	80.0	14.5
	Monocytes	9.0	1.6
	Eosinophils	1.0	0.2
	Basophils	0.0	0.0
	Atypical Lymphocytes	0.0	0.0
	WBC		18.1

WBC corrected for NRBC = or > 10

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 152 QURANTINE
STUDY NO: 152Q

GROUP: 1-M

DRAFT

SEX: MALE

Animal ID	BASELINE
119	Normal Red Blood Cells
120	Normal Red Blood Cells
121	Normal Red Blood Cells
123	Normal Red Blood Cells
125	Normal Red Blood Cells

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
PERIOD: BASELINE

STUDY ID: 152 QURANTINE
STUDY NO: 152Q

DRAFT

SEX: FEMALE

Animal ID	RBC 10^6/mm^3	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RETICS % RBCs	HEINZ BOD. % RBCs	% METHGB % HGB
GROUP: 1-F									
247	5.73	13.1	38.0	66.3	22.9	34.5	1.5	0.0	0.5
248	7.15	15.5	44.7	62.5	21.7	34.7	0.9	0.0	0.8
249	6.25	13.2	37.9	60.6	21.1	34.8	1.1	0.0	0.4
250	6.21	13.5	41.1	66.2	21.7	32.8	1.0	0.0	0.4
251	6.18	14.1	41.5	67.2	22.8	34.0	1.2	0.0	0.7
MEAN	6.30	13.9	40.6	64.6	22.0	34.2	1.1	0.0	0.6
SD	0.518	0.99	2.82	2.86	0.78	0.82	0.23	0.00	0.18
N	5	5	5	5	5	5	5	5	5

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
PERIOD: BASELINE

STUDY ID: 152 QURANTINE
STUDY NO: 152Q

DRAFT

SEX: FEMALE

Animal ID	WBC 10^3/mm^3	M. Neutrop 10^3/mm^3	I. Neutrop 10^3/mm^3	Lymphocyte 10^3/mm^3	Monocytes 10^3/mm^3	Eosinophil 10^3/mm^3	Basophils 10^3/mm^3	PLT 10^3/mm^3
GROUP: 1-F								
247	14.6	2.5	0.0	11.2	0.9	0.0	0.0	1258
248	8.3	0.3	0.0	7.6	0.4	0.0	0.0	853
249	18.0	2.9	0.0	14.4	0.7	0.0	0.0	1188
250	17.8	0.7	0.2	15.3	1.4	0.2	0.0	1025
251	12.2	3.5	0.0	8.3	0.1	0.2	0.0	1113
MEAN	14.2	2.0	0.0	11.4	0.7	0.1	0.0	1087
SD	4.07	1.40	0.09	3.47	0.49	0.11	0.00	157.1
N	5	5	5	5	5	5	5	5

WBC corrected for NRBC = or > 10

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

WHITE DIFFERENTIAL DATA

STUDY ID: 152 QURANTINE
STUDY NO: 152Q

GROUP: 1-F

DRAFT

SEX: FEMALE

Animal ID		BASELINE REL	BASELINE ABS
247	Nucleated Red Cells	1	
	M. Neutrophils	17.0	2.5
	I. Neutrophils	0.0	0.0
	Lymphocytes	77.0	11.2
	Monocytes	6.0	0.9
	Eosinophils	0.0	0.0
	Basophils	0.0	0.0
	Atypical Lymphocytes	0.0	0.0
	WBC		14.6
248	Nucleated Red Cells	0	
	M. Neutrophils	4.0	0.3
	I. Neutrophils	0.0	0.0
	Lymphocytes	91.0	7.6
	Monocytes	5.0	0.4
	Eosinophils	0.0	0.0
	Basophils	0.0	0.0
	Atypical Lymphocytes	0.0	0.0
	WBC		8.3
249	Nucleated Red Cells	0	
	M. Neutrophils	16.0	2.9
	I. Neutrophils	0.0	0.0
	Lymphocytes	80.0	14.4
	Monocytes	4.0	0.7
	Eosinophils	0.0	0.0
	Basophils	0.0	0.0
	Atypical Lymphocytes	0.0	0.0
	WBC		18.0
250	Nucleated Red Cells	0	
	M. Neutrophils	4.0	0.7
	I. Neutrophils	1.0	0.2
	Lymphocytes	86.0	15.3
	Monocytes	8.0	1.4
	Eosinophils	1.0	0.2
	Basophils	0.0	0.0
	Atypical Lymphocytes	0.0	0.0
	WBC		17.8

WBC corrected for NRBC = or > 10

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

WHITE DIFFERENTIAL DATA

STUDY ID: 152 QURANTINE
STUDY NO: 152Q

GROUP: 1-F

DRAFT

SEX: FEMALE

Animal ID		BASELINE REL	BASELINE ABS
251	Nucleated Red Cells	0	
	M. Neutrophils	29.0	3.5
	I. Neutrophils	0.0	0.0
	Lymphocytes	68.0	8.3
	Monocytes	1.0	0.1
	Eosinophils	2.0	0.2
	Basophils	0.0	0.0
	Atypical Lymphocytes	0.0	0.0
	WBC		12.2

WBC corrected for NRBC = or > 10

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 152 QURANTINE
STUDY NO: 152Q

GROUP: 1-F

DRAFT

SEX: FEMALE

Animal ID	BASELINE
247	Normal Red Blood Cells
248	Clumped Platelets, Moderate
249	Normal Red Blood Cells
250	Normal Red Blood Cells
251	Normal Red Blood Cells

DRAFT

APPENDIX L

STATISTICAL ANALYSIS DATA

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Erythrocytes

DRAFT

STUDY ID: UIC-158
STUDY NO: 152
ABBR: RBC

SEX: MALE

UNITS: 10^6/mm^3

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	75.60	7.56	0.460						TREATMENTS	3	1.54	0.51
2-M	10	76.91	7.69	0.270	0.88	7.00	8.00	7.00	8.00	ERROR	36	3.96	0.11
3-M	10	73.14	7.31	0.183	1.66	7.00	8.00	7.00	8.00				
4-M	10	71.93	7.19	0.350	2.47	7.00	8.00*	7.00	8.00	TOTAL	39	5.51	

F Ratio = 4.67 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 4.460 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

1-M	10	82.63	8.26	0.556						TREATMENTS	3	0.60	0.20
2-M	10	83.08	8.31	0.387						ERROR	36	8.18	0.23
3-M	10	81.33	8.13	0.184									
4-M	10	79.93	7.99	0.645						TOTAL	39	8.78	

F Ratio = 0.89 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 5.830 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

1-M	10	83.85	8.39	0.308						TREATMENTS	3	0.11	0.04
2-M	10	82.59	8.26	0.434						ERROR	36	5.14	0.14
3-M	10	82.79	8.28	0.240									
4-M	10	83.52	8.35	0.479						TOTAL	39	5.24	

F Ratio = 0.25 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 4.540 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 27

1-M	NA	0.00	0.00	NA						TREATMENTS	-1	0.00000	
2-M	NA	0.00	0.00	NA						ERROR	0	0.00000	
3-M	NA	0.00	0.00	NA									
4-M	NA	0.00	0.00	NA						TOTAL	-1	0.00000	

F Ratio = 0.00 'F' table values F.01 = 0.00 F.05 = 0.00
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 0.00 P.05 = 0.00

*-Significant Difference from Control P < .05
Error-within groups
NA-Not Applicable

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Hemoglobin

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: HGB

SEX: MALE

UNITS: g/dL

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	157.3	15.7	0.73						TREATMENTS	3	16.24	5.41
2-M	10	158.6	15.9	0.67	0.5	15.0	16.0	15.0	17.0	ERROR	36	14.15	0.39
3-M	10	153.5	15.4	0.38	1.4	15.0	16.0	15.0	17.0				
4-M	10	142.4	14.2	0.66	5.3	15.0	16.0*	15.0	17.0**	TOTAL	39	30.40	

F Ratio = 13.77 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 4.100 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

1-M	10	157.0	15.7	0.89						TREATMENTS	3	10.17	3.39
2-M	10	162.0	16.2	0.56	1.7	15.0	16.0	15.0	17.0	ERROR	36	15.02	0.42
3-M	10	159.8	16.0	0.39	0.0	15.0	16.0	15.0	17.0				
4-M	10	148.7	14.9	0.65	2.9	15.0	16.0*	15.0	17.0	TOTAL	39	25.18	

F Ratio = 8.12 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 4.117 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

1-M	10	152.1	15.2	0.47						TREATMENTS	3	9.13	3.04
2-M	10	154.6	15.5	0.76	1.0	15.0	16.0	14.0	16.0	ERROR	36	10.59	0.29
3-M	10	154.4	15.4	0.45	0.9	15.0	16.0	14.0	16.0				
4-M	10	142.9	14.3	0.42	3.8	15.0	16.0*	14.0	16.0**	TOTAL	39	19.72	

F Ratio = 10.35 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 3.591 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01
Error-within groups

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Hemoglobin

DRAFT

STUDY ID: UIC-158
STUDY NO: 152
ABBR: HGB

SEX: MALE

UNITS: g/dL

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 27

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI
1-M	NA	0.0	0.0	NA			
2-M	NA	0.0	0.0	NA			
3-M	NA	0.0	0.0	NA			
4-M	NA	0.0	0.0	NA			

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	-1	0.00000	
ERROR	0	0.00000	
TOTAL	-1	0.00000	

F Ratio = 0.00 'F' table values F.01 = 0.00 F.05 = 0.00
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 0.00 P.05 = 0.00

Error-within groups
NA-Not Applicable

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Hematocrit

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: HCT

SEX: MALE

UNITS: %

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1-M	10	441.8	44.2	2.19					
2-M	10	457.7	45.8	1.34	1.9	42.0	46.0	42.0	47.0
3-M	10	436.9	43.7	1.91	0.6	42.0	46.0	42.0	47.0
4-M	10	420.7	42.1	1.75	2.6	42.0	46.0*	42.0	47.0

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	69.65	23.22
ERROR	36	120.21	3.34
TOTAL	39	189.86	

F Ratio = 6.95 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 4.160 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1-M	10	436.2	43.6	2.65					
2-M	10	454.7	45.5	2.18	2.0	41.0	46.0	41.0	46.0
3-M	10	451.8	45.2	1.03	1.7	41.0	46.0	41.0	46.0
4-M	10	429.5	43.0	1.85	0.7	41.0	46.0	41.0	46.0

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	44.28	14.76
ERROR	36	146.80	4.08
TOTAL	39	191.08	

F Ratio = 3.62 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 4.558 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1-M	10	443.0	44.3	1.59					
2-M	10	451.4	45.1	2.23	1.1	42.0	46.0	42.0	47.0
3-M	10	458.1	45.8	2.09	1.9	42.0	46.0	42.0	47.0
4-M	10	428.4	42.8	0.81	1.8	42.0	46.0	42.0	47.0

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	49.19	16.40
ERROR	36	112.60	3.13
TOTAL	39	161.79	

F Ratio = 5.24 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 3.972 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 27

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1-M	NA	0.0	0.0	NA					
2-M	NA	0.0	0.0	NA					
3-M	NA	0.0	0.0	NA					
4-M	NA	0.0	0.0	NA					

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	-1	0.00000	
ERROR	0	0.00000	
TOTAL	-1	0.00000	

F Ratio = 0.00 'F' table values F.01 = 0.00 F.05 = 0.00
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 0.00 P.05 = 0.00

*-Significant Difference from Control P < .05
Error-within groups
NA-Not Applicable

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Mean Corpuscular Volume

DRAFT

STUDY IO: UIC-158
STUDY NO: 152
ABBR: MCV

SEX: MALE

UNITS: fL

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	584.9	58.5	1.41						TREATMENTS	3	13.23	4.41
2-M	10	595.8	59.6	2.44						ERROR	36	159.37	4.43
3-M	10	597.3	59.7	2.07									
4-M	10	585.3	58.5	2.34						TOTAL	39	172.60	

F Ratio = 0.00 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 3.561 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

1-M	10	528.1	52.8	0.94						TREATMENTS	3	42.70	14.23
2-M	10	548.0	54.8	2.75						ERROR	36	196.64	5.46
3-M	10	555.9	55.6	2.16									
4-M	10	539.3	53.9	2.95						TOTAL	39	239.34	

F Ratio = 2.61 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 4.306 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

1-M	10	528.6	52.9	1.11						TREATMENTS	3	96.52	32.17
2-M	10	547.2	54.7	2.79	1.7	50.0	56.0	50.0	56.0	ERROR	36	211.18	5.87
3-M	10	553.6	55.4	2.61	2.3	50.0	56.0	50.0	56.0				
4-M	10	514.2	51.4	2.76	1.3	50.0	56.0	50.0	56.0	TOTAL	39	307.70	

F Ratio = 5.48 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 4.520 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 27

1-M	NA	0.0	0.0	NA						TREATMENTS	-1	0.00000	
2-M	NA	0.0	0.0	NA						ERROR	0	0.00000	
3-M	NA	0.0	0.0	NA									
4-M	NA	0.0	0.0	NA						TOTAL	-1	0.00000	

F Ratio = 0.00 'F' table values F.01 = 0.00 F.05 = 0.00
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 0.00 P.05 = 0.00

Error-within groups
NA-Not Applicable

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Mean Corpuscular Hemoglobin

DRAFT

STUDY IO: UIC-15B
STUDY NO: 152
ABBR: MCH

SEX: MALE

UNITS: pg

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	210.1	21.0	1.23						TREATMENTS	3	3.73	1.24
2-M	10	215.5	21.6	1.37						ERROR	36	43.33	1.20
3-M	10	212.8	21.3	0.87									
4-M	10	207.3	20.7	0.82						TOTAL	39	47.06	

F Ratio = 1.03 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 5.189 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	190.3	19.0	0.51						TREATMENTS	3	6.42	2.14
2-M	10	195.2	19.5	0.75	1.6	18.0	20.0	18.0	20.0	ERROR	36	16.58	0.46
3-M	10	196.7	19.7	0.63	2.1	18.0	20.0	18.0	20.0				
4-M	10	186.6	18.7	0.79	1.2	18.0	20.0	18.0	20.0	TOTAL	39	23.00	

F Ratio = 4.65 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 3.531 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	181.4	18.1	0.50						TREATMENTS	3	15.96	5.32
2-M	10	187.4	18.7	0.89	1.9	17.0	19.0	17.0	19.0	ERROR	36	18.23	0.51
3-M	10	186.7	18.7	0.59	1.7	17.0	19.0	17.0	19.0				
4-M	10	171.6	17.2	0.80	3.1	17.0	19.0*	17.0	19.0	TOTAL	39	34.19	

F Ratio = 10.50 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 3.915 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 27

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	NA	0.0	0.0	NA						TREATMENTS	-1	0.00000	
2-M	NA	0.0	0.0	NA						ERROR	0	0.00000	
3-M	NA	0.0	0.0	NA									
4-M	NA	0.0	0.0	NA						TOTAL	-1	0.00000	

F Ratio = 0.00 'F' table values F.01 = 0.00 F.05 = 0.00
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 0.00 P.05 = 0.00

*-Significant Difference from Control P < .05
Error-within groups
NA-Not Applicable

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Mean Corpus. Hemo. Conc.

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: MCHC

SEX: MALE

UNITS: g/dL

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	359.8	36.0	1.48						TREATMENTS	3	3.42	1.14
2-M	10	359.9	36.0	2.10						ERROR	36	84.37	2.34
3-M	10	355.6	35.6	1.23									
4-M	10	353.0	35.3	1.12						TOTAL	39	87.79	

F Ratio = 0.49 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 4.287 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

1-M	10	360.0	36.0	0.48						TREATMENTS	3	10.52	3.51
2-M	10	356.6	35.7	0.70	1.2	35.0	37.0	35.0	37.0	ERROR	36	14.15	0.39
3-M	10	353.7	35.4	0.66	2.2	35.0	37.0	35.0	37.0				
4-M	10	346.1	34.6	0.65	5.0	35.0	37.0*	35.0	37.0**	TOTAL	39	24.68	

F Ratio = 8.92 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 1.771 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

1-M	10	343.3	34.3	0.66						TREATMENTS	3	6.49	2.16
2-M	10	342.5	34.3	0.65	0.3	34.0	35.0	33.0	35.0	ERROR	36	14.01	0.39
3-M	10	337.3	33.7	0.67	2.2	34.0	35.0	33.0	35.0				
4-M	10	333.4	33.3	0.51	3.5	34.0	35.0*	33.0	35.0**	TOTAL	39	20.50	

F Ratio = 5.56 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 1.840 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01
Error-within groups

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Mean Corpus. Hemo. Conc.

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: MCHC

SEX: MALE

UNITS: g/dL

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 27

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	NA	0.0	0.0	NA				TREATMENTS	-1	0.00000	
2-M	NA	0.0	0.0	NA				ERROR	0	0.00000	
3-M	NA	0.0	0.0	NA				TOTAL	-1	0.00000	
4-M	NA	0.0	0.0	NA							

F Ratio = 0.00 'F' table values F.01 = 0.00 F.05 = 0.00
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 0.00 P.05 = 0.00

Error-within groups
NA-Not Applicable

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Reticulocytes

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: RETICS

SEX: MALE

UNITS: % RBCs

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	7.4	0.7	0.28						TREATMENTS	3	4.72	1.58
2-M	10	7.6	0.8	0.25	0.1	0.0	1.0	0.0	1.0	ERROR	36	4.49	0.12
3-M	10	7.7	0.8	0.38	0.2	0.0	1.0	0.0	1.0				
4-M	10	15.5	1.6	0.46	5.1	0.0	1.0*	0.0	1.0**	TOTAL	39	9.22	

F Ratio = 12.62 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 36.997 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	4.4	0.4	0.25						TREATMENTS	3	2.87	0.96
2-M	10	7.0	0.7	0.42	1.5	0.0	1.0	-0.0	1.0	ERROR	36	5.33	0.15
3-M	10	4.9	0.5	0.28	0.3	0.0	1.0	-0.0	1.0				
4-M	10	11.2	1.1	0.52	4.0	0.0	1.0*	-0.0	1.0**	TOTAL	39	8.20	

F Ratio = 6.47 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 55.963 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	6.8	0.7	0.24						TREATMENTS	3	2.83	0.94
2-M	10	6.4	0.6	0.39	0.2	0.0	1.0	0.0	1.0	ERROR	36	5.23	0.15
3-M	10	6.8	0.7	0.25	0.0	0.0	1.0	0.0	1.0				
4-M	10	12.8	1.3	0.55	3.5	0.0	1.0*	0.0	1.0**	TOTAL	39	8.06	

F Ratio = 6.50 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 46.491 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01
Error-within groups

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Reticulocytes

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: RETICS

SEX: MALE

UNITS: % RBCs

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 27

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI
1-M	NA	0.0	0.0	NA			
2-M	NA	0.0	0.0	NA			
3-M	NA	0.0	0.0	NA			
4-M	NA	0.0	0.0	NA			

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	-1	0.00000	
ERROR	0	0.00000	
TOTAL	-1	0.00000	

F Ratio = 0.00 'F' table values F.01 = 0.00 F.05 = 0.00
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 0.00 P.05 = 0.00

Error-within groups
NA-Not Applicable

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Heinz Bodies

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: HEINZ BOD.

SEX: MALE

UNITS: % RBCs

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	0.0	0.0	0.00						TREATMENTS	3	0.00000	0.00000
2-M	10	0.0	0.0	0.00						ERROR	36	0.00000	0.00000
3-M	10	0.0	0.0	0.00									
4-M	10	0.0	0.0	0.00						TOTAL	39	0.00000	

F Ratio = 0.00 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

1-M	10	0.0	0.0	0.00						TREATMENTS	3	0.061	0.020
2-M	10	0.0	0.0	0.00	0.0	-0.0	0.0	-0.0	0.0	ERROR	36	0.209	0.006
3-M	10	0.0	0.0	0.00	0.0	-0.0	0.0	-0.0	0.0				
4-M	10	0.9	0.1	0.15	2.6	-0.0	0.0*	-0.0	0.0	TOTAL	39	0.270	

F Ratio = 3.49 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 338.641 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

1-M	10	0.0	0.0	0.00						TREATMENTS	3	0.009	0.003
2-M	10	0.4	0.0	0.08						ERROR	36	0.109	0.003
3-M	10	0.2	0.0	0.06									
4-M	10	0.1	0.0	0.03						TOTAL	39	0.118	

F Ratio = 0.96 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 314.430 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 27

1-M	NA	0.0	0.0	NA						TREATMENTS	-1	0.00000	
2-M	NA	0.0	0.0	NA						ERROR	0	0.00000	
3-M	NA	0.0	0.0	NA									
4-M	NA	0.0	0.0	NA						TOTAL	-1	0.00000	

F Ratio = 0.00 'F' table values F.01 = 0.00 F.05 = 0.00
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 0.00 P.05 = 0.00

*-Significant Difference from Control P < .05
Error-within groups
NA-Not Applicable

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: % Methemoglobin

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: % METHGB

SEX: MALE

UNITS: % HGB

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	6.4	0.6	0.25						TREATMENTS	3	239.73	79.91
2-M	10	7.4	0.7	0.27	0.3	-0.0	1.0	-0.0	2.0	ERROR	36	14.87	0.41
3-M	10	11.9	1.2	0.19	1.9	-0.0	1.0	-0.0	2.0				
4-M	10	64.9	6.5	1.22	20.4	-0.0	1.0*	-0.0	2.0**	TOTAL	39	254.59	

F Ratio = 193.51 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 28.371 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	8.3	0.8	0.23						TREATMENTS	3	285.61	95.20
2-M	10	8.3	0.8	0.34	0.0	-0.0	2.0	-0.0	2.0	ERROR	36	24.11	0.67
3-M	10	23.6	2.4	0.59	4.2	-0.0	2.0*	-0.0	2.0**				
4-M	10	73.4	7.3	1.47	17.8	-0.0	2.0*	-0.0	2.0**	TOTAL	39	309.72	

F Ratio = 142.15 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 28.816 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	5.6	0.6	0.12						TREATMENTS	3	314.61	104.87
2-M	10	6.0	0.6	0.24	0.1	-0.0	1.0	-0.0	2.0	ERROR	36	19.92	0.55
3-M	10	22.6	2.3	0.33	5.1	-0.0	1.0*	-0.0	2.0**				
4-M	10	74.2	7.4	1.43	20.6	-0.0	1.0*	-0.0	2.0**	TOTAL	39	334.54	

F Ratio = 189.49 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 27.452 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01
Error-within groups

Source-Source of Variation
Treatments-between groups

SUMMARY OF HEMATOLOGY TESTS
TEST: % Methemoglobin

DRAFT

STUDY ID: UIC-158
STUDY NO: 152
ABBR: % METHGB

SEX: MALE

UNITS: % HGB

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 27

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	NA	0.0	0.0	NA				TREATMENTS	-1	0.00000	
2-M	NA	0.0	0.0	NA				ERROR	0	0.00000	
3-M	NA	0.0	0.0	NA							
4-M	NA	0.0	0.0	NA				TOTAL	-1	0.00000	

F Ratio = 0.00 'F' table values F.01 = 0.00 F.05 = 0.00
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 0.00 P.05 = 0.00

Error-within groups
NA-Not Applicable

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Platelets

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: PLT

SEX: MALE
UNITS: 10^3/mm^3

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	9545	955	99.1						TREATMENTS	3	37131	12377
2-M	10	10187	1019	108.7						ERROR	36	366043	10168
3-M	10	9446	945	85.0									
4-M	10	9978	998	108.6						TOTAL	39	403174	

F Ratio = 1.22 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 10.301 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

1-M	10	10413	1041	100.4						TREATMENTS	3	135803	45268
2-M	10	9855	986	100.9	1	932	1150	903	1179	ERROR	36	358610	9961
3-M	10	9319	932	91.4	2	932	1150*	903	1179				
4-M	10	8856	886	106.0	3	932	1150*	903	1179**	TOTAL	39	494413	

F Ratio = 4.54 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 10.385 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

1-M	10	10006	1001	187.1						TREATMENTS	3	191494	63831
2-M	10	9735	974	116.8						ERROR	36	880175	24449
3-M	10	9711	971	158.6									
4-M	10	8242	824	154.9						TOTAL	39	1071669	

F Ratio = 2.61 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 16.593 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01
Error-within groups

Source-Source of Variation
Treatments-between groups

SUMMARY OF HEMATOLOGY TESTS
TEST: Platelets

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: PLT

SEX: MALE

UNITS: 10^3/mm^3

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 27

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI
1-M	NA	0	0	NA			
2-M	NA	0	0	NA			
3-M	NA	0	0	NA			
4-M	NA	0	0	NA			

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	-1	0.00000	
ERROR	0	0.00000	
TOTAL	-1	0.00000	

F Ratio = 0.00 'F' table values F.01 = 0.00 F.05 = 0.00
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 0.00 P.05 = 0.00

Error-within groups
NA-Not Applicable

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Leukocytes

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: WBC

SEX: MALE

UNITS: 10^3/mm^3

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	165.3	16.5	3.01						TREATMENTS	3	612.85	204.28
2-M	10	170.1	17.0	3.43	0.3	12.0	21.0	11.0	22.0	ERROR	36	626.97	17.42
3-M	10	187.8	18.8	3.07	1.2	12.0	21.0	11.0	22.0				
4-M	10	262.7	26.3	6.28	5.2	12.0	21.0*	11.0	22.0**	TOTAL	39	1239.82	

F Ratio = 11.73 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 21.240 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

1-M	10	165.0	16.5	3.08						TREATMENTS	3	660.47	220.16
2-M	10	171.3	17.1	3.62	0.3	12.0	21.0	11.0	22.0	ERROR	36	588.13	16.34
3-M	10	206.1	20.6	2.70	2.3	12.0	21.0	11.0	22.0				
4-M	10	267.4	26.7	5.95	5.7	12.0	21.0*	11.0	22.0**	TOTAL	39	1248.60	

F Ratio = 13.48 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 19.965 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

1-M	10	148.9	14.9	2.40						TREATMENTS	3	728.12	242.71
2-M	10	172.0	17.2	4.21	1.2	10.0	20.0	9.0	21.0	ERROR	36	697.61	19.38
3-M	10	192.5	19.3	3.54	2.2	10.0	20.0	9.0	21.0				
4-M	10	263.0	26.3	6.44	5.8	10.0	20.0*	9.0	21.0**	TOTAL	39	1425.74	

F Ratio = 12.52 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 22.679 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

WBC corrected for NRBC = or > 10
*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01

Error-within groups
Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Act. Partial Thrombo. Time

DRAFT

STUDY IO: UIC-15B
STUOY NO: 152
ABBR: APTT

SEX: MALE

UNITS: sec

ANALYSIS OF VARIANCE FOLLOWEO BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Oev.	OUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Oegree Fdm	Sum of Squares	Mean Square
1-M	NA	0.0	0.0	NA				TREATMENTS	-1	0.00000	
2-M	NA	0.0	0.0	NA				ERROR	0	0.00000	
3-M	NA	0.0	0.0	NA							
4-M	NA	0.0	0.0	NA				TOTAL	-1	0.00000	

F Ratio = 0.00 'F' table values F.01 = 0.00 F.05 = 0.00
Coeff. Var. % = 0.000 Ounnett's 'T' table values P.01 = 0.00 P.05 = 0.00

Week 13

1-M	NA	0.0	0.0	NA				TREATMENTS	-1	660.47	
2-M	NA	0.0	0.0	NA				ERROR	0	588.13	
3-M	NA	0.0	0.0	NA							
4-M	NA	0.0	0.0	NA				TOTAL	-1	1248.60	

F Ratio = 0.00 'F' table values F.01 = 0.00 F.05 = 0.00
Coeff. Var. % = 0.000 Ounnett's 'T' table values P.01 = 0.00 P.05 = 0.00

Week 26

1-M	NA	0.0	0.0	NA				TREATMENTS	-1	728.12	
2-M	NA	0.0	0.0	NA				ERROR	0	697.61	
3-M	NA	0.0	0.0	NA							
4-M	NA	0.0	0.0	NA				TOTAL	-1	1425.74	

F Ratio = 0.00 'F' table values F.01 = 0.00 F.05 = 0.00
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 0.00 P.05 = 0.00

Error-within groups
NA-Not Applicable

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Nucleated Red Cells

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: NRBC

SEX: MALE

UNITS: COUNT

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	0	0	0.0				TREATMENTS	3	0.00000	0.00000
2-M	10	0	0	0.0				ERROR	36	0.00000	0.00000
3-M	10	0	0	0.0							
4-M	10	0	0	0.0				TOTAL	39	0.00000	

F Ratio = 0.00 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	0	0	0.0				TREATMENTS	3	0.10	0.03
2-M	10	0	0	0.0				ERROR	36	1.80	0.05
3-M	10	1	0	0.3							
4-M	10	1	0	0.3				TOTAL	39	1.90	

F Ratio = 0.67 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 447.214 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	0	0	0.0				TREATMENTS	3	0.28	0.09
2-M	10	1	0	0.3				ERROR	36	6.10	0.17
3-M	10	2	0	0.4							
4-M	10	2	0	0.6				TOTAL	39	6.38	

F Ratio = 0.54 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 329.309 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

WBC corrected for NRBC = or > 10
Error-within groups

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: M. Neutrophils

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: M. Neutrop

SEX: MALE

UNITS: 10^3/mm^3

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	27.8	2.8	1.26						TREATMENTS	3	21.94	7.31
2-M	10	21.6	2.2	0.85	0.9	1.0	4.0	1.0	5.0	ERROR	36	77.52	2.15
3-M	10	35.9	3.6	1.66	1.2	1.0	4.0	1.0	5.0				
4-M	10	40.9	4.1	1.88	2.0	1.0	4.0	1.0	5.0	TOTAL	39	99.46	

F Ratio = 3.40 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 46.510 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	22.5	2.3	0.98						TREATMENTS	3	27.34	9.11
2-M	10	24.6	2.5	1.10	0.4	1.0	3.0	1.0	4.0	ERROR	36	43.21	1.20
3-M	10	32.3	3.2	0.73	2.0	1.0	3.0	1.0	4.0				
4-M	10	43.6	4.4	1.44	4.3	1.0	3.0*	1.0	4.0**	TOTAL	39	70.55	

F Ratio = 7.59 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 35.630 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	20.6	2.1	0.83						TREATMENTS	3	23.65	7.88
2-M	10	33.6	3.4	1.44	2.3	1.0	3.0	0.0	4.0	ERROR	36	55.60	1.54
3-M	10	32.2	3.2	1.60	2.1	1.0	3.0	0.0	4.0				
4-M	10	42.2	4.2	0.92	3.9	1.0	3.0*	0.0	4.0**	TOTAL	39	79.25	

F Ratio = 5.10 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 38.655 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

WBC corrected for NRBC = or > 10
*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01

Error-within groups
Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: I. Neutrophils

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: I. Neutrop

SEX: MALE

UNITS: 10^3/mm^3

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	0.2	0.0	0.04						TREATMENTS	3	0.0240	0.0080
2-M	10	0.0	0.0	0.00	0.8	-0.0	0.0	-0.0	0.0	ERROR	36	0.1000	0.0028
3-M	10	0.6	0.1	0.10	1.7	-0.0	0.0	-0.0	0.0				
4-M	10	0.0	0.0	0.00	0.8	-0.0	0.0	-0.0	0.0	TOTAL	39	0.1240	

F Ratio = 2.88 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 263.523 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

1-M	10	0.6	0.1	0.13						TREATMENTS	3	0.011	0.004
2-M	10	0.2	0.0	0.06						ERROR	36	0.317	0.009
3-M	10	0.2	0.0	0.06									
4-M	10	0.3	0.0	0.09						TOTAL	39	0.328	

F Ratio = 0.41 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 288.732 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

1-M	10	0.0	0.0	0.00						TREATMENTS	3	0.0068	0.0023
2-M	10	0.0	0.0	0.00						ERROR	36	0.0810	0.0023
3-M	10	0.0	0.0	0.00									
4-M	10	0.3	0.0	0.09						TOTAL	39	0.0878	

F Ratio = 1.00 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 632.456 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

WBC corrected for NRBC = or > 10
Error-within groups

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Lymphocytes

DRAFT

STUOY ID: UIC-15B
STUOY NO: 152
ABBR: Lymphocyte

SEX: MALE

UNITS: 10^3/mm^3

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	131.1	13.1	2.56						TREATMENTS	3	414.88	138.29
2-M	10	139.7	14.0	2.85	0.6	10.0	17.0	9.0	18.0	ERROR	36	392.30	10.90
3-M	10	146.5	14.7	2.03	1.0	10.0	17.0	9.0	18.0				
4-M	10	212.4	21.2	4.98	5.5	10.0	17.0*	9.0	18.0**	TOTAL	39	807.18	

F Ratio = 12.69 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 20.969 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

1-M	10	138.2	13.8	3.27						TREATMENTS	3	385.78	128.59
2-M	10	141.3	14.1	3.15	0.2	10.0	18.0	9.0	19.0	ERROR	36	530.09	14.72
3-M	10	168.2	16.8	2.70	1.7	10.0	18.0	9.0	19.0				
4-M	10	215.7	21.6	5.57	4.5	10.0	18.0*	9.0	19.0**	TOTAL	39	915.87	

F Ratio = 8.73 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 23.137 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

1-M	10	122.7	12.3	3.15						TREATMENTS	3	468.37	156.12
2-M	10	132.1	13.2	3.04	0.6	8.0	16.0	7.0	17.0	ERROR	36	508.23	14.12
3-M	10	157.0	15.7	2.37	2.0	8.0	16.0	7.0	17.0				
4-M	10	210.8	21.1	5.63	5.2	8.0	16.0*	7.0	17.0**	TOTAL	39	976.59	

F Ratio = 11.06 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 24.139 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

WBC corrected for NRBC = or > 10
*-Significant Oifference from Control P < .05
**-Significant Difference from Control P < .01

Error-within groups
Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Monocytes

DRAFT

STUDY ID: UIC-15B
STUOY NO: 152
ABBR: Monocytes

SEX: MALE

UNITS: 10^3/mm^3

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	5.1	0.5	0.19						TREATMENTS	3	1.03	0.34
2-M	10	7.4	0.7	0.50						ERROR	36	5.83	0.16
3-M	10	5.0	0.5	0.37									
4-M	10	8.8	0.9	0.48						TOTAL	39	6.86	

F Ratio = 2.12 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 61.200 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

1-M	10	2.7	0.3	0.12						TREATMENTS	3	1.03	0.34
2-M	10	4.0	0.4	0.28						ERROR	36	4.99	0.14
3-M	10	4.2	0.4	0.34									
4-M	10	7.1	0.7	0.59						TOTAL	39	6.02	

F Ratio = 2.49 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 82.701 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

1-M	10	2.8	0.3	0.21						TREATMENTS	3	2.36	0.79
2-M	10	3.9	0.4	0.31	0.8	-0.0	1.0	-0.0	1.0	ERROR	36	3.05	0.08
3-M	10	2.2	0.2	0.18	0.5	-0.0	1.0	-0.0	1.0				
4-M	10	8.4	0.8	0.41	4.3	-0.0	1.0*	-0.0	1.0**	TOTAL	39	5.41	

F Ratio = 9.31 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 67.244 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

WBC corrected for NRBC = or > 10
*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01

Error-within groups
Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Eosinophils

DRAFT

STUDY IO: UIC-15B
STUDY NO: 152
ABBR: Eosinophil

SEX: MALE
UNITS: 10^3/mm^3

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	1.0	0.1	0.22				TREATMENTS	3	0.080	0.027
2-M	10	1.4	0.1	0.20				ERROR	36	0.964	0.027
3-M	10	0.2	0.0	0.06				TOTAL	39	1.044	
4-M	10	0.6	0.1	0.13							

F Ratio = 0.00 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 204.549 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

1-M	10	1.1	0.1	0.09				TREATMENTS	3	0.019	0.006
2-M	10	1.3	0.1	0.21				ERROR	36	0.880	0.024
3-M	10	1.1	0.1	0.15				TOTAL	39	0.899	
4-M	10	0.7	0.1	0.15							

F Ratio = 0.26 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 148.902 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

1-M	10	2.7	0.3	0.23				TREATMENTS	3	0.21	0.07
2-M	10	2.4	0.2	0.23				ERROR	36	1.63	0.05
3-M	10	1.3	0.1	0.20				TOTAL	39	1.83	
4-M	10	1.0	0.1	0.19							

F Ratio = 1.51 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 114.878 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

WBC corrected for NRBC = or > 10
Error-within groups

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Basophils

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: Basophils

SEX: MALE

UNITS: 10^3/mm^3

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	0.0	0.0	0.00				TREATMENTS	3	0.00000	0.00000
2-M	10	0.0	0.0	0.00				ERROR	36	0.00000	0.00000
3-M	10	0.0	0.0	0.00							
4-M	10	0.0	0.0	0.00				TOTAL	39	0.00000	

F Ratio = 0.00 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	0.0	0.0	0.00				TREATMENTS	3	0.00000	0.00000
2-M	10	0.0	0.0	0.00				ERROR	36	0.00000	0.00000
3-M	10	0.0	0.0	0.00							
4-M	10	0.0	0.0	0.00				TOTAL	39	0.00000	

F Ratio = 0.00 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	0.0	0.0	0.00				TREATMENTS	3	0.00000	0.00000
2-M	10	0.0	0.0	0.00				ERROR	36	0.00000	0.00000
3-M	10	0.0	0.0	0.00							
4-M	10	0.0	0.0	0.00				TOTAL	39	0.00000	

F Ratio = 0.00 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

WBC corrected for NRBC = or > 10
Error-within groups

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Erythrocytes

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: RBC

SEX: FEMALE

UNITS: 10^6/mm^3

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	73.90	7.39	0.201						TREATMENTS	3	4.21	1.40
2-F	10	74.09	7.41	0.275	0.17	7.00	8.00	7.00	8.00	ERROR	36	2.35	0.07
3-F	10	71.21	7.12	0.290	2.35	7.00	8.00	7.00	8.00				
4-F	10	66.05	6.61	0.248	6.86	7.00	8.00*	7.00	8.00**	TOTAL	39	6.57	

F Ratio = 21.46 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 3.586 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	79.00	7.90	0.375						TREATMENTS	3	2.66	0.89
2-F	10	77.63	7.76	0.509	0.74	7.00	8.00	7.00	8.00	ERROR	36	6.17	0.17
3-F	10	73.78	7.38	0.400	2.82	7.00	8.00*	7.00	8.00				
4-F	10	72.81	7.28	0.355	3.34	7.00	8.00*	7.00	8.00**	TOTAL	39	8.83	

F Ratio = 5.18 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 5.460 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	76.92	7.69	0.367						TREATMENTS	3	0.90	0.30
2-F	10	75.38	7.54	0.272	1.08	7.00	8.00	7.00	8.00	ERROR	36	3.64	0.10
3-F	10	73.28	7.33	0.261	2.56	7.00	8.00*	7.00	8.00				
4-F	10	73.43	7.34	0.358	2.45	7.00	8.00*	7.00	8.00	TOTAL	39	4.55	

F Ratio = 2.97 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 4.256 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01
Error-within groups

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Hemoglobin

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: HGB

SEX: FEMALE

UNITS: g/dL

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1-F	10	159.7	16.0	0.52					
2-F	10	156.6	15.7	0.51	1.2	15.0	17.0	15.0	17.0
3-F	10	154.4	15.4	0.77	2.1	15.0	17.0	15.0	17.0
4-F	10	144.3	14.4	0.40	6.1	15.0	17.0*	15.0	17.0**

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	13.32	4.44
ERROR	36	11.53	0.32
TOTAL	39	24.85	

F Ratio = 13.87 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 3.681 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1-F	10	158.1	15.8	0.62					
2-F	10	153.9	15.4	0.59	1.4	15.0	17.0	15.0	17.0
3-F	9	134.9	15.0	0.91	2.6	15.0	17.0*	15.0	17.0
4-F	10	146.3	14.6	0.63	3.8	15.0	17.0*	15.0	17.0**

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	7.73	2.58
ERROR	35	16.81	0.48
TOTAL	38	24.54	

F Ratio = 5.36 'F' table values F.01 = 4.42 F.05 = 2.88
Coeff. Var. % = 4.556 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1-F	10	152.3	15.2	0.50					
2-F	10	149.5	15.0	0.26	1.2	15.0	16.0	15.0	16.0
3-F	10	147.6	14.8	0.40	2.0	15.0	16.0	15.0	16.0
4-F	10	141.3	14.1	0.76	4.8	15.0	16.0*	15.0	16.0**

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	6.54	2.16
ERROR	36	9.57	0.27
TOTAL	39	16.11	

F Ratio = 8.20 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 3.492 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01
Error-within groups

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Hematocrit

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: HCT

SEX: FEMALE
UNITS: %

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1-F	10	429.0	42.9	1.91					
2-F	10	425.0	42.5	1.35	0.5	41.0	45.0	40.0	45.0
3-F	10	407.4	40.7	1.97	2.8	41.0	45.0*	40.0	45.0
4-F	10	390.9	39.1	1.67	4.9	41.0	45.0*	40.0	45.0**

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	91.97	30.66
ERROR	36	109.01	3.03
TOTAL	39	200.99	

F Ratio = 10.12 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 4.213 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1-F	10	436.2	43.6	1.89					
2-F	10	429.6	43.0	1.57	0.7	41.0	46.0	41.0	46.0
3-F	10	411.4	41.1	2.31	2.7	41.0	46.0*	41.0	46.0
4-F	10	416.1	41.6	2.31	2.2	41.0	46.0	41.0	46.0

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	39.95	13.32
ERROR	36	150.21	4.17
TOTAL	39	190.17	

F Ratio = 3.19 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 4.825 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1-F	10	438.3	43.8	1.74					
2-F	10	431.6	43.2	0.77	0.9	42.0	46.0	41.0	46.0
3-F	10	421.0	42.1	1.44	2.2	42.0	46.0	41.0	46.0
4-F	10	416.0	41.6	2.58	2.8	42.0	46.0*	41.0	46.0

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	30.55	10.18
ERROR	36	111.02	3.08
TOTAL	39	141.58	

F Ratio = 3.30 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 4.115 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01
Source-Source of Variation
Treatments-between groups
Error-within groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Mean Corpuscular Volume

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: MCV

SEX: FEMALE

UNITS: fL

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	580.4	58.0	1.37						TREATMENTS	3	24.60	8.20
2-F	10	573.7	57.4	1.70	0.0	56.0	60.0	56.0	60.0	ERROR	36	87.84	2.44
3-F	10	571.9	57.2	1.04	1.2	56.0	60.0	56.0	60.0				
4-F	10	591.9	59.2	1.97	1.6	56.0	60.0	56.0	60.0	TOTAL	39	112.44	

F Ratio = 3.36 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 2.696 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	552.5	55.3	2.07	TREATMENTS	3	22.31	7.44
2-F	10	554.4	55.4	2.07	ERROR	36	150.21	4.17
3-F	10	558.0	55.8	1.60				
4-F	10	571.6	57.2	2.36	TOTAL	39	172.52	

F Ratio = 1.78 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 3.653 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	570.2	57.0	1.99	TREATMENTS	3	4.03	1.34
2-F	10	573.3	57.3	2.31	ERROR	36	186.21	5.17
3-F	10	574.9	57.5	1.49				
4-F	10	566.6	56.7	3.03	TOTAL	39	190.24	

F Ratio = 0.26 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 3.981 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation

Treatments-between groups

SUMMARY OF HEMATOLOGY TESTS
TEST: Mean Corpuscular Hemoglobin

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: MCH

SEX: FEMALE

UNITS: pg

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	216.1	21.6	0.66						TREATMENTS	3	2.91	0.97
2-F	10	211.4	21.1	0.49						ERROR	36	13.34	0.37
3-F	10	216.9	21.7	0.48									
4-F	10	218.7	21.9	0.75						TOTAL	39	16.25	

F Ratio = 2.61 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 2.821 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	200.5	20.1	0.68						TREATMENTS	3	0.66	0.22
2-F	10	198.5	19.9	0.64						ERROR	35	15.70	0.45
3-F	9	181.9	20.2	0.64									
4-F	10	201.0	20.1	0.71						TOTAL	38	16.36	

F Ratio = 0.49 'F' table values F.01 = 4.42 F.05 = 2.88
Coeff. Var. % = 3.341 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	198.1	19.8	0.58						TREATMENTS	3	4.12	1.37
2-F	10	198.5	19.9	0.69	0.1	19.0	21.0	19.0	21.0	ERROR	36	15.94	0.44
3-F	10	201.5	20.2	0.50	1.1	19.0	21.0	19.0	21.0				
4-F	10	192.6	19.3	0.84	1.8	19.0	21.0	19.0	21.0	TOTAL	39	20.07	

F Ratio = 3.10 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 3.367 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Mean Corpus. Hemo. Conc.

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: MCHC

SEX: FEMALE

UNITS: g/dL

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	372.7	37.3	1.23						TREATMENTS	3	6.63	2.21
2-F	10	368.8	36.9	0.95						ERROR	36	32.21	0.89
3-F	10	379.1	37.9	0.66									
4-F	10	369.5	37.0	0.85						TOTAL	39	38.84	

F Ratio = 2.47 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 2.539 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	362.5	36.3	0.66						TREATMENTS	3	7.72	2.57
2-F	10	358.5	35.9	0.92	1.2	35.0	37.0	35.0	37.0	ERROR	35	19.14	0.55
3-F	9	326.7	36.3	0.61	0.1	35.0	37.0	35.0	37.0				
4-F	10	351.9	35.2	0.72	3.2	35.0	37.0*	35.0	37.0**	TOTAL	38	26.86	

F Ratio = 4.71 'F' table values F.01 = 4.42 F.05 = 2.88
Coeff. Var. % = 2.061 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	347.5	34.8	0.73						TREATMENTS	3	6.58	2.19
2-F	10	346.5	34.7	0.62	0.3	34.0	36.0	34.0	36.0	ERROR	36	18.55	0.52
3-F	10	351.0	35.1	0.75	1.1	34.0	36.0	34.0	36.0				
4-F	10	339.8	34.0	0.76	2.4	34.0	36.0	34.0	36.0	TOTAL	39	25.12	

F Ratio = 4.26 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 2.073 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01
Error-within groups

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Reticulocytes

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: RETICS

SEX: FEMALE

UNITS: % RBCs

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	5.8	0.6	0.19						TREATMENTS	3	4.52	1.51
2-F	10	6.6	0.7	0.23	0.5	0.0	1.0	0.0	1.0	ERROR	36	4.53	0.13
3-F	10	8.6	0.9	0.38	1.8	0.0	1.0	0.0	1.0				
4-F	10	14.4	1.4	0.51	5.4	0.0	1.0*	0.0	1.0**	TOTAL	39	9.05	

F Ratio = 11.99 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 40.074 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	4.8	0.5	0.21						TREATMENTS	3	1.50	0.50
2-F	10	5.8	0.6	0.27	0.6	0.0	1.0	-0.0	1.0	ERROR	36	5.15	0.14
3-F	10	6.1	0.6	0.47	0.8	0.0	1.0	-0.0	1.0				
4-F	10	9.9	0.0	0.48	3.0	0.0	1.0*	-0.0	1.0	TOTAL	39	6.65	

F Ratio = 3.50 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 56.876 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	11.3	1.1	0.22						TREATMENTS	3	3.31	1.10
2-F	10	9.8	0.0	0.36	0.9	1.0	2.0	1.0	2.0	ERROR	36	5.30	0.15
3-F	10	9.2	0.9	0.44	1.2	1.0	2.0	1.0	2.0				
4-F	10	16.5	1.7	0.47	3.0	1.0	2.0*	1.0	2.0	TOTAL	39	8.60	

F Ratio = 7.49 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 32.788 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01
Error-within groups

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Heinz Bodies

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: HEINZ BOD.

SEX: FEMALE

UNITS: % RBCs

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	0.0	0.0	0.00						TREATMENTS	3	0.00000	0.00000
2-F	10	0.0	0.0	0.00						ERROR	36	0.00000	0.00000
3-F	10	0.0	0.0	0.00									
4-F	10	0.0	0.0	0.00						TOTAL	39	0.00000	

F Ratio = 0.00 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

1-F	10	0.1	0.0	0.03						TREATMENTS	3	0.066	0.022
2-F	10	0.1	0.0	0.03	0.0	-0.0	0.0	-0.0	0.0	ERROR	36	0.178	0.005
3-F	10	0.0	0.0	0.00	0.3	-0.0	0.0	-0.0	0.0				
4-F	10	1.0	0.1	0.13	2.9	-0.0	0.0*	-0.0	0.0	TOTAL	39	0.244	

F Ratio = 4.45 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 234.389 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

1-F	10	0.0	0.0	0.00						TREATMENTS	3	0.075	0.025
2-F	10	0.0	0.0	0.00	0.0	-0.0	0.0	-0.0	0.0	ERROR	36	0.220	0.006
3-F	10	0.0	0.0	0.00	0.0	-0.0	0.0	-0.0	0.0				
4-F	10	1.0	0.1	0.16	2.9	-0.0	0.0*	-0.0	0.0	TOTAL	39	0.295	

F Ratio = 4.09 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 312.694 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

*-Significant Difference from Control P < .05
Error-within groups

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: % Methemoglobin

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: % METHGB

SEX: FEMALE

UNITS: % HGB

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	7.6	0.8	0.14						TREATMENTS	3	192.06	64.02
2-F	10	7.2	0.7	0.21	0.1	-0.0	2.0	-0.0	2.0	ERROR	36	18.52	0.51
3-F	10	11.8	1.2	0.26	1.3	-0.0	2.0	-0.0	2.0				
4-F	10	59.3	5.9	1.39	16.1	-0.0	2.0*	-0.0	2.0**	TOTAL	39	210.58	

F Ratio = 124.47 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 33.396 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

1-F	10	4.3	0.4	0.27						TREATMENTS	3	295.82	98.61
2-F	10	4.8	0.5	0.34	0.2	-0.0	1.0	-0.0	1.0	ERROR	36	14.42	0.40
3-F	10	16.4	1.6	0.32	4.3	-0.0	1.0*	-0.0	1.0**				
4-F	10	70.3	7.0	1.15	23.3	-0.0	1.0*	-0.0	1.0**	TOTAL	39	310.24	

F Ratio = 246.14 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 26.427 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

1-F	10	6.4	0.6	0.51						TREATMENTS	3	369.79	123.26
2-F	10	6.2	0.6	0.32	0.0	-1.0	2.0	-1.0	2.0	ERROR	36	43.94	1.22
3-F	10	18.3	1.8	0.60	2.4	-1.0	2.0	-1.0	2.0				
4-F	10	79.6	8.0	2.04	14.8	-1.0	2.0*	-1.0	2.0**	TOTAL	39	413.73	

F Ratio = 100.98 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 39.995 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01
Error-within groups

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Platelets

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: PLT

SEX: FEMALE

UNITS: 10^3/mm^3

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	10888	1089	139.2				TREATMENTS	3	161652	53884
2-F	10	10659	1066	130.9				ERROR	36	837694	23269
3-F	10	9503	950	216.9				TOTAL	39	999347	
4-F	10	11178	1118	97.6							

F Ratio = 2.32 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 14.449 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	9540	954	158.7				TREATMENTS	3	143157	47719
2-F	10	9499	950	139.7				ERROR	36	697145	19365
3-F	10	8865	887	79.0				TOTAL	39	840303	
4-F	10	10537	1054	162.9							

F Ratio = 2.46 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 14.480 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	9797	980	133.1				TREATMENTS	3	40686	13562
2-F	10	9026	903	146.2				ERROR	36	592127	16448
3-F	10	9415	942	94.9				TOTAL	39	632814	
4-F	10	9795	980	133.1							

F Ratio = 0.82 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 13.488 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Leukocytes

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: WBC

SEX: FEMALE

UNITS: 10^3/mm^3

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	158.9	15.9	3.41						TREATMENTS	3	1094.89	364.96
2-F	10	158.9	15.9	2.91	0.0	12.0	20.0	10.0	21.0	ERROR	36	567.15	15.75
3-F	10	148.6	14.9	2.63	0.6	12.0	20.0	10.0	21.0				
4-F	10	275.9	27.6	6.01	6.6	12.0	20.0*	10.0	21.0**	TOTAL	39	1662.04	

F Ratio = 23.17 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 21.388 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	152.8	15.3	4.16						TREATMENTS	3	980.74	326.91
2-F	10	154.1	15.4	3.79	0.1	10.0	20.0	9.0	22.0	ERROR	36	733.51	20.38
3-F	10	139.3	13.9	2.10	0.7	10.0	20.0	9.0	22.0				
4-F	10	262.3	26.2	6.74	5.4	10.0	20.0*	9.0	22.0**	TOTAL	39	1714.24	

F Ratio = 16.04 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 25.484 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	126.0	12.6	3.82						TREATMENTS	3	662.57	220.86
2-F	10	109.8	11.0	3.01	1.2	9.0	16.0	8.0	17.0	ERROR	36	336.43	9.35
3-F	10	109.7	11.0	1.55	1.2	9.0	16.0	8.0	17.0				
4-F	10	207.9	20.8	3.37	6.0	9.0	16.0*	8.0	17.0**	TOTAL	39	998.99	

F Ratio = 23.63 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 22.096 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

WBC corrected for NRBC = or > 10
*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01

Error-within groups
Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Act. Partial Thrombo. Time

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: APTT

SEX: FEMALE

UNITS: sec

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	NA	0.0	0.0	NA				TREATMENTS	-1	0.00000	
2-F	NA	0.0	0.0	NA				ERROR	0	0.00000	
3-F	NA	0.0	0.0	NA							
4-F	NA	0.0	0.0	NA				TOTAL	-1	0.00000	

F Ratio = 0.00 'F' table values F.01 = 0.00 F.05 = 0.00
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 0.00 P.05 = 0.00

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	NA	0.0	0.0	NA				TREATMENTS	-1	980.74	
2-F	NA	0.0	0.0	NA				ERROR	0	733.51	
3-F	NA	0.0	0.0	NA							
4-F	NA	0.0	0.0	NA				TOTAL	-1	1714.24	

F Ratio = 0.00 'F' table values F.01 = 0.00 F.05 = 0.00
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 0.00 P.05 = 0.00

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	NA	0.0	0.0	NA				TREATMENTS	-1	662.57	
2-F	NA	0.0	0.0	NA				ERROR	0	336.43	
3-F	NA	0.0	0.0	NA							
4-F	NA	0.0	0.0	NA				TOTAL	-1	998.99	

F Ratio = 0.00 'F' table values F.01 = 0.00 F.05 = 0.00
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 0.00 P.05 = 0.00

Error-within groups
NA-Not Applicable

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Nucleated Red Cells

DRAFT

STUDY ID: UIC-158
STUDY NO: 152
ABBR: NRBC

SEX: FEMALE

UNITS: COUNT

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	0	0	0.0				TREATMENTS	3	0.10	0.03
2-F	10	1	0	0.3				ERROR	36	1.80	0.05
3-F	10	1	0	0.3							
4-F	10	0	0	0.0				TOTAL	39	1.90	

F Ratio = 0.67 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 447.214 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	0	0	0.0				TREATMENTS	3	0.00000	0.00000
2-F	10	0	0	0.0				ERROR	36	0.00000	0.00000
3-F	10	0	0	0.0							
4-F	10	0	0	0.0				TOTAL	39	0.00000	

F Ratio = 0.00 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	3	0	0.7				TREATMENTS	3	0.50	0.17
2-F	10	4	0	0.0				ERROR	36	15.00	0.42
3-F	10	1	0	0.3							
4-F	10	2	0	0.4				TOTAL	39	15.50	

F Ratio = 0.40 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 258.199 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

WBC corrected for NRBC = or > 10
Error-within groups

Source-Source of Variation
Treatments-between groups

SUMMARY OF HEMATOLOGY TESTS
TEST: M. Neutrophils

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: M. Neutrop

SEX: FEMALE

UNITS: 10^3/mm^3

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	26.8	2.7	1.72						TREATMENTS	3	42.39	14.13
2-F	10	17.4	1.7	1.07	1.6	1.0	4.0	1.0	4.0	ERROR	36	59.95	1.67
3-F	10	19.5	2.0	0.93	1.3	1.0	4.0	1.0	4.0				
4-F	10	43.6	4.4	1.30	2.9	1.0	4.0*	1.0	4.0	TOTAL	39	102.34	

F Ratio = 8.48 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 48.106 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	16.2	1.6	0.95						TREATMENTS	3	11.84	3.95
2-F	10	14.4	1.4	0.69	0.4	1.0	3.0	0.0	3.0	ERROR	36	32.02	0.89
3-F	10	24.0	2.4	0.58	1.8	1.0	3.0	0.0	3.0				
4-F	10	27.6	2.8	1.36	2.7	1.0	3.0*	0.0	3.0	TOTAL	39	43.86	

F Ratio = 4.43 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 45.896 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	22.2	2.2	1.37						TREATMENTS	3	22.90	7.63
2-F	10	14.0	1.4	0.87	1.7	1.0	3.0	1.0	4.0	ERROR	36	40.18	1.12
3-F	10	24.6	2.5	0.69	0.5	1.0	3.0	1.0	4.0				
4-F	10	35.2	3.5	1.17	2.8	1.0	3.0*	1.0	4.0	TOTAL	39	63.08	

F Ratio = 6.84 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 44.017 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

WBC corrected for NRBC = or > 10
*-Significant Difference from Control P < .05
Error-within groups

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: I. Neutrophils

DRAFT

STUDY ID: UIC-158
STUDY NO: 152
ABBR: I. Neutrop

SEX: FEMALE

UNITS: 10^3/mm^3

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	0.2	0.0	0.06						TREATMENTS	3	0.024	0.008
2-F	10	0.0	0.0	0.00						ERROR	36	0.360	0.010
3-F	10	0.0	0.0	0.00									
4-F	10	0.6	0.1	0.19						TOTAL	39	0.384	

F Ratio = 0.80 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 500.000 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

1-F	10	0.0	0.0	0.00						TREATMENTS	3	0.045	0.015
2-F	10	0.0	0.0	0.00	0.0	-0.0	0.0	-0.0	0.0	ERROR	36	0.185	0.005
3-F	10	0.1	0.0	0.03	0.3	-0.0	0.0	-0.0	0.0				
4-F	10	0.8	0.1	0.14	2.5	-0.0	0.0*	-0.0	0.0	TOTAL	39	0.230	

F Ratio = 2.90 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 318.605 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

1-F	10	0.0	0.0	0.00						TREATMENTS	3	0.00000	0.00000
2-F	10	0.0	0.0	0.00						ERROR	36	0.00000	0.00000
3-F	10	0.0	0.0	0.00									
4-F	10	0.0	0.0	0.00						TOTAL	39	0.00000	

F Ratio = 0.00 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

WBC corrected for NRBC = or > 10
*-Significant Difference from Control P < .05
Error-within groups
Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Lymphocytes

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: Lymphocyte

SEX: FEMALE
UNITS: 10^3/mm^3

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	127.5	12.8	2.26						TREATMENTS	3	666.91	222.30
2-F	10	136.9	13.7	2.51	0.6	9.0	17.0	8.0	18.0	ERROR	36	469.70	13.05
3-F	10	125.4	12.5	2.03	0.1	9.0	17.0	8.0	18.0				
4-F	10	223.7	22.4	6.05	6.0	9.0	17.0*	8.0	18.0**	TOTAL	39	1136.61	

F Ratio = 17.04 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 23.551 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	133.0	13.3	3.47						TREATMENTS	3	816.04	272.01
2-F	10	134.9	13.5	3.56	0.1	9.0	18.0	7.0	19.0	ERROR	36	659.09	18.31
3-F	10	111.7	11.2	2.07	1.1	9.0	18.0	7.0	19.0				
4-F	10	228.7	22.9	6.65	5.0	9.0	18.0*	7.0	19.0**	TOTAL	39	1475.13	

F Ratio = 14.86 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 28.136 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	100.5	10.1	2.97						TREATMENTS	3	473.24	157.75
2-F	10	93.0	9.3	2.46	0.6	7.0	13.0	6.0	14.0	ERROR	36	260.28	7.23
3-F	10	82.6	8.3	1.24	1.5	7.0	13.0	6.0	14.0				
4-F	10	170.1	17.0	3.53	5.8	7.0	13.0*	6.0	14.0**	TOTAL	39	733.52	

F Ratio = 21.82 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 24.104 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

WBC corrected for NRBC = or > 10
*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01

Error-within groups
Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Monocytes

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: Monocytes

SEX: FEMALE

UNITS: 10^3/mm^3

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	2.5	0.3	0.18						TREATMENTS	3	1.60	0.53
2-F	10	4.0	0.4	0.41	0.0	-0.0	1.0	-0.0	1.0	ERROR	36	4.07	0.11
3-F	10	2.5	0.3	0.15	0.0	-0.0	1.0	-0.0	1.0				
4-F	10	7.4	0.7	0.48	3.3	-0.0	1.0*	-0.0	1.0**	TOTAL	39	5.68	

F Ratio = 4.72 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 82.049 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

1-F	10	2.8	0.3	0.15						TREATMENTS	3	0.21	0.07
2-F	10	3.2	0.3	0.24						ERROR	36	2.38	0.07
3-F	10	2.7	0.3	0.18									
4-F	10	4.5	0.5	0.39						TOTAL	39	2.58	

F Ratio = 1.04 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 77.883 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

1-F	10	2.2	0.2	0.17						TREATMENTS	3	0.02	0.01
2-F	10	1.8	0.2	0.09						ERROR	36	1.16	0.03
3-F	10	1.6	0.2	0.18									
4-F	10	2.0	0.2	0.24						TOTAL	39	1.18	

F Ratio = 0.21 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 94.314 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

WBC corrected for NRBC = or > 10
*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01

Error-within groups
Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Eosinophils

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: Eosinophil

SEX: FEMALE
UNITS: 10^3/mm^3

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	1.5	0.2	0.14				TREATMENTS	3	0.104	0.035
2-F	10	0.7	0.1	0.08				ERROR	36	0.712	0.020
3-F	10	1.7	0.2	0.21							
4-F	10	0.5	0.1	0.11				TOTAL	39	0.816	

F Ratio = 1.75 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 127.849 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	1.2	0.1	0.12				TREATMENTS	3	0.011	0.004
2-F	10	1.2	0.1	0.09				ERROR	36	0.777	0.022
3-F	10	0.8	0.1	0.13							
4-F	10	1.1	0.1	0.21				TOTAL	39	0.788	

F Ratio = 0.17 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 136.663 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	1.2	0.1	0.11				TREATMENTS	3	0.019	0.006
2-F	10	0.9	0.1	0.07				ERROR	36	0.389	0.011
3-F	10	1.0	0.1	0.08							
4-F	10	0.6	0.1	0.13				TOTAL	39	0.408	

F Ratio = 0.58 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 112.378 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

WBC corrected for NRBC = or > 10
Error-within groups

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Basophils

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: Basophils

SEX: FEMALE
UNITS: 10^3/mm^3

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	0.2	0.0	0.06				TREATMENTS	3	0.0030	0.0010
2-F	10	0.0	0.0	0.00				ERROR	36	0.0360	0.0010
3-F	10	0.0	0.0	0.00							
4-F	10	0.0	0.0	0.00				TOTAL	39	0.0390	

F Ratio = 1.00 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 632.456 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	0.0	0.0	0.00				TREATMENTS	3	0.00000	0.00000
2-F	10	0.0	0.0	0.00				ERROR	36	0.00000	0.00000
3-F	10	0.0	0.0	0.00							
4-F	10	0.0	0.0	0.00				TOTAL	39	0.00000	

F Ratio = 0.00 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	0.0	0.0	0.00				TREATMENTS	3	0.00000	0.00000
2-F	10	0.0	0.0	0.00				ERROR	36	0.00000	0.00000
3-F	10	0.0	0.0	0.00							
4-F	10	0.0	0.0	0.00				TOTAL	39	0.00000	

F Ratio = 0.00 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

WBC corrected for NRBC = or > 10
Error-within groups

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Alanine Aminotransferase

DRAFT

STUDY ID: UIC-158
STUDY NO: 152
ABBR: ALT

SEX: MALE

UNITS: IU/L

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	529	53	8.7				TREATMENTS	3	207.08	69.03
2-M	10	524	52	9.8				ERROR	36	2368.70	65.80
3-M	10	529	53	7.2							
4-M	10	475	48	6.3				TOTAL	39	2575.78	

F Ratio = 1.05 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 15.774 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	651	65	14.3	TREATMENTS	3	1643.40	547.80
2-M	10	622	62	13.1	ERROR	36	8030.20	223.06
3-M	10	603	60	9.4				
4-M	10	768	77	20.7	TOTAL	39	9673.60	

F Ratio = 2.46 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 22.595 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	753	75	15.7	TREATMENTS	3	2995	998
2-M	10	807	81	42.5	ERROR	36	28276	785
3-M	10	648	65	14.4				
4-M	10	886	89	29.7	TOTAL	39	31271	

F Ratio = 1.27 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 36.233 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation

Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Sorbitol Dehydrogenase

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: SDH

SEX: MALE
UNITS: IU/L

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	155.1	15.5	8.40				TREATMENTS	3	90.21	30.07
2-M	10	186.8	18.7	8.53				ERROR	36	2648.30	73.56
3-M	10	162.8	16.3	10.71							
4-M	10	190.0	19.0	6.02				TOTAL	39	2738.51	

F Ratio = 0.41 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 49.385 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	200.7	20.1	13.31				TREATMENTS	3	84.72	28.24
2-M	10	164.2	16.4	7.08				ERROR	36	3038.52	84.40
3-M	10	182.1	18.2	8.55							
4-M	10	166.8	16.7	6.10				TOTAL	39	3123.24	

F Ratio = 0.33 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 51.483 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	130.1	13.0	4.44				TREATMENTS	3	122.43	40.81
2-M	10	159.7	16.0	7.60				ERROR	35	1566.73	44.76
3-M	10	124.2	12.4	6.57							
4-M	9	148.4	16.5	7.74				TOTAL	38	1689.16	

F Ratio = 0.91 'F' table values F.01 = 4.42 F.05 = 2.88
Coeff. Var. % = 46.396 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation

Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Total Protein

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: TP

SEX: MALE

UNITS: g/dL

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	77.3	7.7	0.78				TREATMENTS	3	0.34	0.11
2-M	10	78.2	7.8	0.48				ERROR	36	10.95	0.30
3-M	10	76.9	7.7	0.41							
4-M	10	79.3	7.9	0.45				TOTAL	39	11.29	

F Ratio = 0.37 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 7.077 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	83.3	8.3	0.60				TREATMENTS	3	1.26	0.42
2-M	10	79.0	7.9	0.37				ERROR	36	9.56	0.27
3-M	10	79.8	8.0	0.57							
4-M	10	79.0	7.9	0.49				TOTAL	39	10.82	

F Ratio = 1.59 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 6.418 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	75.9	7.6	0.56				TREATMENTS	3	0.93	0.31
2-M	10	73.3	7.3	0.61				ERROR	36	10.11	0.28
3-M	10	76.0	7.6	0.45							
4-M	10	72.6	7.3	0.48				TOTAL	39	11.04	

F Ratio = 1.10 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 7.119 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation

Treatments-between groups

DRAFT

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Albumin

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: ALB

SEX: MALE

UNITS: g/dL

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	39.8	4.0	0.36				TREATMENTS	3	0.19	0.06
2-M	10	39.4	3.9	0.23				ERROR	36	2.40	0.07
3-M	10	40.5	4.1	0.25							
4-M	10	41.2	4.1	0.15				TOTAL	39	2.59	

F Ratio = 0.94 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 6.420 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	42.9	4.3	0.40				TREATMENTS	3	0.22	0.07
2-M	10	41.1	4.1	0.21				ERROR	36	3.65	0.10
3-M	10	42.0	4.2	0.36							
4-M	10	42.9	4.3	0.26				TOTAL	39	3.87	

F Ratio = 0.73 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 7.538 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	42.1	4.2	0.28				TREATMENTS	3	0.25	0.08
2-M	10	39.9	4.0	0.24				ERROR	36	2.49	0.07
3-M	10	41.3	4.1	0.31							
4-M	10	40.9	4.1	0.21				TOTAL	39	2.74	

F Ratio = 1.21 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 6.404 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Total Bile Acids

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: TBA

SEX: MALE

UNITS: umol/L

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	246.9	24.7	7.58				TREATMENTS	3	609	203
2-M	10	341.3	34.1	24.94				ERROR	36	10959	304
3-M	10	338.2	33.8	20.01							
4-M	10	330.1	33.0	11.72				TOTAL	39	11568	

F Ratio = 0.67 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 55.542 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	444.0	44.4	20.18				TREATMENTS	3	3902	1301
2-M	10	463.1	46.3	24.88				ERROR	36	21818	606
3-M	10	672.8	67.3	26.35							
4-M	10	621.8	62.2	26.53				TOTAL	39	25720	

F Ratio = 2.15 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 44.726 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	597.8	59.8	35.22						TREATMENTS	3	12280	4093
2-M	10	482.2	48.2	19.59	0.8	25.0	94.0	16.0	104.0	ERROR	36	36123	1003
3-M	10	602.6	60.3	31.87	0.0	25.0	94.0	16.0	104.0				
4-M	10	949.9	95.0	37.05	2.5	25.0	94.0*	16.0	104.0	TOTAL	39	48403	

F Ratio = 4.08 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 48.132 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

*-Significant Difference from Control P < .05
Error-within groups

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Alkaline Phosphatase

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: ALKP

SEX: MALE

UNITS: IU/L

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	3682	368	98.7				TREATMENTS	3	12432	4144
2-M	10	3404	340	41.0				ERROR	36	322513	8959
3-M	10	3635	364	122.7				TOTAL	39	334944	
4-M	10	3247	325	96.8							

F Ratio = 0.46 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 27.105 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	2361	236	80.9				TREATMENTS	3	2017	672
2-M	10	2217	222	46.8				ERROR	36	191215	5312
3-M	10	2359	236	98.0				TOTAL	39	193232	
4-M	10	2219	222	54.0							

F Ratio = 0.13 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 31.839 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	2037	204	76.0				TREATMENTS	3	5990	1997
2-M	10	1733	173	56.5				ERROR	36	181559	5043
3-M	10	1914	191	90.1				TOTAL	39	187549	
4-M	10	2027	203	55.5							

F Ratio = 0.40 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 36.839 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Lactate Dehydrogenase

DRAFT

STUDY ID: UIC-158
STUDY NO: 152
ABBR: LDH

SEX: MALE

UNITS: IU/L

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	1706	171	146.3				TREATMENTS	3	3306	1102
2-M	10	1630	163	101.5				ERROR	36	625414	17373
3-M	10	1764	176	159.6							
4-M	10	1879	188	111.1				TOTAL	39	628720	

F Ratio = 0.06 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 75.544 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	4729	473	515.2				TREATMENTS	3	121140	40380
2-M	10	4127	413	289.8				ERROR	36	3663614	101767
3-M	10	3326	333	142.3							
4-M	10	4603	460	193.4				TOTAL	39	3784753	

F Ratio = 0.40 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 76.023 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	5163	516	359.7				TREATMENTS	3	73058	24353
2-M	10	4214	421	321.1				ERROR	36	3079580	85544
3-M	10	4053	405	210.9							
4-M	10	4598	460	255.3				TOTAL	39	3152638	

F Ratio = 0.28 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 64.894 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Creatine Kinase

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: CK

SEX: MALE

UNITS: IU/L

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI
1 M	10	2423	242	173.4			
2-M	10	3041	304	293.8			
3-M	10	1701	170	140.2			
4-M	10	1665	167	182.7			

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	129201	43067
ERROR	36	1524898	42358
TOTAL	39	1654100	

F Ratio = 1.02 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 93.233 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI
1 M	10	3120	312	249.1			
2-M	10	4561	456	392.0			
3-M	10	3809	381	335.6			
4-M	10	2256	226	159.0			

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	289701	96567
ERROR	36	3182166	88394
TOTAL	39	3471867	

F Ratio = 1.09 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 86.515 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI
1 M	10	5018	502	397.4			
2-M	10	3775	378	358.6			
3-M	10	3328	333	380.8			
4-M	10	6061	606	654.3			

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	459597	153199
ERROR	36	7736515	214903
TOTAL	39	8196112	

F Ratio = 0.71 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 101.986 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation

Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Blood Urea Nitrogen

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: BUN

SEX: MALE

UNITS: mg/dL

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1 M	10	183.4	18.3	1.67					
2-M	10	173.0	17.3	1.62	1.3	16.0	20.0	16.0	21.0
3-M	10	169.7	17.0	1.31	1.7	16.0	20.0	16.0	21.0
4-M	10	158.3	15.8	2.52	3.1	16.0	20.0*	16.0	21.0

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	32.07	10.69
ERROR	36	121.15	3.37
TOTAL	39	153.22	

F Ratio = 3.18 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 10.721 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1 M	10	209.9	21.0	3.61					
2-M	10	170.1	17.0	2.73	3.0	18.0	24.0*	17.0	25.0
3-M	10	180.6	18.1	2.91	2.2	18.0	24.0	17.0	25.0
4-M	10	153.6	15.4	2.54	4.2	18.0	24.0*	17.0	25.0**

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	168.09	56.03
ERROR	36	318.71	8.85
TOTAL	39	486.80	

F Ratio = 6.33 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 16.664 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1 M	10	180.6	18.1	2.48					
2-M	10	154.9	15.5	3.38	2.2	15.0	21.0	15.0	22.0
3-M	10	157.7	15.8	1.95	2.0	15.0	21.0	15.0	22.0
4-M	10	140.3	14.0	2.23	3.5	15.0	21.0*	15.0	22.0**

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	83.32	27.77
ERROR	36	236.93	6.58
TOTAL	39	320.25	

F Ratio = 4.22 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 16.199 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01
Error-within groups

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Creatinine

DRAFT

STUOY IO: UIC-15B
STUOY NO: 152
ABBR: CREAT

SEX: MALE

UNITS: mg/dL

ANALYSIS OF VARIANCE FOLLOWED BY OUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	5.38	0.54	0.069				TREATMENTS	3	0.027	0.009
2-M	10	5.55	0.56	0.094				ERROR	36	0.278	0.008
3-M	10	5.22	0.52	0.042							
4-M	10	5.92	0.59	0.125				TOTAL	39	0.305	

F Ratio = 1.17 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 15.913 Ounnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

1 M	10	5.74	0.57	0.071				TREATMENTS	3	0.021	0.007
2-M	10	5.21	0.52	0.044				ERROR	36	0.146	0.004
3-M	10	5.78	0.58	0.079							
4-M	10	5.70	0.57	0.055				TOTAL	39	0.168	

F Ratio = 1.75 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 11.376 Ounnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

1 M	10	6.02	0.60	0.046				TREATMENTS	3	0.011	0.004
2-M	10	5.73	0.57	0.049				ERROR	36	0.149	0.004
3-M	10	6.16	0.62	0.102							
4-M	10	5.82	0.58	0.042				TOTAL	39	0.160	

F Ratio = 0.91 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 10.851 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Sodium

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: NA

SEX: MALE

UNITS: mEq/L

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	1443	144	3.5				TREATMENTS	3	77.60	25.87
2-M	10	1469	147	3.3				ERROR	36	374.00	10.39
3-M	10	1453	145	2.2				TOTAL	39	451.60	
4-M	10	1479	148	3.7							

F Ratio = 2.49 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 2.206 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

1 M	10	1451	145	1.2					TREATMENTS	3	6.27	2.09
2-M	10	1452	145	1.5					ERROR	36	66.70	1.85
3-M	10	1453	145	1.3					TOTAL	39	72.97	
4-M	10	1443	144	1.4								

F Ratio = 1.13 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 0.939 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

1 M	10	1466	147	1.4						TREATMENTS	3	29.60	9.87
2-M	10	1464	146	1.3	0	145	148	144	149	ERROR	36	84.80	2.36
3-M	10	1458	146	2.0	1	145	148	144	149	TOTAL	39	114.40	
4-M	10	1444	144	1.2	3	145	148*	144	149**				

F Ratio = 4.19 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 1.053 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01
Error-within groups

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Potassium

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: K

SEX: MALE
UNITS: mEq/L

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1 M	10	62.04	6.20	0.489					
2-M	10	61.79	6.18	0.552	0.11	6.00	7.00	6.00	7.00
3-M	10	56.66	5.67	0.476	2.36	6.00	7.00	6.00	7.00
4-M	10	63.98	6.40	0.515	0.85	6.00	7.00	6.00	7.00

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	2.94	0.98
ERROR	36	9.32	0.26
TOTAL	39	12.25	

F Ratio = 3.78 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 8.324 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.
1 M	10	60.11	6.01	0.493
2-M	10	58.79	5.88	0.559
3-M	10	57.45	5.75	0.533
4-M	10	59.49	5.95	0.446

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	0.39	0.13
ERROR	36	9.35	0.26
TOTAL	39	9.74	

F Ratio = 0.50 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 8.643 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.
1 M	10	58.88	5.89	0.387
2-M	10	58.00	5.80	0.316
3-M	10	58.37	5.84	0.418
4-M	10	56.04	5.60	0.251

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	0.46	0.15
ERROR	36	4.39	0.12
TOTAL	39	4.85	

F Ratio = 1.27 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 6.037 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation

Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Chloride

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: CL

SEX: MALE

UNITS: mEq/L

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	1052	105	2.5						TREATMENTS	3	31.28	10.43
2-M	10	1041	104	4.1						ERROR	36	335.10	9.31
3-M	10	1065	107	2.9									
4-M	10	1047	105	2.4						TOTAL	39	366.38	

F Ratio = 1.12 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 2.902 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	1057	106	5.1						TREATMENTS	3	401.00	133.67
2-M	10	999	100	4.4	2	100	111*	98	113	ERROR	36	993.00	27.58
3-M	10	1058	106	5.7	0	100	111	98	113				
4-M	10	1086	109	5.6	1	100	111	98	113	TOTAL	39	1394.00	

F Ratio = 4.85 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 5.002 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	1031	103	2.7						TREATMENTS	3	55.68	18.56
2-M	10	1031	103	3.7						ERROR	36	444.30	12.34
3-M	10	1053	105	3.0									
4-M	10	1056	106	4.4						TOTAL	39	499.98	

F Ratio = 1.50 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 3.369 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

*-Significant Difference from Control P < .05
Error-within groups

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Calcium

DRAFT

STUDY ID: UIC-158
STUDY NO: 152
ABBR: CA

SEX: MALE

UNITS: mg/dL

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	112.7	11.3	0.49				TREATMENTS	3	0.38	0.13
2-M	10	113.5	11.4	0.51				ERROR	36	6.56	0.18
3-M	10	111.4	11.1	0.34							
4-M	10	111.1	11.1	0.33				TOTAL	39	6.94	

F Ratio = 0.69 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 3.805 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

1 M	10	108.6	10.9	0.41				TREATMENTS	3	1.03	0.34
2-M	10	108.9	10.9	0.34				ERROR	36	4.50	0.12
3-M	10	108.2	10.8	0.40							
4-M	10	104.9	10.5	0.24				TOTAL	39	5.53	

F Ratio = 2.76 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 3.284 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

1 M	10	114.8	11.5	0.47				TREATMENTS	3	0.73	0.24
2-M	10	116.5	11.7	0.31				ERROR	36	4.94	0.14
3-M	10	115.5	11.6	0.37							
4-M	10	112.8	11.3	0.32				TOTAL	39	5.68	

F Ratio = 1.78 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 3.225 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation

Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Inorganic Phosphorus

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: IP

SEX: MALE
UNITS: mg/dL

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	96.1	9.6	0.57				TREATMENTS	3	1.42	0.47
2-M	10	93.8	9.4	0.58				ERROR	36	15.91	0.44
3-M	10	96.0	9.6	0.54							
4-M	10	91.5	9.2	0.90				TOTAL	39	17.33	

F Ratio = 1.07 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 7.046 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

1 M	10	77.7	7.8	0.98				TREATMENTS	3	2.52	0.84
2-M	10	74.3	7.4	0.74				ERROR	36	23.06	0.64
3-M	10	80.2	8.0	0.44							
4-M	10	80.6	8.1	0.93				TOTAL	39	25.58	

F Ratio = 1.31 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 10.235 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

1 M	10	85.9	8.6	0.90				TREATMENTS	3	0.82	0.27
2-M	10	85.0	8.5	1.06				ERROR	36	40.51	1.13
3-M	10	87.8	8.8	1.33							
4-M	10	83.9	8.4	0.90				TOTAL	39	41.33	

F Ratio = 0.24 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 12.386 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation

Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Glucose

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: GLU

SEX: MALE

UNITS: mg/dL

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	1609	161	39.1				TREATMENTS	3	3684	1228
2-M	10	1449	145	11.1				ERROR	36	21230	590
3-M	10	1512	151	23.8							
4-M	10	1345	135	11.7				TOTAL	39	24914	

F Ratio = 2.08 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 16.422 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	1696	170	51.3				TREATMENTS	3	8780	2927
2-M	10	1431	143	47.3				ERROR	36	57740	1604
3-M	10	1645	165	34.2							
4-M	10	1337	134	19.6				TOTAL	39	66520	

F Ratio = 1.82 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 26.223 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	1916	192	43.4				TREATMENTS	3	5591	1864
2-M	10	1843	184	52.5				ERROR	36	77840	2162
3-M	10	1863	186	54.3							
4-M	10	1608	161	32.6				TOTAL	39	83431	

F Ratio = 0.86 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 25.726 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation

Treatments-between groups

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Globulin

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: GLOB

SEX: MALE

UNITS: g/dL

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	37.5	3.8	0.49				TREATMENTS	3	0.31	0.10
2-M	10	38.8	3.9	0.34				ERROR	36	6.43	0.18
3-M	10	36.4	3.6	0.44				TOTAL	39	6.74	
4-M	10	38.1	3.8	0.41							

F Ratio = 0.58 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 11.214 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	40.4	4.0	0.31				TREATMENTS	3	0.94	0.31
2-M	10	37.9	3.8	0.27	1.8	4.0 4.0	4.0 4.0	ERROR	36	3.46	0.10
3-M	10	37.8	3.8	0.32	1.9	4.0 4.0	4.0 4.0	TOTAL	39	4.40	
4-M	10	36.1	3.6	0.33	3.1	4.0 4.0*	4.0 4.0**				

F Ratio = 3.27 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 8.145 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	33.8	3.4	0.78				TREATMENTS	3	0.47	0.16
2-M	10	33.4	3.3	0.75				ERROR	36	17.52	0.49
3-M	10	34.7	3.5	0.65				TOTAL	39	18.00	
4-M	10	31.7	3.2	0.60							

F Ratio = 0.32 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 20.888 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01
Error-within groups

Source-Source of Variation
Treatments-between groups

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: A/G Ratio

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: A/G

SEX: MALE

UNITS: -

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	10.69	1.07	0.097				TREATMENTS	3	0.068	0.023
2-M	10	10.20	1.02	0.089				ERROR	36	0.674	0.019
3-M	10	11.34	1.13	0.200				TOTAL	39	0.742	
4-M	10	10.94	1.09	0.132							

F Ratio = 1.22 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 12.676 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	10.65	1.07	0.108				TREATMENTS	3	0.098	0.033
2-M	10	10.90	1.09	0.088	0.56	1.00 1.00	1.00 1.00	ERROR	36	0.360	0.010
3-M	10	11.14	1.11	0.101	1.10	1.00 1.00	1.00 1.00	TOTAL	39	0.459	
4-M	10	11.97	1.20	0.101	2.95	1.00 1.00*	1.00 1.00				

F Ratio = 3.28 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 8.960 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1 M	10	13.23	1.32	0.375				TREATMENTS	3	0.06	0.02
2-M	10	12.59	1.26	0.327				ERROR	36	4.37	0.12
3-M	10	12.51	1.25	0.365				TOTAL	39	4.43	
4-M	10	13.44	1.34	0.324							

F Ratio = 0.18 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 26.922 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

*-Significant Difference from Control P < .05
Error-within groups

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Alanine Aminotransferase

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: ALT

SEX: FEMALE

UNITS: IU/L

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	512	51	7.3						TREATMENTS	3	542.88	180.96
2-F	10	478	48	8.4	1	43	59	41	62	ERROR	36	2000.50	55.57
3-F	10	491	49	3.5	1	43	59	41	62				
4-F	10	574	57	9.3	2	43	59	41	62	TOTAL	39	2543.38	

F Ratio = 3.26 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 14.510 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

1-F	10	643	64	13.4						TREATMENTS	3	606.67	202.22
2-F	10	600	60	8.6						ERROR	36	5655.10	157.09
3-F	10	675	68	11.4									
4-F	10	705	71	15.6						TOTAL	39	6261.78	

F Ratio = 1.29 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 19.113 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

1-F	10	1130	113	51.6						TREATMENTS	3	5053	1684
2-F	10	984	98	72.3						ERROR	36	126538	3515
3-F	10	1171	117	73.2									
4-F	10	891	89	28.6						TOTAL	39	131592	

F Ratio = 0.48 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 56.788 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation

Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Sorbitol Dehydrogenase

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: SDH

SEX: FEMALE

UNITS: IU/L

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	149.3	14.9	3.48						TREATMENTS	3	108.54	36.18
2-F	10	147.6	14.8	1.60						ERROR	36	556.55	15.46
3-F	10	152.4	15.2	6.40									
4-F	10	187.6	18.8	2.49						TOTAL	39	665.09	

F Ratio = 2.34 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 24.694 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	122.0	12.2	4.18						TREATMENTS	3	301.99	100.66
2-F	10	131.3	13.1	6.69	0.4	6.0	19.0	4.0	20.0	ERROR	36	1204.20	33.45
3-F	10	186.7	18.7	8.11	2.5	6.0	19.0*	4.0	20.0				
4-F	10	174.3	17.4	2.40	2.0	6.0	19.0	4.0	20.0	TOTAL	39	1506.20	

F Ratio = 3.01 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 37.660 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	87.4	8.7	6.12	TREATMENTS	3	62.78	20.93
2-F	10	87.4	8.7	4.19	ERROR	36	1040.49	28.90
3-F	10	69.9	7.0	5.30				
4-F	10	57.8	5.8	5.70	TOTAL	39	1103.27	

F Ratio = 0.72 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 71.089 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

*-Significant Difference from Control P < .05
Error-within groups

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Total Protein

DRAFT

STUDY IO: UIC-15B
STUDY NO: 152
ABBR: TP

SEX: FEMALE

UNITS: g/dL

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		DUNNETT'S RANGES LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	73.0	7.3	0.41						TREATMENTS	3	0.09	0.03
2-F	10	72.3	7.2	0.56						ERROR	36	7.33	0.20
3-F	10	73.5	7.4	0.40									
4-F	10	72.4	7.2	0.41						TOTAL	39	7.42	

F Ratio = 0.15 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 6.198 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		DUNNETT'S RANGES LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	77.3	7.7	0.65						TREATMENTS	3	0.87	0.29
2-F	10	80.4	8.0	0.55						ERROR	36	15.17	0.42
3-F	10	77.3	7.7	0.73									
4-F	10	76.6	7.7	0.65						TOTAL	39	16.04	

F Ratio = 0.69 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 8.333 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		DUNNETT'S RANGES LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	98.6	9.9	0.85						TREATMENTS	3	5.15	1.72
2-F	10	91.5	9.2	0.51	2.5	9.0	11.0*	9.0	11.0	ERROR	36	14.57	0.40
3-F	10	98.0	9.8	0.56	0.2	9.0	11.0	9.0	11.0				
4-F	10	90.8	9.1	0.58	2.7	9.0	11.0*	9.0	11.0	TOTAL	39	19.72	

F Ratio = 4.25 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 6.715 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

*-Significant Difference from Control P < .05
Error-within groups

Source-Source of Variation
Treatments-between groups

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Albumin

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: ALB

SEX: FEMALE

UNITS: g/dL

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	40.7	4.1	0.29				TREATMENTS	3	0.08	0.03
2-F	10	39.9	4.0	0.28				ERROR	36	2.80	0.08
3-F	10	40.5	4.1	0.26				TOTAL	39	2.88	
4-F	10	39.6	4.0	0.28							

F Ratio = 0.34 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 6.941 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	45.6	4.6	0.30				TREATMENTS	3	0.13	0.04
2-F	10	45.9	4.6	0.40				ERROR	36	4.96	0.14
3-F	10	45.0	4.5	0.43				TOTAL	39	5.09	
4-F	10	44.4	4.4	0.33							

F Ratio = 0.32 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 8.205 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	46.5	4.7	0.28				TREATMENTS	3	0.06	0.02
2-F	10	46.2	4.6	0.23				ERROR	36	2.44	0.07
3-F	10	47.3	4.7	0.20				TOTAL	39	2.51	
4-F	10	46.7	4.7	0.31							

F Ratio = 0.32 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 5.581 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation

Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Total Bile Acids

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: TBA

SEX: FEMALE
UNITS: umol/L

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	255.7	25.6	13.51				TREATMENTS	3	1124.86	374.95
2-F	10	227.1	22.7	7.13				ERROR	36	7621.08	211.70
3-F	10	294.5	29.5	16.51							
4-F	10	368.4	36.8	18.47				TOTAL	39	8745.94	

F Ratio = 1.77 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 50.798 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	451.4	45.1	30.14				TREATMENTS	3	14071	4690
2-F	10	866.4	86.6	89.41				ERROR	36	99250	2757
3-F	10	597.0	59.7	25.49							
4-F	10	901.7	90.2	38.40				TOTAL	39	113321	

F Ratio = 1.70 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 74.570 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	938.8	93.9	44.84				TREATMENTS	3	35186	11729
2-F	10	823.1	82.3	34.15				ERROR	36	284821	7912
3-F	10	824.9	82.5	38.92							
4-F	10	1538.6	153.9	164.18				TOTAL	39	320007	

F Ratio = 1.48 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 86.244 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Alkaline Phosphatase

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: ALKP

SEX: FEMALE

UNITS: IU/L

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	2133	213	44.4				TREATMENTS	3	10881	3627
2-F	10	2368	237	70.5				ERROR	36	276026	7667
3-F	10	2418	242	116.7				TOTAL	39	286907	
4-F	10	2595	260	100.6							

F Ratio = 0.47 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 36.815 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	1280	128	26.5				TREATMENTS	3	14244	4748
2-F	10	1761	176	90.7				ERROR	36	190188	5283
3-F	10	1511	151	79.6				TOTAL	39	204432	
4-F	10	1706	171	76.5							

F Ratio = 0.90 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 46.458 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	1101	110	36.5				TREATMENTS	3	12163	4054
2-F	10	1140	114	50.0				ERROR	36	147810	4106
3-F	10	1364	136	93.3				TOTAL	39	159974	
4-F	10	1531	153	62.3							

F Ratio = 0.99 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 49.904 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation

Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Lactate Dehydrogenase

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: LDH

SEX: FEMALE

UNITS: IU/L

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI
1-F	10	2525	253	211.0			
2-F	10	2398	240	110.8			
3-F	10	3920	392	254.2			
4-F	10	1825	183	86.7			

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	237150	79050
ERROR	36	1160223	32228
TOTAL	39	1397372	

F Ratio = 2.45 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 67.313 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI
1-F	10	4435	444	197.3			
2-F	10	4573	457	242.7			
3-F	10	3200	320	163.4			
4-F	10	3752	375	190.0			

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	121866	40622
ERROR	36	1445662	40157
TOTAL	39	1567528	

F Ratio = 1.01 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 50.224 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI
1-F	10	4831	483	270.4			
2-F	10	5497	550	249.7			
3-F	10	4859	486	243.2			
4-F	10	4865	487	218.5			

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	31300	10433
ERROR	36	2181642	60601
TOTAL	39	2212942	

F Ratio = 0.17 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 49.107 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Creatine Kinase

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: CK

SEX: FEMALE

UNITS: IU/L

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	2113	211	167.9				TREATMENTS	3	88191	29397
2-F	10	1471	147	47.2				ERROR	36	716370	19899
3-F	10	2595	260	216.3							
4-F	10	1487	149	48.7				TOTAL	39	804561	

F Ratio = 1.48 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 73.605 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

1-F	10	4272	427	461.4				TREATMENTS	3	340010	113337
2-F	10	4890	489	525.6				ERROR	36	5111786	141994
3-F	10	4079	408	242.1							
4-F	10	2400	240	142.1				TOTAL	39	5451797	

F Ratio = 0.80 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 96.367 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

1-F	10	2981	298	232.5				TREATMENTS	3	723170	241057
2-F	10	4785	479	462.0				ERROR	36	14542512	403959
3-F	10	6526	653	921.2							
4-F	10	5888	589	707.0				TOTAL	39	15265682	

F Ratio = 0.60 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 125.982 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation

Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Blood Urea Nitrogen

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: BUN

SEX: FEMALE

UNITS: mg/dL

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	183.9	18.4	1.50				TREATMENTS	3	12.84	4.28
2-F	10	183.1	18.3	1.85				ERROR	36	131.49	3.65
3-F	10	194.8	19.5	1.72							
4-F	10	179.7	18.0	2.44				TOTAL	39	144.33	

F Ratio = 1.17 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 10.310 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	167.5	16.8	3.18				TREATMENTS	3	65.84	21.95
2-F	10	183.3	18.3	3.89				ERROR	36	340.89	9.47
3-F	10	188.1	18.8	2.26							
4-F	10	155.8	15.6	2.76				TOTAL	39	406.73	

F Ratio = 2.32 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 17.718 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	187.5	18.8	1.96						TREATMENTS	3	53.44	17.81
2-F	10	181.4	18.1	2.18	0.7	17.0	21.0	16.0	22.0	ERROR	36	143.94	4.00
3-F	10	187.5	18.8	2.10	0.0	17.0	21.0	16.0	22.0				
4-F	10	159.4	15.9	1.72	3.1	17.0	21.0*	16.0	22.0**	TOTAL	39	197.38	

F Ratio = 4.46 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 11.174 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01
Error-within groups

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Creatinine

DRAFT

STUDY ID: UIC-158
STUDY NO: 152
ABBR: CREAT

SEX: FEMALE

UNITS: mg/dL

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	5.47	0.55	0.028				TREATMENTS	3	0.0049	0.0016
2-F	10	5.57	0.56	0.047				ERROR	36	0.0580	0.0016
3-F	10	5.74	0.57	0.054				TOTAL	39	0.0629	
4-F	10	5.72	0.57	0.023							

F Ratio = 1.02 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 7.137 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

1-F	10	5.97	0.60	0.088				TREATMENTS	3	0.032	0.011
2-F	10	5.52	0.55	0.107				ERROR	36	0.272	0.008
3-F	10	6.27	0.63	0.075				TOTAL	39	0.303	
4-F	10	5.71	0.57	0.074							

F Ratio = 1.40 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 14.805 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

1-F	10	6.48	0.65	0.096				TREATMENTS	3	0.010	0.003
2-F	10	6.50	0.65	0.066				ERROR	36	0.226	0.006
3-F	10	6.71	0.67	0.065				TOTAL	39	0.236	
4-F	10	6.27	0.63	0.086							

F Ratio = 0.52 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 12.205 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation

Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Sodium

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: NA

SEX: FEMALE

UNITS: mEq/L

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	1441	144	1.2				TREATMENTS	3	0.88	0.29
2-F	10	1439	144	1.3				ERROR	36	65.50	1.82
3-F	10	1438	144	1.8							
4-F	10	1437	144	1.1				TOTAL	39	66.38	

F Ratio = 0.16 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 0.938 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	1448	145	1.7				TREATMENTS	3	26.60	8.87
2-F	10	1449	145	1.5				ERROR	36	171.00	4.75
3-F	10	1461	146	2.8							
4-F	10	1438	144	2.4				TOTAL	39	197.60	

F Ratio = 1.87 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 1.504 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	1455	146	2.1				TREATMENTS	3	17.47	5.82
2-F	10	1463	146	1.6				ERROR	36	95.90	2.66
3-F	10	1461	146	1.4							
4-F	10	1446	145	1.3				TOTAL	39	113.37	

F Ratio = 2.19 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 1.121 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation

Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Potassium

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: K

SEX: FEMALE

UNITS: mEq/L

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	54.68	5.47	0.241				TREATMENTS	3	0.40	0.13
2-F	10	54.57	5.46	0.288				ERROR	36	3.50	0.10
3-F	10	56.88	5.69	0.417							
4-F	10	56.31	5.63	0.272				TOTAL	39	3.91	

F Ratio = 1.39 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 5.610 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	58.06	5.81	0.438				TREATMENTS	3	0.80	0.27
2-F	10	54.52	5.45	0.391				ERROR	36	5.39	0.15
3-F	10	54.74	5.47	0.457							
4-F	10	55.36	5.54	0.214				TOTAL	39	6.19	

F Ratio = 1.78 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 6.951 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	56.13	5.61	0.671				TREATMENTS	3	0.27	0.09
2-F	10	55.77	5.58	0.448				ERROR	36	9.33	0.26
3-F	10	55.12	5.51	0.465							
4-F	10	57.37	5.74	0.413				TOTAL	39	9.60	

F Ratio = 0.34 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 9.077 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation

Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Chloride

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: CL

SEX: FEMALE

UNITS: mEq/L

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	1035	104	3.6				TREATMENTS	3	7.40	2.47
2-F	10	1037	104	3.7				ERROR	36	410.60	11.41
3-F	10	1046	105	2.9							
4-F	10	1042	104	3.2				TOTAL	39	418.00	

F Ratio = 0.22 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 3.247 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	994	99	2.5				TREATMENTS	3	49.00	16.33
2-F	10	1006	101	2.8				ERROR	36	271.00	7.53
3-F	10	1023	102	2.9							
4-F	10	1017	102	2.8				TOTAL	39	320.00	

F Ratio = 2.17 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 2.717 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	1044	104	3.9				TREATMENTS	3	51.87	17.29
2-F	10	1025	103	1.6				ERROR	36	449.90	12.50
3-F	10	1047	105	5.4							
4-F	10	1021	102	1.9				TOTAL	39	501.77	

F Ratio = 1.38 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 3.418 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation

Treatments-between groups

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Calcium

DRAFT

STUDY ID: UIC-158
STUDY NO: 152
ABBR: CA

SEX: FEMALE

UNITS: mg/dL

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	107.6	10.8	0.33				TREATMENTS	3	0.18	0.06
2-F	10	108.1	10.8	0.23				ERROR	36	4.22	0.12
3-F	10	109.3	10.9	0.41				TOTAL	39	4.40	
4-F	10	108.9	10.9	0.37							

F Ratio = 0.50 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 3.157 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

1-F	10	109.9	11.0	0.66				TREATMENTS	3	0.41	0.14
2-F	10	109.5	11.0	0.56				ERROR	36	9.68	0.27
3-F	10	112.1	11.2	0.47				TOTAL	39	10.09	
4-F	10	111.0	11.1	0.34							

F Ratio = 0.51 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 4.688 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

1-F	10	111.0	11.1	0.32				TREATMENTS	3	0.23	0.08
2-F	10	110.4	11.0	0.32				ERROR	36	3.24	0.09
3-F	10	109.3	10.9	0.24				TOTAL	39	3.47	
4-F	10	109.2	10.9	0.31							

F Ratio = 0.85 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 2.728 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Inorganic Phosphorus

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: IP

SEX: FEMALE

UNITS: mg/dL

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	77.9	7.8	0.88				TREATMENTS	3	2.19	0.73
2-F	10	79.8	8.0	0.52				ERROR	36	21.38	0.59
3-F	10	83.7	8.4	0.97							
4-F	10	82.9	8.3	0.63				TOTAL	39	23.57	

F Ratio = 1.23 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 9.504 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	79.4	7.9	1.08				TREATMENTS	3	1.44	0.48
2-F	10	76.7	7.7	0.73				ERROR	36	26.22	0.73
3-F	10	81.9	8.2	0.54							
4-F	10	80.4	8.0	0.96				TOTAL	39	27.66	

F Ratio = 0.66 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 10.721 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	91.8	9.2	0.84				TREATMENTS	3	1.68	0.56
2-F	10	86.3	8.6	1.13				ERROR	36	36.61	1.02
3-F	10	90.6	9.1	1.12							
4-F	10	89.9	9.0	0.91				TOTAL	39	38.29	

F Ratio = 0.55 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 11.249 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation

Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Glucose

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: GLU

SEX: FEMALE

UNITS: mg/dL

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	1287	129	18.2				TREATMENTS	3	1693	564
2-F	10	1328	133	14.7				ERROR	36	15176	422
3-F	10	1458	146	24.4							
4-F	10	1394	139	23.3				TOTAL	39	16869	

F Ratio = 1.34 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 15.022 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	1421	142	30.3				TREATMENTS	3	3521	1174
2-F	10	1444	144	23.9				ERROR	36	48370	1344
3-F	10	1657	166	43.0							
4-F	10	1465	147	45.1				TOTAL	39	51891	

F Ratio = 0.87 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 24.490 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	1531	153	32.5				TREATMENTS	3	2994	998
2-F	10	1391	139	26.5				ERROR	36	38494	1069
3-F	10	1573	157	38.9							
4-F	10	1373	137	31.7				TOTAL	39	41488	

F Ratio = 0.93 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 22.290 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY
OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: Globulin

DRAFT

STUDY ID: UIC-158
STUDY NO: 152
ABBR: GLOB

SEX: FEMALE

UNITS: g/dL

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	32.3	3.2	0.26				TREATMENTS	3	0.03	0.01
2-F	10	32.4	3.2	0.35				ERROR	36	2.38	0.07
3-F	10	33.0	3.3	0.19							
4-F	10	32.8	3.3	0.20				TOTAL	39	2.41	

F Ratio = 0.17 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 7.883 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	31.7	3.2	0.44				TREATMENTS	3	0.46	0.15
2-F	10	34.5	3.5	0.36				ERROR	36	7.16	0.20
3-F	10	32.3	3.2	0.50							
4-F	10	32.2	3.2	0.47				TOTAL	39	7.63	

F Ratio = 0.78 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 13.652 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	52.1	5.2	0.76				TREATMENTS	3	4.66	1.55
2-F	10	45.3	4.5	0.47	2.8	5.0 6.0*	4.0 6.0	ERROR	36	10.56	0.29
3-F	10	50.7	5.1	0.49	0.6	5.0 6.0	4.0 6.0				
4-F	10	44.1	4.4	0.37	3.3	5.0 6.0*	4.0 6.0**	TOTAL	39	15.22	

F Ratio = 5.29 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 11.272 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01
Error-within groups
Source-Source of Variation
Treatments-between groups

SUMMARY OF CLINICAL CHEMISTRY TESTS
TEST: A/G Ratio

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: A/G

SEX: FEMALE

UNITS: -

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	12.66	1.27	0.133						TREATMENTS	3	0.017	0.006
2-F	10	12.39	1.24	0.104						ERROR	36	0.356	0.010
3-F	10	12.28	1.23	0.065									
4-F	10	12.09	1.21	0.083						TOTAL	39	0.373	

F Ratio = 0.57 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 8.046 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	14.60	1.46	0.188						TREATMENTS	3	0.07	0.02
2-F	10	13.44	1.34	0.189						ERROR	36	1.57	0.04
3-F	10	14.21	1.42	0.253									
4-F	10	14.03	1.40	0.198						TOTAL	39	1.64	

F Ratio = 0.53 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 14.836 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	9.07	0.91	0.121						TREATMENTS	3	0.162	0.054
2-F	10	10.30	1.03	0.123	2.59	1.00	1.00*	1.00	1.00	ERROR	36	0.405	0.011
3-F	10	9.40	0.94	0.089	0.70	1.00	1.00	1.00	1.00				
4-F	10	10.63	1.06	0.085	3.29	1.00	1.00*	1.00	1.00**	TOTAL	39	0.567	

F Ratio = 4.81 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 10.763 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01
Error-within groups

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Act. Partial Thrombo. Time

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: APTT

SEX: MALE

UNITS: sec

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 27

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	181.7	18.2	3.54						TREATMENTS	3	37.70	12.57
2-M	10	198.1	19.8	1.21	1.8	16.0	20.0	15.0	21.0	ERROR	36	152.55	4.24
3-M	10	192.6	19.3	1.21	1.2	16.0	20.0	15.0	21.0				
4-M	10	173.0	17.3	1.24	0.9	16.0	20.0	15.0	21.0	TOTAL	39	190.25	

F Ratio = 2.97 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 11.047 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation

Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Act. Partial Thrombo. Time

DRAFT

STUDY ID: UIC-158
STUDY NO: 152
ABBR: APTT

SEX: FEMALE

UNITS: sec

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 27

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI
1-F	10	163.3	16.3	1.93			
2-F	10	183.8	18.4	5.16			
3-F	10	189.1	18.9	3.40			
4-F	10	169.6	17.0	3.13			

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	43.39	14.46
ERROR	36	464.97	12.92
TOTAL	39	508.36	

F Ratio = 1.12 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 20.368 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Error-within groups
Source-Source of Variation

Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Atypical Lymphocytes

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: Atypical L

SEX: MALE

UNITS: 10^3/mm^3

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	0.0	0.0	0.00				TREATMENTS	3	0.00000	0.00000
2-M	10	0.0	0.0	0.00				ERROR	36	0.00000	0.00000
3-M	10	0.0	0.0	0.00							
4-M	10	0.0	0.0	0.00				TOTAL	39	0.00000	

F Ratio = 0.00 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	0.0	0.0	0.00				TREATMENTS	3	0.00000	0.00000
2-M	10	0.0	0.0	0.00				ERROR	36	0.00000	0.00000
3-M	10	0.0	0.0	0.00							
4-M	10	0.0	0.0	0.00				TOTAL	39	0.00000	

F Ratio = 0.00 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	0.0	0.0	0.00				TREATMENTS	3	0.00000	0.00000
2-M	10	0.0	0.0	0.00				ERROR	36	0.00000	0.00000
3-M	10	0.0	0.0	0.00							
4-M	10	0.0	0.0	0.00				TOTAL	39	0.00000	

F Ratio = 0.00 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

WBC corrected for NRBC = or > 10
Error-within groups

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
TEST: Atypical Lymphocytes

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: Atypical L

SEX: FEMALE

UNITS: 10^3/mm^3

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 4

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	0.0	0.0	0.00				TREATMENTS	3	0.00000	0.00000
2-F	10	0.0	0.0	0.00				ERROR	36	0.00000	0.00000
3-F	10	0.0	0.0	0.00							
4-F	10	0.0	0.0	0.00				TOTAL	39	0.00000	

F Ratio = 0.00 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 13

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	0.0	0.0	0.00				TREATMENTS	3	0.00000	0.00000
2-F	10	0.0	0.0	0.00				ERROR	36	0.00000	0.00000
3-F	10	0.0	0.0	0.00							
4-F	10	0.0	0.0	0.00				TOTAL	39	0.00000	

F Ratio = 0.00 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

Week 26

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	0.0	0.0	0.00				TREATMENTS	3	0.00000	0.00000
2-F	10	0.0	0.0	0.00				ERROR	36	0.00000	0.00000
3-F	10	0.0	0.0	0.00							
4-F	10	0.0	0.0	0.00				TOTAL	39	0.00000	

F Ratio = 0.00 'F' table values F.01 = 4.38 F.05 = 2.86
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 3.09 P.05 = 2.44

WBC corrected for NRBC = or > 10
Error-within groups

Source-Source of Variation
Treatments-between groups

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

ORGAN WEIGHT SUMMARY

STUDY: 152
SEX: MALE

ALL FATES DAYS: 183-185 ALL BALANCES
ANALYSIS OF VARIANCE USING DUNNETT'S PROCEDURE

DRAFT

BODY WEIGHT (G)

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1-M	20	14308	715	55.3					
2-M	20	13971	699	64.0	1	672	759	661	770
3-M	20	13165	658**	50.7	3**	672	759*	661	770**
4-M	19	10100	532**	61.7	10**	671	760*	660	771**

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	400017	133339
ERROR	75	253408	3379
TOTAL	78	653426	

F Ratio = 39.46 'F' table values F.01 = 4.08** F.05 = 2.74*
Coeff. Var. % = 8.909 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

Adrenal Glands (G)

Group	N	Total	Mean	Std. Dev.
1-M	20	1.232	0.062	0.0088
2-M	20	1.313	0.066	0.0128
3-M	20	1.203	0.060	0.0185
4-M	19	1.314	0.069	0.0180

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	0.0010	0.0003
ERROR	75	0.0169	0.0002
TOTAL	78	0.0178	

F Ratio = 1.44 'F' table values F.01 = 4.08 F.05 = 2.74
Coeff. Var. % = 23.408 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

Brain (G)

Group	N	Total	Mean	Std. Dev.
1-M	20	44.448	2.222	0.1605
2-M	20	44.045	2.202	0.1069
3-M	20	44.199	2.210	0.1426
4-M	19	41.310	2.174	0.1142

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	0.02	0.01
ERROR	75	1.33	0.02
TOTAL	78	1.35	

F Ratio = 0.46 'F' table values F.01 = 4.08 F.05 = 2.74
Coeff. Var. % = 6.041 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

Heart (G)

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1-M	20	36.570	1.829	0.2062					
2-M	20	34.846	1.742	0.1810	1.484	1.690	1.967	1.656	2.001
3-M	20	33.309	1.665*	0.0950	2.808*	1.690	1.967*	1.656	2.001
4-M	19	30.590	1.610**	0.2270	3.714**	1.688	1.969*	1.654	2.003**

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	0.53	0.18
ERROR	75	2.53	0.03
TOTAL	78	3.06	

F Ratio = 5.25 'F' table values F.01 = 4.08** F.05 = 2.74*
Coeff. Var. % = 10.721 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

* - Significant difference P<.05 ** - Significant difference P<.01

LABCAT OW3.14 27-MAR-1996

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

ORGAN WEIGHT SUMMARY

STUDY: 152
SEX: MALE

ALL FATES DAYS: 183-185 ALL BALANCES
ANALYSIS OF VARIANCE USING DUNNETT'S PROCEDURE

DRAFT

Kidneys (G)

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	20	83.306	4.165	0.3983						TREATMENTS	3	3.46	1.15
2-M	20	82.756	4.138	0.3960	0.163	3.764	4.567	3.665	4.666	ERROR	75	21.32	0.28
3-M	20	90.705	4.535	0.3602	2.194	3.764	4.567	3.665	4.666				
4-M	19	87.407	4.600*	0.8453	2.547*	3.759	4.572*	3.658	4.673	TOTAL	78	24.78	

F Ratio = 4.05 'F' table values F.01 = 4.08 F.05 = 2.74*
Coeff. Var. % = 12.238 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

Lungs/Bronchi (G)

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	20	46.328	2.316	0.2856						TREATMENTS	3	90.56	30.19
2-M	20	48.938	2.447	0.3396	0.162	0.402	4.231	-0.072	4.705	ERROR	75	485.15	6.47
3-M	20	89.736	4.487*	4.9359	2.699*	0.402	4.231*	-0.072	4.705				
4-M	19	86.565	4.556*	1.0143	2.749*	0.377	4.256*	-0.104	4.736	TOTAL	78	575.71	

F Ratio = 4.67 'F' table values F.01 = 4.08** F.05 = 2.74*
Coeff. Var. % = 73.988 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

Liver (G)

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	20	501.898	25.095	2.9526						TREATMENTS	3	61.22	20.41
2-M	20	480.224	24.011	2.8975						ERROR	75	1220.18	16.27
3-M	20	484.305	24.215	5.5883									
4-M	19	429.731	22.617	4.0939						TOTAL	78	1281.41	

F Ratio = 1.25 'F' table values F.01 = 4.08 F.05 = 2.74
Coeff. Var. % = 16.805 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

Spleen (G)

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	20	19.386	0.969	0.1863						TREATMENTS	3	32.86	10.95
2-M	20	18.966	0.948	0.1432	0.182	0.694	1.244	0.626	1.313	ERROR	75	10.02	0.13
3-M	20	23.970	1.199	0.1500	1.983	0.694	1.244	0.626	1.313				
4-M	19	48.068	2.530**	0.6890	13.326**	0.691	1.248*	0.621	1.317**	TOTAL	78	42.88	

F Ratio = 81.97 'F' table values F.01 = 4.08** F.05 = 2.74*
Coeff. Var. % = 26.160 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

* - Significant difference P<.05 ** - Significant difference P<.01

LABCAT OW3.14 27-MAR-1996

ORGAN WEIGHT SUMMARY

STUDY: 152
SEX: MALE

ALL FATES DAYS: 183-185 ALL BALANCES
ANALYSIS OF VARIANCE USING DUNNETT'S PROCEDURE

DRAFT

Testes with Epididymides (G)

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	DUNNETT'S RANGES LO -99%- HI
1-M	20	107.357	5.368	0.5011			
2-M	20	105.370	5.269	0.3792			
3-M	20	109.491	5.475	0.5326			
4-M	19	99.329	5.228	0.5896			

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	0.72	0.24
ERROR	75	19.15	0.26
TOTAL	78	19.87	

F Ratio = 0.94 'F' table values F.01 = 4.08 F.05 = 2.74
Coeff. Var. % = 9.470 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

ORGAN WEIGHT SUMMARY (% BRAIN WEIGHT)

STUDY: 152
SEX: MALE

ALL FATES DAYS: 183-185 ALL BALANCES
ANALYSIS OF VARIANCE USING DUNNETT'S PROCEDURE

DRAFT

Adrenal Glands (% BRAIN WEIGHT)

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	20	55.38	2.77	0.319						TREATMENTS	3	2.61	0.87
2-M	20	59.61	2.98	0.591						ERROR	75	33.28	0.44
3-M	20	54.46	2.72	0.822									
4-M	19	60.48	3.18	0.812						TOTAL	78	35.89	

F Ratio = 1.96 'F' table values F.01 = 4.08 F.05 = 2.74
Coeff. Var. % = 22.886 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

Heart (% BRAIN WEIGHT)

1-M	20	1649.87	82.49	9.525						TREATMENTS	3	814.49	271.50
2-M	20	1582.55	79.13	7.466	1.22	75.91	89.08	74.28	90.71	ERROR	75	5740.61	76.54
3-M	20	1513.79	75.69*	6.856	2.46*	75.91	89.08*	74.28	90.71				
4-M	19	1409.19	74.17**	10.710	2.97**	75.82	89.16*	74.17	90.82**	TOTAL	78	6555.10	

F Ratio = 3.55 'F' table values F.01 = 4.08 F.05 = 2.74*
Coeff. Var. % = 11.228 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

Kidneys (% BRAIN WEIGHT)

1-M	20	3752.51	187.63	15.277						TREATMENTS	3	8710	2903
2-M	20	3764.25	188.21	18.890	0.08	170.11	205.14	165.77	209.49	ERROR	75	40631	542
3-M	20	4119.76	205.99*	20.407	2.49*	170.11	205.14*	165.77	209.49				
4-M	19	4014.92	211.31**	34.564	3.18**	169.88	205.37*	165.48	209.77**	TOTAL	78	49341	

F Ratio = 5.36 'F' table values F.01 = 4.08** F.05 = 2.74*
Coeff. Var. % = 11.748 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

Lungs/Bronchi (% BRAIN WEIGHT)

1-M	20	2090.80	104.54	13.301						TREATMENTS	3	195494	65165
2-M	20	2225.12	111.26	15.623	0.18	14.97	194.11	-0.24	216.32	ERROR	75	1062305	14164
3-M	20	4103.69	205.18*	231.794	2.67*	14.97	194.11*	-0.24	216.32				
4-M	19	3978.59	209.40*	43.117	2.75*	13.80	195.28*	-0.70	217.78	TOTAL	78	1257799	

F Ratio = 4.60 'F' table values F.01 = 4.08** F.05 = 2.74*
Coeff. Var. % = 75.834 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

* - Significant difference P<.05 ** - Significant difference P<.01

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ORGAN WEIGHT SUMMARY (% BRAIN WEIGHT)

STUDY: 152
SEX: MALE

ALL FATES DAYS: 183-185 ALL BALANCES
ANALYSIS OF VARIANCE USING DUNNETT'S PROCEDURE

DRAFT

Liver (% BRAIN WEIGHT)

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI	
1-M	20	22584.94	1129.25	106.800					
2-M	20	21815.81	1090.79	131.674					
3-M	20	22001.92	1100.10	267.811					
4-M	19	19792.28	1041.70	188.636					

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	77093	25698
ERROR	75	2549369	33992
TOTAL	78	2626462	

F Ratio = 0.76 'F' table values F.01 = 4.08 F.05 = 2.74
Coeff. Var. % = 16.898 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

Spleen (% BRAIN WEIGHT)

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI	
1-M	20	868.73	43.44	5.976					
2-M	20	860.98	43.05	5.915	0.08	31.22	55.65	28.19	58.68
3-M	20	1087.66	54.38	7.282	2.13	31.22	55.65	28.19	58.68
4-M	19	2208.29	116.23**	31.092	14.00**	31.06	55.81*	28.00	58.88**

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	70897	23632
ERROR	75	19752	263
TOTAL	78	90649	

F Ratio = 89.73 'F' table values F.01 = 4.08** F.05 = 2.74*
Coeff. Var. % = 25.510 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

Testes with Epididymides (% BRAIN WEIGHT)

Group	N	Total	Mean	Std. Dev.
1-M	20	4846.69	242.33	25.829
2-M	20	4792.65	239.63	19.127
3-M	20	4964.45	248.22	24.124
4-M	19	4583.36	241.23	31.324

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	839	280
ERROR	75	48345	645
TOTAL	78	49185	

F Ratio = 0.43 'F' table values F.01 = 4.08 F.05 = 2.74
Coeff. Var. % = 10.454 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

* - Significant difference P<.05 ** - Significant difference P<.01

LABCAT OW3.14 27-MAR-1996

SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS

ORGAN WEIGHT SUMMARY

STUDY: 152
SEX: FEMALE

ALL FATES DAYS: 183-185 ALL BALANCES
ANALYSIS OF VARIANCE USING DUNNETT'S PROCEDURE

DRAFT

BODY WEIGHT (G)

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	20	7788	389	44.1						TREATMENTS	3	58452	19484
2-F	20	7408	370	49.7	1	358	421	350	429	ERROR	76	131853	1735
3-F	20	7531	377	46.1	1	358	421	350	429				
4-F	20	6368	318**	20.1	5**	358	421*	350	429**	TOTAL	79	190305	

F Ratio = 11.23 'F' table values F.01 = 4.08** F.05 = 2.74*
Coeff. Var. % = 11.453 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

Adrenal Glands (G)

1-F	20	1.406	0.070	0.0181						TREATMENTS	3	0.0064	0.0021
2-F	20	1.576	0.079	0.0139	1.675	0.058	0.082	0.055	0.085	ERROR	76	0.0196	0.0003
3-F	20	1.454	0.073	0.0177	0.473	0.058	0.082	0.055	0.085				
4-F	20	1.867	0.093**	0.0141	4.542**	0.058	0.082*	0.055	0.085**	TOTAL	79	0.0260	

F Ratio = 8.31 'F' table values F.01 = 4.08** F.05 = 2.74*
Coeff. Var. % = 20.370 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

Brain (G)

1-F	20	40.278	2.014	0.1057						TREATMENTS	3	0.041	0.014
2-F	20	39.313	1.966	0.0959						ERROR	76	0.771	0.010
3-F	20	40.491	2.025	0.1021									
4-F	20	39.837	1.992	0.0990						TOTAL	79	0.812	

F Ratio = 1.34 'F' table values F.01 = 4.08 F.05 = 2.74
oeff. Var. % = 5.039 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

Heart (G)

1-F	20	22.244	1.112	0.1140						TREATMENTS	3	0.228	0.076
2-F	20	23.123	1.156	0.1391	1.234	1.027	1.197	1.006	1.218	ERROR	76	0.964	0.013
3-F	20	21.647	1.082	0.0961	0.838	1.027	1.197	1.006	1.218				
4-F	20	20.192	1.010*	0.0958	2.880*	1.027	1.197*	1.006	1.218	TOTAL	79	1.192	

F Ratio = 5.98 'F' table values F.01 = 4.08** F.05 = 2.74*
Coeff. Var. % = 10.334 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

* - Significant difference P<.05 ** - Significant difference P<.01

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ORGAN WEIGHT SUMMARY

STUDY: 152
SEX: FEMALE

ALL FATES DAYS: 183-185 ALL BALANCES
ANALYSIS OF VARIANCE USING DUNNETT'S PROCEDURE

DRAFT

Kidneys (G)

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	20	51.162	2.558	0.3257						TREATMENTS	3	0.59	0.20
2-F	20	49.130	2.457	0.3230						ERROR	76	6.83	0.09
3-F	20	51.308	2.565	0.2844									
4-F	20	53.982	2.699	0.2612						TOTAL	79	7.43	

F Ratio = 2.20 'F' table values F.01 = 4.08 F.05 = 2.74
Coeff. Var. % = 11.667 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

Lungs/Bronchi (G)

1-F	20	34.179	1.709	0.2221						TREATMENTS	3	37.51	12.50
2-F	20	34.232	1.712	0.2045	0.022	1.420	1.998	1.348	2.070	ERROR	76	11.22	0.15
3-F	20	53.193	2.660**	0.3839	7.825**	1.420	1.998*	1.348	2.070**				
4-F	20	66.607	3.330**	0.5932	13.346**	1.420	1.998*	1.348	2.070**	TOTAL	79	48.73	

F Ratio = 84.71 'F' table values F.01 = 4.08** F.05 = 2.74*
Coeff. Var. % = 16.330 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

Liver (G)

1-F	20	261.757	13.088	1.6747						TREATMENTS	3	3.62	1.21
2-F	20	258.554	12.928	2.0458						ERROR	76	242.65	3.19
3-F	20	264.471	13.224	1.9904									
4-F	20	253.048	12.652	1.3488						TOTAL	79	246.27	

F Ratio = 0.38 'F' table values F.01 = 4.08 F.05 = 2.74
Coeff. Var. % = 13.774 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

Ovaries (G)

1-F	20	2.024	0.101	0.0251						TREATMENTS	3	0.0017	0.0006
2-F	20	2.184	0.109	0.0306						ERROR	76	0.0705	0.0009
3-F	20	2.275	0.114	0.0363									
4-F	20	2.207	0.110	0.0287						TOTAL	79	0.0722	

F Ratio = 0.61 'F' table values F.01 = 4.08 F.05 = 2.74
Coeff. Var. % = 28.040 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

* - Significant difference P<.05 ** - Significant difference P<.01

LABCAT OW3.14 27-MAR-1996

ORGAN WEIGHT SUMMARY

STUDY: 152
SEX: FEMALE

ALL FATES DAYS: 183-185 ALL BALANCES
ANALYSIS OF VARIANCE USING DUNNETT'S PROCEDURE

DRAFT

Spleen (G)

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI	
1-F	20	11.307	0.565	0.0886					
2-F	20	11.422	0.571	0.0878	0.126	0.457	0.674	0.430	0.701
3-F	20	13.518	0.676*	0.0994	2.420*	0.457	0.674*	0.430	0.701
4-F	20	25.476	1.274**	0.2409	15.509**	0.457	0.674*	0.430	0.701**

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	3	6.88	2.29
ERROR	76	1.59	0.02
TOTAL	79	8.47	

F Ratio = 109.93 'F' table values F.01 = 4.08** F.05 = 2.74*
Coeff. Var. % = 18.723 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

* - Significant difference P<.05 ** - Significant difference P<.01

LABCAT OW3.14 27-MAR-1996

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

ORGAN WEIGHT SUMMARY (% BRAIN WEIGHT)

STUDY: 152
SEX: FEMALE

ALL FATES DAYS: 183-185 ALL BALANCES
ANALYSIS OF VARIANCE USING DUNNETT'S PROCEDURE

DRAFT

Adrenal Glands (% BRAIN WEIGHT)

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	20	69.80	3.49	0.867						TREATMENTS	3	17.76	5.92
2-F	20	80.18	4.01	0.701	2.07	2.89	4.09	2.74	4.24	ERROR	76	47.99	0.63
3-F	20	71.98	3.60	0.881	0.43	2.89	4.09	2.74	4.24				
4-F	20	93.83	4.69**	0.713	4.78**	2.89	4.09*	2.74	4.24**	TOTAL	79	65.75	

F Ratio = 9.38 'F' table values F.01 = 4.08** F.05 = 2.74*
Coeff. Var. % = 20.130 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

Heart (% BRAIN WEIGHT)

1-F	20	1105.81	55.29	5.677						TREATMENTS	3	701.69	233.90
2-F	20	1178.91	58.95	7.725	1.94	50.80	59.78	49.68	60.90	ERROR	76	2709.73	35.65
3-F	20	1070.88	53.54	4.921	0.92	50.80	59.78	49.68	60.90				
4-F	20	1015.54	50.78*	5.148	2.39*	50.80	59.78*	49.68	60.90	TOTAL	79	3411.42	

F Ratio = 6.56 'F' table values F.01 = 4.08** F.05 = 2.74*
Coeff. Var. % = 10.928 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

Kidneys (% BRAIN WEIGHT)

1-F	20	2543.04	127.15	15.763						TREATMENTS	3	1420	473
2-F	20	2500.84	125.04	15.598						ERROR	76	17585	231
3-F	20	2537.08	126.85	13.871									
4-F	20	2717.99	135.90	15.535						TOTAL	79	19005	

F Ratio = 2.05 'F' table values F.01 = 4.08 F.05 = 2.74
Coeff. Var. % = 11.816 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

Lungs/Bronchi (% BRAIN WEIGHT)

1-F	20	1694.10	84.71	8.564						TREATMENTS	3	93407	31136
2-F	20	1743.12	87.16	10.243	0.42	70.69	98.72	67.22	102.19	ERROR	76	26339	347
3-F	20	2629.90	131.50**	18.434	7.95**	70.69	98.72*	67.22	102.19**				
4-F	20	3345.65	167.28**	29.464	14.03**	70.69	98.72*	67.22	102.19**	TOTAL	79	119745	

F Ratio = 89.84 'F' table values F.01 = 4.08** F.05 = 2.74*
Coeff. Var. % = 15.822 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

* - Significant difference P<.05 ** - Significant difference P<.01

LABCAT OW3.14 27-MAR-1996

ORGAN WEIGHT SUMMARY (% BRAIN WEIGHT)

STUDY: 152
SEX: FEMALE

ALL FATES DAYS: 183-185 ALL BALANCES
ANALYSIS OF VARIANCE USING DUNNETT'S PROCEDURE

DRAFT

Liver (% BRAIN WEIGHT)

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	20	13011.66	650.58	80.273				TREATMENTS	3	4733	1578
2-F	20	13169.10	658.46	104.675				ERROR	76	623428	8203
3-F	20	13066.84	653.34	93.187							
4-F	20	12752.08	637.60	82.022				TOTAL	79	628161	

F Ratio = 0.19 'F' table values F.01 = 4.08 F.05 = 2.74
Coeff. Var. % = 13.934 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

Ovaries (% BRAIN WEIGHT)

1-F	20	100.42	5.02	1.204					TREATMENTS	3	4.98	1.66
2-F	20	111.75	5.59	1.684					ERROR	76	186.80	2.46
3-F	20	112.65	5.63	1.812								
4-F	20	111.24	5.56	1.504					TOTAL	79	191.78	

F Ratio = 0.67 'F' table values F.01 = 4.08 F.05 = 2.74
Coeff. Var. % = 28.763 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

Spleen (% BRAIN WEIGHT)

1-F	20	562.27	28.11	4.591						TREATMENTS	3	17381	5794
2-F	20	581.75	29.09	4.392	0.44	22.86	33.37	21.56	34.67	ERROR	76	3701	49
3-F	20	667.89	33.39*	4.672	2.39*	22.86	33.37*	21.56	34.67				
4-F	20	1278.56	63.93**	11.515	16.23**	22.86	33.37*	21.56	34.67**	TOTAL	79	21082	

F Ratio = 118.97 'F' table values F.01 = 4.08** F.05 = 2.74*
Coeff. Var. % = 18.064 Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38

* - Significant difference P<.05 ** - Significant difference P<.01

LABCAT OW3.14 27-MAR-1996

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 152 SEX: MALE

ANALYSIS OF VARIANCE

DAY 1

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	6304	252	16.6						TREATMENTS	3	272	91
2-M	25	6219	249	13.5	0.8					ERROR	96	20002	208
3-M	25	6211	248	12.8	0.9								
4-M	25	6200	248	14.6	1.0					TOTAL	99	20274	
'F' table values				F.01 =	3.98	F.05 =	2.70			Coeff. Var. % =		5.789	
Dunnett's 'T' table values				P.01 =	2.97	P.05 =	2.38			F Ratio =		0.44	

DAY 8

1-M	25	7657	306	20.7						TREATMENTS	3	3085	1028
2-M	25	7443	298	24.5	1.5					ERROR	96	38546	402
3-M	25	7466	299	15.7	1.3								
4-M	25	7265	291	18.1	2.8					TOTAL	99	41631	
'F' table values				F.01 =	3.98	F.05 =	2.70			Coeff. Var. % =		6.717	
Dunnett's 'T' table values				P.01 =	2.97	P.05 =	2.38			F Ratio =		2.56	

DAY 15

1-M	25	8816	353	26.9						TREATMENTS	3	14081	4694
2-M	25	8544	342	28.0	1.6	337	369	333	373	ERROR	96	53703	559
3-M	25	8561	342	18.9	1.5	337	369	333	373				
4-M	25	8002	320**	19.4	4.9	337	369*	333	373**	TOTAL	99	67784	
table values				F.01 =	3.98**	F.05 =	2.70*			Coeff. Var. % =		6.972	
Dunnett's 'T' table values				P.01 =	2.97	P.05 =	2.38			F Ratio =		8.39	

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 152 SEX: MALE

ANALYSIS OF VARIANCE

DAY 22

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	9757	390	29.6						TREATMENTS	3	38503	12834
2-M	25	9443	378	33.2	1.6	372	409	367	413	ERROR	96	71360	743
3-M	25	9470	379	20.6	1.5	372	409	367	413				
4-M	25	8460	338**	23.8	6.7	372	409*	367	413**	TOTAL	99	109863	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 7.343
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 17.27

DAY 29

1-M	25	10474	419	34.9						TREATMENTS	3	57910	19303
2-M	25	10213	409	36.7	1.2	398	440	392	446	ERROR	96	97515	1016
3-M	25	10281	411	24.8	0.9	398	440	392	446				
4-M	25	8951	358**	29.7	6.8	398	440*	392	446**	TOTAL	99	155425	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 7.984
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 19.00

DAY 36

1-M	25	11141	446	38.5						TREATMENTS	3	86137	28712
2-M	25	10943	438	38.9	0.8	422	469	416	475	ERROR	96	117756	1227
3-M	25	10940	438	29.3	0.8	422	469	416	475				
4-M	25	9324	373**	32.5	7.3	422	469*	416	475**	TOTAL	99	203893	

table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 8.270
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 23.41

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

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SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 152 SEX: MALE

ANALYSIS OF VARIANCE

DAY 43

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	12123	485	44.1						TREATMENTS	3	122957	40986
2-M	25	11809	472	41.0	1.2	459	511	453	517	ERROR	96	142578	1485
3-M	25	11641	466	31.4	1.8	459	511	453	517				
4-M	25	9873	395**	36.5	8.3	459	511*	453	517**	TOTAL	99	265535	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 8.480
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 27.60

DAY 50

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	12647	506	46.8						TREATMENTS	3	169233	56411
2-M	25	12398	496	40.0	0.9	479	532	473	539	ERROR	96	148816	1550
3-M	25	12057	482	30.6	2.1	479	532	473	539				
4-M	25	10042	402**	38.4	9.4	479	532*	473	539**	TOTAL	99	318049	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 8.351
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 36.39

DAY 57

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	13244	530	51.0						TREATMENTS	3	210770	70257
2-M	25	13035	521	41.9	0.7	501	559	494	566	ERROR	96	178832	1863
3-M	25	12558	502	30.9	2.2	501	559	494	566				
4-M	25	10358	414**	46.2	9.5	501	559*	494	566**	TOTAL	99	389602	

table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 8.773
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 37.71

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

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SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 152 SEX: MALE

ANALYSIS OF VARIANCE

DAY 64

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	13692	548	53.3						TREATMENTS	3	242829	80943
2-M	25	13598	544	42.7	0.3	516	579	509	587	ERROR	96	206894	2155
3-M	25	13032	521	32.6	2.0	516	579	509	587				
4-M	25	10656	426**	53.8	9.2	516	579*	509	587**	TOTAL	99	449723	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 9.107
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 37.56

DAY 71

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	14244	570	54.2						TREATMENTS	3	286410	95470
2-M	25	14143	566	45.0	0.3	537	603	528	611	ERROR	96	233968	2437
3-M	25	13427	537	34.1	2.3	537	603	528	611				
4-M	25	10935	437**	60.2	9.5	537	603*	528	611**	TOTAL	99	520378	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 9.359
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 39.17

DAY 78

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	14584	583	60.7						TREATMENTS	3	322034	107345
2-M	25	14524	581	44.8	0.2	550	617	541	625	ERROR	96	238652	2486
3-M	25	13802	552	34.7	2.2	550	617	541	625				
4-M	25	11105	444**	55.2	9.9	550	617*	541	625**	TOTAL	99	560686	

table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 9.231
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 43.18

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

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SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 152 SEX: MALE

ANALYSIS OF VARIANCE

DAY 85

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	14977	599	61.7						TREATMENTS	3	334182	111394
2-M	25	14954	598	46.7	0.1	566	633	557	641	ERROR	96	237648	2476
3-M	25	14081	563*	36.5	2.5	566	633*	557	641				
4-M	25	11439	458**	50.8	10.1	566	633*	557	641**	TOTAL	99	571830	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 8.973
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 45.00

DAY 92

1-M	25	15138	606	65.1						TREATMENTS	3	343634	114545
2-M	25	14989	600	50.6	0.4	571	640	562	649	ERROR	96	255312	2660
3-M	25	14109	564*	37.4	2.8	571	640*	562	649				
4-M	25	11485	459**	49.4	10.0	571	640*	562	649**	TOTAL	99	598946	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 9.255
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 43.07

DAY 99

1-M	25	15555	622	63.7						TREATMENTS	3	367400	122467
2-M	25	15542	622	53.5	0.0	586	658	578	667	ERROR	96	270444	2817
3-M	25	14435	577**	39.4	3.0	586	658*	578	667**				
4-M	25	11839	474**	52.8	9.9	586	658*	578	667**	TOTAL	99	637844	

table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 9.251
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 43.47

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 152 SEX: MALE

ANALYSIS OF VARIANCE

DAY 106

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	15751	630	64.1						TREATMENTS	3	402310	134103
2-M	25	15773	631	56.1	0.1	594	666	585	675	ERROR	96	273652	2851
3-M	25	14555	582**	40.9	3.2	594	666*	585	675**				
4-M	25	11879	475**	49.7	10.3	594	666*	585	675**	TOTAL	99	675962	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 9.212
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 47.04

DAY 113

1-M	25	16106	644	64.7						TREATMENTS	3	400252	133417
2-M	25	16060	642	57.4	0.1	608	681	598	690	ERROR	96	284752	2966
3-M	25	14790	592**	39.4	3.4	608	681*	598	690**				
4-M	25	12209	488**	53.2	10.1	608	681*	598	690**	TOTAL	99	685004	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 9.205
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 44.98

DAY 120

1-M	25	16252	650	62.6						TREATMENTS	3	427036	142345
2-M	25	16337	653	56.9	0.2	614	686	605	696	ERROR	96	280884	2926
3-M	25	14898	596**	40.4	3.5	614	686*	605	696**				
4-M	25	12294	492**	53.9	10.3	614	686*	605	696**	TOTAL	99	707920	

table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 9.048
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 48.65

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 152 SEX: MALE

ANALYSIS OF VARIANCE

DAY 127

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	16331	653	63.4						TREATMENTS	3	441354	147118
2-M	25	16477	659	59.4	0.4	617	690	608	699	ERROR	96	283276	2951
3-M	25	14952	598**	37.8	3.6	617	690*	608	699**				
4-M	25	12339	494**	53.2	10.4	617	690*	608	699**	TOTAL	99	724630	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 9.039
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 49.86

DAY 134

1-M	25	16555	662	65.5						TREATMENTS	3	458895	152965
2-M	25	16695	668	60.4	0.3	624	700	615	710	ERROR	96	308372	3212
3-M	25	15179	607**	39.0	3.4	624	700*	615	710**				
4-M	25	12479	499**	58.3	10.2	624	700*	615	710**	TOTAL	99	767267	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 9.305
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 47.62

DAY 141

1-M	25	16820	673	67.2						TREATMENTS	3	459447	153149
2-M	25	17060	682	63.4	0.6	634	712	624	721	ERROR	95	317908	3346
3-M	25	15446	618**	40.3	3.4	634	712*	624	721**				
4-M	24	12230	510**	56.8	9.9	633	712*	624	722**	TOTAL	98	777355	

table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 9.304
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 45.77

* P less than .05
** P less than .01

Analysis of Variance using OUNNETT'S Procedure

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 152 SEX: FEMALE

ANALYSIS OF VARIANCE

DAY 1

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	4561	182	10.2				TREATMENTS	3	148	49
2-F	25	4550	182	11.0	0.1			ERROR	96	10638	111
3-F	25	4545	182	10.3	0.2						
4-F	25	4483	179	10.6	1.0			TOTAL	99	10786	

'F' table values	F.01 =	3.98	F.05 =	2.70	Coeff. Var. % = 5.803
Dunnett's 'T' table values	P.01 =	2.97	P.05 =	2.38	F Ratio = 0.45

DAY 8

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	5107	204	12.6				TREATMENTS	3	516	172
2-F	25	5072	203	13.8	0.4			ERROR	96	14510	151
3-F	25	5053	202	12.6	0.6						
4-F	25	4954	198	9.8	1.8			TOTAL	99	15026	

'F' table values	F.01 =	3.98	F.05 =	2.70	Coeff. Var. % = 6.090
Dunnett's 'T' table values	P.01 =	2.97	P.05 =	2.38	F Ratio = 1.14

DAY 15

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	5539	222	12.7				TREATMENTS	3	1385	462
2-F	25	5520	221	16.0	0.2			ERROR	96	18841	196
3-F	25	5519	221	14.5	0.2						
4-F	25	5312	212	12.6	2.3			TOTAL	99	20226	

table values	F.01 =	3.98	F.05 =	2.70	Coeff. Var. % = 6.400
Dunnett's 'T' table values	P.01 =	2.97	P.05 =	2.38	F Ratio = 2.35

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 152 SEX: FEMALE

ANALYSIS OF VARIANCE

DAY 22

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	5894	236	14.4						TREATMENTS	3	2645	882
2-F	25	5850	234	16.7	0.4	226	246	223	248	ERROR	96	21605	225
3-F	25	5880	235	15.4	0.1	226	246	223	248				
4-F	25	5580	223*	13.3	3.0	226	246*	223	248	TOTAL	99	24250	

'F' table values F.01 = 3.98 F.05 = 2.70* Coeff. Var. % = 6.465
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 3.92

DAY 29

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	6163	247	15.4		TREATMENTS	3	2330	777
2-F	25	6176	247	18.5	0.1	ERROR	96	27618	288
3-F	25	6228	249	19.4	0.5				
4-F	25	5916	237	14.0	2.1	TOTAL	99	29948	

'F' table values F.01 = 3.98 F.05 = 2.70 Coeff. Var. % = 6.928
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 2.70

DAY 36

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	6307	252	16.1						TREATMENTS	3	5266	1755
2-F	25	6322	253	19.3	0.1	240	264	238	267	ERROR	96	29662	309
3-F	25	6303	252	20.0	0.0	240	264	238	267				
4-F	25	5892	236**	14.4	3.3	240	264*	238	267**	TOTAL	99	34928	

table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 7.081
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 5.68

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 152 SEX: FEMALE

ANALYSIS OF VARIANCE

DAY 43

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	6700	268	16.0						TREATMENTS	3	5363	1788
2-F	25	6722	269	22.6	0.2	255	281	252	284	ERROR	96	36270	378
3-F	25	6679	267	22.4	0.2	255	281	252	284				
4-F	25	6279	251**	15.6	3.1	255	281*	252	284**	TOTAL	99	41633	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 7.368
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 4.73

DAY 50

1-F	25	6836	273	18.5						TREATMENTS	3	8638	2879
2-F	25	6895	276	25.8	0.4	259	288	255	291	ERROR	96	43907	457
3-F	25	6923	277	24.4	0.6	259	288	255	291				
4-F	25	6353	254**	15.1	3.2	259	288*	255	291**	TOTAL	99	52545	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 7.919
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 6.30

DAY 57

1-F	25	7097	284	20.9						TREATMENTS	3	11855	3952
2-F	25	7179	287	27.8	0.5	268	300	264	304	ERROR	96	53206	554
3-F	25	7129	285	27.6	0.2	268	300	264	304				
4-F	25	6510	260**	15.7	3.5	268	300*	264	304**	TOTAL	99	65061	

table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 8.433
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 7.13

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 152 SEX: FEMALE

ANALYSIS OF VARIANCE

DAY 64

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	7338	294	22.2						TREATMENTS	3	13526	4509
2-F	25	7334	293	26.9	0.0	277	310	273	314	ERROR	96	56218	586
3-F	25	7349	294	29.8	0.1	277	310	273	314				
4-F	25	6669	267**	15.4	3.9	277	310*	273	314**	TOTAL	99	69744	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 8.435
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 7.70

DAY 71

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	7475	299	22.7						TREATMENTS	3	15267	5089
2-F	25	7447	298	28.4	0.2	282	316	277	321	ERROR	96	63077	657
3-F	25	7458	298	32.3	0.1	282	316	277	321				
4-F	25	6747	270**	16.2	4.0	282	316*	277	321**	TOTAL	99	78344	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 8.800
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 7.75

DAY 78

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	7631	305	24.9						TREATMENTS	3	17778	5926
2-F	25	7655	306	29.9	0.1	287	324	282	328	ERROR	96	72285	753
3-F	25	7534	301	34.9	0.5	287	324	282	328				
4-F	25	6844	274**	16.6	4.1	287	324*	282	328**	TOTAL	99	90063	

table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 9.250
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 7.87

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 152 SEX: FEMALE

ANALYSIS OF VARIANCE

DAY 85

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	7815	313	26.2						TREATMENTS	3	18686	6229
2-F	25	7794	312	32.0	0.1	294	332	289	336	ERROR	96	77019	802
3-F	25	7710	308	34.2	0.5	294	332	289	336				
4-F	25	6989	280**	18.2	4.1	294	332*	289	336**	TOTAL	99	95705	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 9.346
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 7.76

DAY 92

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	7915	317	27.5						TREATMENTS	3	25414	8471
2-F	25	7833	313	31.1	0.4	298	336	293	340	ERROR	96	76719	799
3-F	25	7780	311	31.4	0.7	298	336	293	340				
4-F	25	6929	277**	22.1	4.9	298	336*	293	340**	TOTAL	99	102133	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 9.282
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 10.60

DAY 99

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	7876	315	26.7						TREATMENTS	3	18131	6044
2-F	25	7788	312	30.8	0.5	296	334	292	338	ERROR	96	73310	764
3-F	25	7700	308	32.8	0.9	296	334	292	338				
4-F	25	7024	281**	17.7	4.4	296	334*	292	338**	TOTAL	99	91441	

table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 9.094
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 7.91

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 152 SEX: FEMALE

ANALYSIS OF VARIANCE

DAY 106

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	7895	316	27.2						TREATMENTS	3	21788	7263
2-F	25	7856	314	30.3	0.2	297	334	293	339	ERROR	96	71469	744
3-F	25	7772	311	31.2	0.6	297	334	293	339				
4-F	25	6995	280**	18.6	4.7	297	334*	293	339**	TOTAL	99	93257	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 8.941
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 9.76

DAY 113

1-F	25	8249	330	27.6						TREATMENTS	3	27732	9244
2-F	25	8240	330	33.5	0.0	311	349	306	354	ERROR	96	79189	825
3-F	25	8102	324	33.3	0.7	311	349	306	354				
4-F	25	7245	290**	17.5	4.9	311	349*	306	354**	TOTAL	99	106921	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 9.021
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 11.21

DAY 120

1-F	25	8415	337	30.9						TREATMENTS	3	33118	11039
2-F	25	8336	333	34.7	0.4	316	357	311	363	ERROR	96	92262	961
3-F	25	8247	330	36.6	0.8	316	357	311	363				
4-F	25	7291	292**	18.7	5.1	316	357*	311	363**	TOTAL	99	125380	

table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 9.601
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 11.49

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 152 SEX: FEMALE

ANALYSIS OF VARIANCE

DAY 127

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	8515	341	31.9						TREATMENTS	3	40106	13369
2-F	25	8417	337	36.5	0.4	319	362	313	368	ERROR	96	100282	1045
3-F	25	8381	335	39.3	0.6	319	362	313	368				
4-F	25	7287	291**	16.9	5.4	319	362*	313	368**	TOTAL	99	140388	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 9.914
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 12.80

DAY 134

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	8672	347	33.8						TREATMENTS	3	44204	14735
2-F	25	8549	342	35.5	0.5	324	369	319	375	ERROR	96	106961	1114
3-F	25	8567	343	41.3	0.4	324	369	319	375				
4-F	25	7387	295**	18.6	5.4	324	369*	319	375**	TOTAL	99	151165	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 10.062
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 13.22

DAY 141

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	8816	353	34.7						TREATMENTS	3	53697	17899
2-F	25	8692	348	36.9	0.5	330	376	324	381	ERROR	96	111011	1156
3-F	25	8676	347	41.8	0.6	330	376	324	381				
4-F	25	7396	296**	17.8	5.9	330	376*	324	381**	TOTAL	99	164708	

table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 10.127
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 15.48

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 152 SEX: FEMALE

ANALYSIS OF VARIANCE

DAY 148

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	8948	358	38.7						TREATMENTS	3	56835	18945
2-F	25	8803	352	38.7	0.6	334	382	328	388	ERROR	96	123527	1287
3-F	25	8831	353	42.3	0.5	334	382	328	388				
4-F	25	7490	300**	18.9	5.7	334	382*	328	388**	TOTAL	99	180362	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 10.528
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 14.72

DAY 155

1-F	25	9104	364	40.0						TREATMENTS	3	54903	18301
2-F	25	8835	353	42.1	1.0	338	390	332	396	ERROR	96	139794	1456
3-F	25	8946	358	46.0	0.6	338	390	332	396				
4-F	25	7627	305**	18.3	5.5	338	390*	332	396**	TOTAL	99	194697	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 11.057
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 12.57

DAY 162

1-F	25	9005	360	40.7						TREATMENTS	3	51737	17246
2-F	25	8834	353	42.4	0.6	334	386	328	393	ERROR	96	143227	1492
3-F	25	8883	355	45.5	0.4	334	386	328	393				
4-F	25	7602	304**	21.1	5.1	334	386*	328	393**	TOTAL	99	194964	

table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 11.253
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 11.56

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 152 SEX: FEMALE

ANALYSIS OF VARIANCE

DAY 169

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	9114	365	42.6						TREATMENTS	3	55123	18374
2-F	25	8970	359	42.3	0.5	338	391	332	397	ERROR	96	144128	1501
3-F	25	8969	359	44.0	0.5	338	391	332	397				
4-F	25	7669	307**	21.3	5.3	338	391*	332	397**	TOTAL	99	199251	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 11.159
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 12.24

DAY 176

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	9386	375	46.4						TREATMENTS	3	64515	21505
2-F	25	9215	369	44.5	0.6	347	404	340	411	ERROR	96	167485	1745
3-F	25	9184	367	48.1	0.7	347	404	340	411				
4-F	25	7806	312**	22.9	5.3	347	404*	340	411**	TOTAL	99	232000	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 11.736
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 12.33

DAY 182

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	20	7715	386	44.4						TREATMENTS	3	56809	18936
2-F	20	7404	370	51.9	1.2	354	417	347	425	ERROR	76	132196	1739
3-F	20	7480	374	44.6	0.9	354	417	347	425				
4-F	20	6331	317**	17.4	5.2	354	417*	347	425**	TOTAL	79	189005	

table values F.01 = 4.04** F.05 = 2.72* Coeff. Var. % = 11.533
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 10.89

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

DRAFT

SUMMARY OF DAILY MEAN FOOD CONSUMPTION (Grams)

STUDY: 152 SEX: MALE

ANALYSIS OF VARIANCE

DAY 8

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	629	25	1.8						TREATMENTS	3	97	32
2-M	25	607	24	3.6	1.3	24	27	23	27	ERROR	96	565	6
3-M	25	611	24	1.5	1.0	24	27	23	27				
4-M	25	562	22**	2.3	3.9	24	27*	23	27**	TOTAL	99	662	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 10.069
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 5.52

DAY 15

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	655	26	2.3						TREATMENTS	3	442	147
2-M	25	621	25	3.2	2.1	25	28	24	28	ERROR	96	513	5
3-M	25	632	25	1.6	1.4	25	28	24	28				
4-M	25	518	21**	1.8	8.4	25	28*	24	28**	TOTAL	99	955	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 9.533
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 27.54

DAY 22

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	664	27	1.9						TREATMENTS	3	689	230
2-M	24	619	26	2.3	1.3	25	28	25	28	ERROR	95	389	4
3-M	25	664	27	1.9	0.0	25	28	25	28				
4-M	25	507	20**	2.0	11.0	25	28*	25	28**	TOTAL	98	1078	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 8.167
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 56.06

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

DRAFT

SUMMARY OF DAILY MEAN FOOD CONSUMPTION (Grams)

STUDY: 152 SEX: MALE

ANALYSIS OF VARIANCE

DAY 29

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	655	26	2.7						TREATMENTS	3	674	225
2-M	25	656	26	3.5	0.1	24	28	24	29	ERROR	96	720	7
3-M	25	647	26	1.9	0.4	24	28	24	29				
4-M	25	503	20**	2.5	7.9	24	28*	24	29**	TOTAL	99	1394	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 11.127
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 29.96

DAY 36

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	658	26	2.9						TREATMENTS	3	606	202
2-M	25	630	25	2.7	1.3	24	28	24	29	ERROR	96	915	10
3-M	25	653	26	3.9	0.2	24	28	24	29				
4-M	25	507	20**	2.7	6.9	24	28*	24	29**	TOTAL	99	1521	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 12.612
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 21.19

DAY 43

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	719	29	3.1						TREATMENTS	3	605	202
2-M	25	677	27	2.7	2.2	27	31	26	31	ERROR	96	716	7
3-M	25	679	27	2.2	2.1	27	31	26	31				
4-M	25	555	22**	2.8	8.5	27	31*	26	31**	TOTAL	99	1321	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 10.382
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 27.06

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

DRAFT

SUMMARY OF DAILY MEAN FOOD CONSUMPTION (Grams)

STUDY: 152 SEX: MALE

ANALYSIS OF VARIANCE

DAY 50

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	711	28	3.2						TREATMENTS	3	624	208
2-M	25	714	29	2.6	0.1	26	30	26	31	ERROR	96	801	8
3-M	25	672	27	2.0	1.9	26	30	26	31				
4-M	25	560	22**	3.5	7.4	26	30*	26	31**	TOTAL	99	1425	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 10.871
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 24.91

DAY 57

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	735	29	3.5						TREATMENTS	3	1000	333
2-M	25	729	29	2.6	0.3	27	31	27	32	ERROR	96	837	9
3-M	25	691	28	1.8	2.1	27	31	27	32				
4-M	25	540	22**	3.6	9.3	27	31*	27	32**	TOTAL	99	1837	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 10.957
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 38.21

DAY 64

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	713	29	3.0						TREATMENTS	3	967	322
2-M	25	713	29	2.6	0.0	26	31	26	31	ERROR	96	896	9
3-M	25	694	28	1.9	0.9	26	31	26	31				
4-M	25	528	21**	4.3	8.6	26	31*	26	31**	TOTAL	99	1863	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 11.535
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 34.56

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

DRAFT

SUMMARY OF DAILY MEAN FOOD CONSUMPTION (Grams)

STUDY: 152 SEX: MALE

ANALYSIS OF VARIANCE

DAY 71

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	718	29	2.9						TREATMENTS	3	905	302
2-M	25	732	29	2.9	0.6	26	31	26	32	ERROR	96	1065	11
3-M	25	695	28	1.8	1.0	26	31	26	32				
4-M	25	544	22**	4.9	7.4	26	31*	26	32**	TOTAL	99	1970	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 12.384
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 27.21

DAY 78

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	729	29	5.1						TREATMENTS	3	725	242
2-M	25	738	30	2.6	0.4	27	32	26	32	ERROR	96	1267	13
3-M	25	719	29	1.9	0.4	27	32	26	32				
4-M	25	574	23**	4.0	6.0	27	32*	26	32**	TOTAL	99	1992	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 13.163
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 18.31

DRAFT

SUMMARY OF DAILY MEAN FOOD CONSUMPTION (Grams)

STUDY: 152 SEX: MALE

ANALYSIS OF VARIANCE

DAY 85

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	709	28	3.3						TREATMENTS	3	389	130
2-M	25	725	29	2.8	0.8	26	30	26	31	ERROR	96	842	9
3-M	25	723	29	2.9	0.7	26	30	26	31				
4-M	25	606	24**	2.8	4.9	26	30*	26	31**	TOTAL	99	1231	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 10.720
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 14.79

DAY 92

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	684	27	3.8						TREATMENTS	3	657	219
2-M	25	665	27	5.0	0.7	25	30	24	30	ERROR	96	1321	14
3-M	25	650	26	2.1	1.3	25	30	24	30				
4-M	25	521	21**	3.2	6.2	25	30*	24	30**	TOTAL	99	1978	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 14.721
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 15.91

DAY 99

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	685	27	3.0						TREATMENTS	3	430	143
2-M	25	699	28	3.0	0.7	25	29	25	30	ERROR	96	820	9
3-M	25	659	26	2.2	1.3	25	29	25	30				
4-M	25	566	23**	3.3	5.8	25	29*	25	30**	TOTAL	99	1250	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 11.205
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 16.76

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

DRAFT

SUMMARY OF DAILY MEAN FOOD CONSUMPTION (Grams)

STUDY: 152 SEX: MALE

ANALYSIS OF VARIANCE

DAY 106

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	672	27	2.6						TREATMENTS	3	407	136
2-M	25	678	27	3.4	0.3	25	29	24	29	ERROR	96	916	10
3-M	25	666	27	3.0	0.3	25	29	24	29				
4-M	25	556	22**	3.3	5.3	25	29*	24	29**	TOTAL	99	1323	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 12.007
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 14.21

DAY 113

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	677	27	2.7						TREATMENTS	3	258	86
2-M	25	681	27	2.9	0.2	25	29	25	29	ERROR	96	677	7
3-M	25	681	27	2.1	0.2	25	29	25	29				
4-M	25	587	23**	2.8	4.8	25	29*	25	29**	TOTAL	99	935	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 10.114
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 12.19

DAY 120

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	681	27	3.6						TREATMENTS	3	339	113
2-M	25	686	27	2.4	0.2	25	29	25	30	ERROR	96	811	8
3-M	25	651	26	2.6	1.5	25	29	25	30				
4-M	25	571	23**	2.9	5.4	25	29*	25	30**	TOTAL	99	1150	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 11.227
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 13.37

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

DRAFT

SUMMARY OF DAILY MEAN FOOD CONSUMPTION (Grams)

STUDY: 152 SEX: MALE

ANALYSIS OF VARIANCE

DAY 127

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	645	26	2.7						TREATMENTS	3	325	108
2-M	25	671	27	2.6	1.5	24	27	24	28	ERROR	96	584	6
3-M	25	626	25	2.1	1.1	24	27	24	28				
4-M	25	550	22**	2.5	5.4	24	27*	24	28**	TOTAL	99	909	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 9.900
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 17.80

DAY 134

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	659	26	2.8						TREATMENTS	3	426	142
2-M	25	664	27	2.0	0.2	24	28	24	29	ERROR	96	904	9
3-M	25	666	27	2.1	0.3	24	28	24	29				
4-M	25	544	22**	4.6	5.3	24	28*	24	29**	TOTAL	99	1330	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 12.116
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 15.07

DAY 141

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	651	26	2.8						TREATMENTS	3	376	125
2-M	25	694	28	2.9	2.2	24	28	24	28	ERROR	95	721	8
3-M	25	681	27	1.9	1.5	24	28	24	28				
4-M	24	545	23**	3.3	4.2	24	28*	24	28**	TOTAL	98	1097	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 10.608
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 16.51

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

DRAFT

SUMMARY OF DAILY MEAN FOOD CONSUMPTION (Grams)

STUDY: 152 SEX: MALE

ANALYSIS OF VARIANCE

DAY 148

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	692	28	2.5				TREATMENTS	3	71	24
2-M	25	695	28	3.7	0.1			ERROR	95	881	9
3-M	25	692	28	2.0	0.0						
4-M	24	618	26	3.7	2.2			TOTAL	98	952	

'F' table values F.01 = 3.98 F.05 = 2.70 Coeff. Var. % = 11.181
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 2.54

DAY 155

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	701	28	2.4				TREATMENTS	3	260	87
2-M	25	697	28	3.0	0.2	26 30	26 30	ERROR	95	705	7
3-M	25	701	28	2.0	0.0	26 30	26 30				
4-M	24	581	24**	3.3	4.9	26 30*	26 30**	TOTAL	98	965	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 10.060
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 11.69

DAY 162

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-M	25	649	26	3.1				TREATMENTS	3	272	91
2-M	25	652	26	3.4	0.2	24 28	24 28	ERROR	95	760	8
3-M	25	641	26	2.2	0.4	24 28	24 28				
4-M	24	529	22**	2.4	4.8	24 28*	24 28**	TOTAL	98	1032	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 11.328
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 11.35

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

DRAFT

SUMMARY OF DAILY MEAN FOOD CONSUMPTION (Grams)

STUDY: 152 SEX: MALE

ANALYSIS OF VARIANCE

DAY 169

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree fdm	Sum of Squares	Mean Square
1-M	25	638	26	3.1						TREATMENTS	3	258	86
2-M	25	642	26	3.6	0.2	24	27	23	28	ERROR	95	819	9
3-M	25	640	26	2.0	0.1	24	27	23	28				
4-M	24	524	22**	2.8	4.4	24	28*	23	28**	TOTAL	98	1077	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 11.894
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 9.99

DAY 176

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree fdm	Sum of Squares	Mean Square
1-M	25	661	26	2.9						TREATMENTS	3	185	62
2-M	25	630	25	4.3	1.3	24	29	24	29	ERROR	95	1031	11
3-M	25	653	26	2.1	0.3	24	29	24	29				
4-M	24	550	23**	3.6	3.7	24	29*	24	29**	TOTAL	98	1216	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 13.075
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 5.68

DAY 182

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	Source	Degree fdm	Sum of Squares	Mean Square
1-M	20	545	27	2.4		TREATMENTS	3	41	14
2-M	20	520	26	3.5	1.3	ERROR	75	655	9
3-M	20	550	28	2.8	0.3				
4-M	19	492	26	3.1	1.4	TOTAL	78	696	

'F' table values F.01 = 4.04 F.05 = 2.72 Coeff. Var. % = 11.076
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 1.56

DRAFT

SUMMARY OF DAILY MEAN FOOD CONSUMPTION (Grams)

STUDY: 152 SEX: FEMALE

ANALYSIS OF VARIANCE

DAY 8

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	464	19	2.7						TREATMENTS	3	97	32
2-F	25	442	18	1.7	1.3	17	20	17	21	ERROR	96	530	6
3-F	25	446	18	3.1	1.1	17	20	17	21				
4-F	25	397	16**	1.6	4.0	17	20*	17	21**	TOTAL	99	627	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 13.429
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 5.88

DAY 15

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	455	18	2.7		TREATMENTS	3	11	4
2-F	25	442	18	2.0	0.6	ERROR	96	929	10
3-F	25	461	18	4.2	0.3				
4-F	25	442	18	3.1	0.6	TOTAL	99	940	

'F' table values F.01 = 3.98 F.05 = 2.70 Coeff. Var. % = 17.283
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 0.38

DAY 22

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	476	19	3.5						TREATMENTS	3	175	58
2-F	25	462	18	3.0	0.6	17	21	16	22	ERROR	96	916	10
3-F	25	493	20	3.6	0.8	17	21	16	22				
4-F	25	405	16**	1.8	3.3	17	21*	16	22**	TOTAL	99	1091	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 16.827
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 6.11

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

DRAFT

SUMMARY OF DAILY MEAN FOOD CONSUMPTION (Grams)

STUDY: 152 SEX: FEMALE

ANALYSIS OF VARIANCE

DAY 29

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	438	18	2.1						TREATMENTS	3	56	19
2-F	25	446	18	1.7	0.6	16	19	16	19	ERROR	96	325	3
3-F	25	456	18	2.2	1.4	16	19	16	19				
4-F	25	406	16*	1.2	2.5	16	19*	16	19	TOTAL	99	381	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 10.534
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 5.53

DAY 36

1-F	25	445	18	3.3						TREATMENTS	3	91	30
2-F	25	421	17	1.5	1.1	16	20	15	20	ERROR	96	885	9
3-F	25	462	18	4.3	0.8	16	20	15	20				
4-F	25	399	16	2.4	2.1	16	20	15	20	TOTAL	99	976	

'F' table values F.01 = 3.98 F.05 = 2.70* Coeff. Var. % = 17.577
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 3.30

DAY 43

1-F	24	425	18	2.1						TREATMENTS	3	103	34
2-F	25	485	19**	1.9	3.2	16	19*	16	19**	ERROR	95	334	4
3-F	25	481	19*	1.8	2.9	16	19*	16	19				
4-F	25	425	17	1.7	1.3	16	19	16	19	TOTAL	98	437	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 10.215
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 9.76

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

DRAFT

SUMMARY OF DAILY MEAN FOOD CONSUMPTION (Grams)

STUDY: 152 SEX: FEMALE

ANALYSIS OF VARIANCE

DAY 50

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	476	19	3.9						TREATMENTS	3	7	2
2-F	25	476	19	2.3	0.0					ERROR	96	956	10
3-F	25	491	20	2.9	0.7								
4-F	25	488	20	3.4	0.5					TOTAL	99	963	

'F' table values F.01 = 3.98 F.05 = 2.70 Coeff. Var. % = 16.342
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 0.25

DAY 57

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	491	20	2.7						TREATMENTS	3	153	51
2-F	25	492	20	2.1	0.1	18	21	18	21	ERROR	96	466	5
3-F	25	488	20	2.0	0.2	18	21	18	21				
4-F	25	419	17**	2.0	4.6	18	21*	18	21**	TOTAL	99	619	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 11.657
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 10.51

DAY 64

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	483	19	2.4						TREATMENTS	3	127	42
2-F	25	479	19	2.6	0.3	18	21	17	21	ERROR	96	462	5
3-F	25	484	19	2.1	0.1	18	21	17	21				
4-F	25	417	17**	1.4	4.3	18	21*	17	21**	TOTAL	99	589	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 11.775
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 8.82

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

DRAFT

SUMMARY OF DAILY MEAN FOOD CONSUMPTION (Grams)

STUDY: 152 SEX: FEMALE

ANALYSIS OF VARIANCE

DAY 71

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	472	19	2.6						TREATMENTS	3	73	24
2-F	25	466	19	2.2	0.4	17	20	17	21	ERROR	96	441	5
3-F	25	469	19	2.1	0.2	17	20	17	21				
4-F	25	420	17**	1.5	3.4	17	20*	17	21**	TOTAL	99	514	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 11.731
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 5.28

DAY 78

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	530	21	5.6						TREATMENTS	3	130	43
2-F	25	519	21	2.4	0.4	19	24	18	24	ERROR	95	1185	12
3-F	25	517	21	2.8	0.5	19	24	18	24				
4-F	24	438	18*	2.2	2.9	19	24*	18	24	TOTAL	98	1315	

'F' table values F.01 = 3.98 F.05 = 2.70* Coeff. Var. % = 17.444
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 3.47

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

DRAFT

SUMMARY OF DAILY MEAN FOOD CONSUMPTION (Grams)

STUDY: 152 SEX: FEMALE

ANALYSIS OF VARIANCE

DAY 85

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	517	21	3.5				TREATMENTS	3	57	19
2-F	25	497	20	2.4	1.0			ERROR	96	795	8
3-F	25	508	20	2.2	0.4						
4-F	25	467	19	3.3	2.5			TOTAL	99	852	

'F' table values F.01 = 3.98 F.05 = 2.70 Coeff. Var. % = 14.468
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 2.29

DAY 92

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	483	19	6.1				TREATMENTS	3	289	96
2-F	25	471	19	3.4	0.4	17 22	16 23	ERROR	96	1575	16
3-F	25	473	19	3.5	0.3	17 22	16 23				
4-F	25	378	15**	2.2	3.7	17 22*	16 23**	TOTAL	99	1864	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 22.442
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 5.88

DAY 99

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	446	18	4.1				TREATMENTS	3	74	25
2-F	25	427	17	1.6	1.0	16 20	16 20	ERROR	96	650	7
3-F	25	436	17	2.5	0.5	16 20	16 20				
4-F	25	389	16**	1.4	3.1	16 20*	16 20**	TOTAL	99	724	

'F' table values F.01 = 3.98 F.05 = 2.70* Coeff. Var. % = 15.319
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 3.67

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF DAILY MEAN FOOD CONSUMPTION (Grams)

STUDY: 152 SEX: FEMALE

ANALYSIS OF VARIANCE

DAY 106

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	447	18	5.2						TREATMENTS	3	102	34
2-F	24	445	19	2.7	0.7	16	20	15	21	ERROR	95	1059	11
3-F	25	460	18	2.5	0.6	16	20	15	21				
4-F	25	400	16	2.1	2.0	16	20	15	21	TOTAL	98	1161	

'F' table values F.01 = 3.98 F.05 = 2.70* Coeff. Var. % = 18.863
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 3.06

DAY 113

1-F	25	472	19	4.7						TREATMENTS	3	76	25
2-F	25	485	19	2.2	0.6					ERROR	96	989	10
3-F	25	505	20	3.3	1.5								
4-F	25	445	18	1.9	1.2					TOTAL	99	1065	

'F' table values F.01 = 3.98 F.05 = 2.70 Coeff. Var. % = 16.828
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 2.46

DAY 120

1-F	25	483	19	2.3						TREATMENTS	3	71	24
2-F	25	478	19	2.0	0.3	18	21	17	21	ERROR	96	584	6
3-F	25	500	20	2.5	1.0	18	21	17	21				
4-F	25	442	18	2.9	2.4	18	21	17	21	TOTAL	99	655	

'F' table values F.01 = 3.98 F.05 = 2.70* Coeff. Var. % = 12.955
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 3.92

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

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SUMMARY OF DAILY MEAN FOOD CONSUMPTION (Grams)

STUDY: 152 SEX: FEMALE

ANALYSIS OF VARIANCE

DAY 127

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	467	19	2.0						TREATMENTS	3	158	53
2-F	25	457	18	1.7	0.8	17	20	17	20	ERROR	96	314	3
3-F	25	482	19	2.1	1.2	17	20	17	20				
4-F	25	399	16**	1.3	5.3	17	20*	17	20**	TOTAL	99	472	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 10.027
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 16.10

DAY 134

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	493	20	3.8						TREATMENTS	3	172	57
2-F	25	471	19	1.9	1.1	18	22	17	22	ERROR	96	727	8
3-F	25	501	20	2.5	0.4	18	22	17	22				
4-F	25	417	17**	2.5	3.9	18	22*	17	22**	TOTAL	99	899	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 14.620
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 7.57

DAY 141

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	475	19	3.0						TREATMENTS	3	208	69
2-F	25	477	19	1.8	0.1	17	21	17	21	ERROR	96	745	8
3-F	25	517	21	3.4	2.1	17	21	17	21				
4-F	25	416	17**	2.7	3.0	17	21*	17	21**	TOTAL	99	953	

'F' table values F.01 = 3.98** F.05 = 2.70* Coeff. Var. % = 14.779
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 8.92

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

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SUMMARY OF DAILY MEAN FOOD CONSUMPTION (Grams)

STUDY: 152 SEX: FEMALE

ANALYSIS OF VARIANCE

DAY 148

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	498	20	3.8				TREATMENTS	3	100	33
2-F	25	488	20	1.9	0.4			ERROR	96	1481	15
3-F	25	552	22	4.7	1.9						
4-F	25	499	20	4.6	0.0			TOTAL	99	1581	

'F' table values F.01 = 3.98 F.05 = 2.70 Coeff. Var. % = 19.281
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 2.17

DAY 155

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	489	20	4.8				TREATMENTS	3	102	34
2-F	23	427	19	2.4	1.1	17 22	17 22	ERROR	94	933	10
3-F	25	506	20	2.6	0.8	17 22	17 22				
4-F	25	439	18	2.0	2.2	17 22	17 22	TOTAL	97	1035	

'F' table values F.01 = 3.98 F.05 = 2.70* Coeff. Var. % = 16.586
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 3.44

DAY 162

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI	LO -99%- HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	400	16	3.8				TREATMENTS	3	62	21
2-F	23	397	17	2.5	1.5			ERROR	94	845	9
3-F	25	442	18	3.4	2.0						
4-F	25	396	16	1.9	0.2			TOTAL	97	907	

'F' table values F.01 = 3.98 F.05 = 2.70 Coeff. Var. % = 17.974
Dunnett's 'T' table values P.01 = 2.97 P.05 = 2.38 F Ratio = 2.30

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

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SUMMARY OF DAILY MEAN FOOD CONSUMPTION (Grams)

STUDY: 152 SEX: FEMALE

ANALYSIS OF VARIANCE

DAY 169

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	431	17	4.2						TREATMENTS	3	57	19
2-F	25	436	17	2.5	0.2					ERROR	96	782	8
3-F	25	456	18	2.4	1.2								
4-F	25	403	16	1.8	1.4					TOTAL	99	839	

'F' table values	F.01 =	3.98	F.05 =	2.70	Coeff. Var. % = 16.535
Dunnett's 'T' table values	P.01 =	2.97	P.05 =	2.38	F Ratio = 2.35

DAY 176

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	25	475	19	3.1						TREATMENTS	3	69	23
2-F	25	475	19	1.9	0.0	17	21	17	21	ERROR	96	564	6
3-F	25	488	20	2.5	0.8	17	21	17	21				
4-F	25	433	17*	2.0	2.5	17	21*	17	21	TOTAL	99	633	

'F' table values	F.01 =	3.98	F.05 =	2.70*	Coeff. Var. % = 12.951
Dunnett's 'T' table values	P.01 =	2.97	P.05 =	2.38	F Ratio = 3.91

DAY 182

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	20	423	21	3.5						TREATMENTS	3	98	33
2-F	20	420	21	2.9	0.2	19	23	18	24	ERROR	76	737	10
3-F	20	464	23	3.2	2.1	19	23	18	24				
4-F	20	404	20	2.7	1.0	19	23	18	24	TOTAL	79	835	

'F' table values	F.01 =	4.04	F.05 =	2.72*	Coeff. Var. % = 14.560
Dunnett's 'T' table values	P.01 =	2.97	P.05 =	2.38	F Ratio = 3.37

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

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APPENDIX M

PROTOCOL AND AMENDMENTS

Contract No.: DAMD17-92-C-2001
Task Order No.: UIC-15B
UIC/TRL Study No.: 152

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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS

1.0 PURPOSE OF THE STUDY:

The purpose of this study is to determine specific target organ toxicity, dose-response relationships, and a no observed adverse effect level of WR238605 succinate in CD® rats following six months of daily administration by gavage. This study will be conducted in accordance with the specifications of the Sponsor as described in Task Order UIC-15. The protocol for this study was approved by the UIC Animal Care Committee (Appendix 1).

2.0 SPONSOR:

2.1	Name:	U.S. Army Medical Materiel Development Activity
2.2	Address:	Fort Detrick Frederick, MD 21702-5009
2.3	Representative:	George J. Schieferstein, Ph.D.

3.0 TESTING FACILITY:

3.1	Name:	Toxicology Research Laboratory (TRL)
3.2	Address:	University of Illinois at Chicago (UIC) Department of Pharmacology 1940 W. Taylor St. Chicago, IL 60612-7353
3.3	Study Director:	Barry S. Levine, D.Sc., D.A.B.T.

4.0 DATES:

4.1	Proposed Initiation of Dosing:	08/02/95
4.2	Proposed Necropsy Date(s):	01/31/96 - 02/02/96
4.3	Proposed Study Completion Date (Draft Study Report):	05/03/96

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5.0 TEST ARTICLE

5.1 Name or Code No: WR238605 Succinate (mole fraction = 0.8)
8-[4-Amino-1-methylbutyl)amino]-2,6-dimethoxy-4-methyl-5-(3-trifluoromethyl-phenoxy)quinoline succinate
Bottle No. BM12562
CAS No. 106635-81-8

5.2 TRL Chemical No: 0720614

5.3 Physical Description: Pale yellow powder.

5.4 Stability and Handling of Test Article:

5.4.1 Storage Conditions to Maintain Stability:

5.4.1.1 Temperature: 0 - 4°C.

5.4.1.2 Humidity: Ambient conditions.

5.4.1.3 Light: Protect from light; amber bottle or silver foil covering.

5.4.1.4 Special Requirements: None

5.4.2 Special Handling Procedures: Standard safety precautions including gloves, eye protection, mask, and lab coats.

5.4.3 Log of Test Article: The amount, date, identity of person(s) removing aliquots and the purpose for which each aliquot of the test article was removed from the batch will be documented. At termination of the study, all unused test article will be returned to the Sponsor if requested.

6.0 PERSONNEL:

Principal Investigator	Barry S. Levine, D.Sc., D.A.B.T.
Study Director	Barry S. Levine, D.Sc., D.A.B.T.
Pathologist	Robert L. Morrissey, D.V.M., Ph.D., D.A.C.V.P.
Pathology Support	Ralph M. Bunte, D.V.M., D.A.C.V.P.
Analytical Chemist	Adam Negrusz, Ph.D.
Clinical Veterinarian	James E. Artwohl, D.V.M., M.S., D.A.C.V.P.
Ophthalmologist	Samuel J. Vainisi D.V.M., D.A.V.C.O.
Veterinarian Support	Documented in raw data
Clinical Laboratory	Maria Lang, A.H.T., C.V.T.
Tox. Lab Supervisor	Soudabeh Soura, B.S.
Lead Technician	Teresa O'Neill, B.S.
Chemistry Specialist	Thomas Tolhurst, B.S.
Quality Assurance	Ronald C. Schoenbeck

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7.0 TEST SYSTEM:

7.1 Species: Rat

7.2 Strain: CD® (Virus Antibody Free)

7.3 Number and Sex: 105 Males and 105 Females (includes 5/sex for quarantine/pretest clinical pathology measurements).

7.4 Age of Animals: At least 7 weeks old at dosing initiation.

7.5 Weight of Animals: Approximately 225 - 275 g (males) and approximately 150 - 200g (females) at dosing initiation.

7.6 Source of Animals: Charles River Breeding Laboratories. Kingston, N.Y.

7.7 Justification for Selection of Test System: The FDA requires the use of two animal species in preclinical toxicology studies. The rat is a standard and accepted rodent species for regulatory toxicology studies. and is specified by the Sponsor. This is a successive chronic toxicity study to a thirteen week oral toxicity study of WR238605 which included a thirteen week recovery period in rats (UIC/TRL Study No. 098).

7.8 Procedure for Unique Identification of Test System: Upon arrival, each animal will be given a study-unique quarantine/pretest number. During the animal selection process, each animal will be assigned an animal number unique to it within the population making up the study. This number will be coded on a subcutaneously implanted microchip. It will appear on a cage card visible on the front of each cage. The cage card will additionally contain the study number. test article identification. treatment group number. sex and dose level. Cage cards will be color-coded as a function of treatment group. Raw data records and specimens will also be identified by the unique test animal number.

7.9 Housing: The animals will be housed in an AAALAC-accredited facility. Animals will be singly housed in polycarbonate cages with Anderson-bed-a-cob bedding (Heinold. Kankakee. Illinois) in a temperature (65-78°F) and humidity (30-70%) controlled room with a 14 hour light/10 hour dark cycle. The cage size, 840 cm^2 area and 20 cm height. is adequate to house rats at the upper weight range as described in the *Guide for the Care and Use of Laboratory Animals*. DHEW (NIH) No. 86.23. All animals will be routinely transferred to clean cages with fresh bedding once weekly.

7.10 Quarantine Procedure: Animals will be quarantined for approximately two weeks. During that time. the animals will be observed daily for signs of illness, and all unusual observations will be reported to the Study Director or Clinical Veterinarian. Animals will be examined during quarantine and approved for use by the Clinical Veterinarian prior to being placed on test. Any sickly animals will be eliminated prior to the test animal selection process. If a selected animal appears sickly prior to initiation of treatment. it will be replaced by a healthy animal prior to initiation of treatment under the direction of the Study Director. In addition, during the

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the quarantine/pretest period, hematology and clinical chemistry parameters (see Section 8.7.7) will be measured for five rats/sex to determine the suitability of the rat shipment for use in this study. These rats, however, will not be used in the dosing portion of the study. Quarantine release will be documented on the Clinical Veterinarian Log by the veterinarian prior to study initiation.

7.11 Food: Certified Rodent Chow No. 5002 (PMI Feeds, Inc., St. Louis, MO) will be provided *ad libitum* from arrival until termination.

7.12 Water: Tap water from an automatic watering system in which the room distribution lines are flushed daily will be provided *ad libitum* from arrival until termination. The water is not treated with additional chlorine or HCl.

7.13 There are no known contaminants in the feed or water which are expected to influence the study. A copy of the feed certification will be kept with the study records. The results of bimonthly comprehensive chemical analyses of Chicago water performed by the City of Chicago are documented in files maintained by Quality Assurance.

7.14 It is not known if the animals will experience pain or distress during the study. Analgesic or anesthetic agents will confound the ability to determine the toxic potential of the test article, and therefore will not be used. If an animal is in severe pain or distress, following consultation with the veterinary staff. it will be euthanized in accordance with standard operating procedures.

8.0 EXPERIMENTAL DESIGN:

8.1 Treatment Groups:

Treatment Group	Dose Level (mg base/kg/day)	Dose Conc. (mg base/ml)	Dose Volume (ml/kg/day)	Number of Males	Number of Females
1	0	0	5	20 + 5*	20 + 5*
2	0.5	0.1	5	20 + 5*	20 + 5*
3	2.0	0.4	5	20 + 5*	20 + 5*
4	9.0	1.8	5	20 + 5*	20 + 5*

* Five satellite rats/sex/dose will be utilized for the collection of blood samples for plasma drug level analysis and will be euthanized after the last set of samples are collected in week 25. The other observations. tests and measurements will be performed on these animals except for the collection of blood samples for clinical pathology measurements, ophthalmology examinations and pathology evaluations. The remaining 20 rats/sex/dose will be used in the core toxicity study.

Dose levels are selected by the Sponsor based upon the results of a previous thirteen week oral toxicity study of WR238605 with a thirteen week recovery period in rats (UIC/TRL Study No. 098). The number of animals in the core toxicity study, 20/sex/dose, is routinely used in chronic regulatory toxicity studies, and is also the number of animals for this species indicated in the 1993 *OECD Guidelines for Testing of Chemicals;* Chronic Toxicity Studies. No such FDA document exists for the testing of drugs.

8.2 Frequency and Route of Administration of the Test Article: The test article will be administered by gavage once daily starting with day 1 for at least twenty-six weeks. Control animals will receive the test article vehicle (aqueous 1% methylcellulose/0.2% Tween 80). All animals will receive vehicle by gavage for at least 3 days during week -1 to acclimate them to the procedure. All animals will be dosed up to and including the day prior to their scheduled necropsy on days 183, 184 and 185. Dosing volume will be 5 ml/kg/day, adjusted on the basis of each animal's most recent body weight. The actual volume (ml) administered will be documented in the raw data. Gavage needles will be cleaned with ethanol in-between use.

8.3 Justification of Route(s): Oral treatment is the intended clinical route of administration and is specified by the Sponsor.

8.4 Procedure to Control Bias during the Assignment of Animals to Treatment Groups: During the quarantine/pretest period, the animals will be randomized by sex into the four groups shown in Section 8.1 using a computer-generated randomization procedure on the basis of body weight.

8.5 Test Article Vehicle: Aqueous 1% methylcellulose/0.2% Tween 80. Both chemicals will be obtained from Sigma Chemical Co. If another source is used, it will be identified in the raw data.

8.6 Test Article Dosage Form Preparation and Analyses: Dosing formulation calculations of the test article will be adjusted for purity of the test article and the base mole fraction. The control materials will be assumed to be 100% pure for dosing calculations. Formulations will be prepared weekly and will be administered daily by gavage, at 5 ml/kg/day, 7 days a week. The 1% methylcellulose/0.2% Tween 80 vehicle will be prepared at least weekly by placing the required amount of deionized water in a beaker and then adding the required amount of methylcellulose and volume of Tween 80, using its specific gravity of 1.08 (1.0 g of methylcellulose and 0.2 g Tween 80 per 100 ml of deionized water). One lot no. each of methylcellulose and Tween 80 will be used. The mixture will be stirred while being heated until homogeneous and then refrigerated.

The test article dosing suspensions will be prepared weekly. Stability data from a previously conducted dog toxicity study by gastric intubation demonstrated that WR238605 Succinate suspensions were stable for at least 28 days (UIC/TRL Study No. 047). Homogeneity data also obtained from UIC/TRL Study No. 47 demonstrated that the test article suspensions are homogeneous (coefficients of variation for sampling in the top, middle and bottom of several test suspensions were typically less than 4%).

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Each test article dosing suspension will be prepared individually by adding the appropriate amount of WR238605 Succinate to the required volume of the 1.0% methylcellulose/0.2% Tween 80 vehicle in a pre-calibrated beaker. The contents will be mixed with an Omni-Mixer homogenizer, for at least 5 minutes. All suspensions will be stored at 2 - 8°C. All suspensions will be allowed to warm to room temperature and stirred continuously before and during gavage administration. Samples of all dosing suspensions prepared weekly will be analyzed, and only suspensions within 10% of their target concentration will be used. Weekly samples will also be analyzed for test article concentration after use. Tolerance of sample analysis after use will also be 10%, i.e., 10% of the "before use" assay value.

8.7 Type and Frequency of Observations, Tests, Analyses and Measurements:

8.7.1 Mortality Check: All animals will be observed for moribundity/mortality prior to dosing in the morning and in the afternoon.

8.7.2 Clinical Signs: All animals will be observed once daily for clinical signs of toxicity approximately 1 - 2 hours after dosing.

8.7.3 Clinical Observations: All animals will be subjected to a physical examination including examination of eyes and all orifices, weekly starting in week -1.

8.7.4 Body Weight: Body weights of all animals will be recorded weekly starting in week -1 and at scheduled necropsy.

8.7.5 Food Consumption: Food consumption for all animals will be measured weekly commencing in week -1.

8.7.6 Ophthalmologic Examinations: The core toxicity study rats will be examined by indirect ophthalmoscopy prior to study initiation, and in weeks 13 and 26.

8.7.7 Clinical Pathology: Hematology and clinical chemistry parameters will be measured in 10 animals/sex/group in the core toxicity study during weeks 4, 13 and 26. The same animals will be used throughout the study, unless substitution is necessary, i.e. death or moribund sacrifice. The non-fasted animals will be anesthetized by carbon dioxide inhalation (70% CO_2:30% O_2), and approximately 1.5 - 2.0 ml of blood will be collected from the orbital sinus to measure the following parameters. The left eye will be routinely used. If the right eye is necessary for a particular animal(s), it will be documented in the raw data. The samples will be processed in the same random order as collected.

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Hematology

[a]Erythrocyte count and morphology
Hematocrit
Hemoglobin
Leukocyte count, total and differential
Reticulocyte count
Mean corpuscular volume (MCV)
Mean corpuscular hemoglobin (MCH)
Mean corpuscular hemoglobin concentration (MCHC)
Heinz bodies
Platelet count
[b]Methemoglobin

[a]Includes nucleated RBCs.
[b]To be measured with a Co-oximeter (Instrumentation Laboratory Model No. 482). The assay will be performed within one hour of sample collection. The specimens will be kept on wet ice prior to analysis.

Clinical Chemistry

Alanine aminotransferase (ALT)
Albumin
Albumin/Globulin ratio (calculated)
Alkaline phosphatase
Calcium
Chloride
Creatinine
Creatine kinase (CK)
Glucose
Inorganic phosphorus
Lactate dehydrogenase
Potassium
Sodium
Sorbitol dehydrogenase (SDH)
Total bile acids
Total protein
Urea nitrogen (BUN)

Activated partial thromboplastin time will be measured in the same 10 rats/sex/group used for clinical chemistry and hematology measurements. Blood samples will be collected from the vena cava at their scheduled necropsy in week 27.

Clinical chemistry and hematology tests and activated partial thromboplastin time will be measured in 5 rats/sex during the quarantine/pretest period to assess the suitability of the shipment. These animals will not be used in the dosing phase of the study.

8.7.8 Plasma Drug Levels: Blood samples (1.0 - 2.0 ml) will be collected from the orbital sinus from the 5 satellite rats/sex/group designated for the determination of plasma drug levels in week -1, ≈24 hours after the first day of dosing, and ≈24 hours after dosing at the following time-points: weeks 3, 7, 18 and 25. Blood samples will be collected immediately prior to dosing, i.e., ≈ 24 hours after the previous dose, due to the anticipated long half-life of the test article. The plasma samples will be stored at -65° to -70°C, and sent in at least two shipment as directed by the Sponsor to Dr. Emil Lin, University of California at San Francisco (UCSF) for measurement of drug levels. The UCSF-generated report may be included in the UIC-generated final study report at the discretion of the Sponsor.

8.7.9 Pathology: All core toxicity animals which die on test or are sacrificed if moribund will be necropsied on that day. Surviving core toxicity animals will be sacrificed and necropsied in random order over three consecutive days

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at the onset of week 27 (days 183 - 185). If a rat in the satellite groups (used for plasma drug level determinations) is found dead or sacrificed moribund, it will not be necropsied.

Euthanasia will be accomplished by carbon dioxide asphyxiation, and an extensive necropsy will be performed under the direction and supervision of the pathologist. Terminal body weights will be collected prior to routine sacrifice.

The necropsy procedure will be a thorough and systematic examination and dissection of the animal viscera and carcass, and collection and fixation of the following tissues/organs in 10% neutral buffered formalin.

*Adrenal glands
Animal identification
*Brain
Cecum
Colon
Diaphragm
Duodenum
Esophagus
Eyes with harderian glands
Femoral marrow smear
*Heart
Gross lesions
Ileum
Jejunum
*Kidneys
*Liver
*Lungs/Bronchi
Lymph node (mesenteric)
*Ovaries
Pancreas
Pituitary
Prostate
Rib with costochondral junction
Salivary gland (submaxillary)
Sciatic nerve
Skeletal muscle
Skin with mammary gland
Spinal cord (thoracic)
*Spleen
Sternum with marrow
Stomach
*Testes with epididymides
Thymus
Thyroid gland/Parathyroids
Tongue
Trachea
Urinary bladder
Uterus

*Weighed at scheduled necropsy. Paired organs will be weighed as a unit.

All tissues and organs collected at necropsy will be examined microscopically in all control and high dose animals. If treatment-related lesions are observed, those tissues will be examined microscopically in mid and low dose animals. Animals found dead or subjected to a moribund sacrifice may also be processed for microscopic examination following discussions with the Sponsor. Gross lesions will be examined microscopically in all animals.

Femoral bone marrow smears will be prepared for all animals at scheduled necropsy and for moribund sacrificed animals. The myeloid:erythroid (M:E) ratio will be determined in control and high dose animals. If treatment-related changes are seen. M:E ratios will also be determined in mid and low dose animals.

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8.8 Statistical Analyses: For each sex, Analysis of Variance tests will be conducted on body weight, food consumption, hematology, clinical chemistry and organ weight data. Organ weight analyses will consider weights relative to brain weight. If a significant F ratio is obtained ($p \leq 0.05$), Dunnett's t test will be used for pair-wise comparisons to the concurrent control group. Frequency data such as incidence of mortality, gross necropsy observations and tissue morphology observations will be compared by Fisher's Exact Test or Chi-square analyses as necessary.

All statistical analysis procedures will compare treated to control animals at each time point. Data will not be corrected for baseline values, except that body weight analysis will include absolute values, weekly changes and total weight changes. Baseline clinical data will be used to assess the general health of the animals, and may be used qualitatively to assist in the interpretation of potential drug-related changes following the initiation of treatment.

8.9 Deliverables: Quantitative data will be tabulated and presented in the report, which will include historical control clinical pathology data. In addition to the written report, individual data tables in "ASCII" form and summary data tables of parameters and variability will be transmitted to the Sponsor on magnetic media (computer diskette). The transcribed data on disk will no longer be considered GLP compliant.

The following will be included in the study reports: references for all statistical methods; computer software identification used for carrying out the statistical analyses; historical control data for clinical pathology measurements; and ANOVA tables in an appendix.

9.0 RECORDS TO BE MAINTAINED:

All data generated during the conduct study, except those that are generated as direct computer input, shall be recorded directly, promptly, and accurately in ink in bound books with prenumbered pages or on worksheets that shall be bound during or at the conclusion of the nonclinical laboratory study. All appropriate computer and machine output shall be bound during or at the conclusion of the study. All data entries shall be dated on the day of entry and signed or initialed by the person entering the data. Any changes in entries for whatever reason (e.g., to correct an error or transposition) shall be made so as not to obscure the original entry, shall indicate the reason for such change, and shall be dated and signed or identified at the time of data input. In computer driven collection systems, the operator responsible for direct input shall be identified at the time of data input. Any changes in computer entries for whatever reason (e.g, to correct an error or transposition) shall be made in such manner so as not to obscure the original entry, if possible, shall indicate the reason for such change, and shall be dated and the responsible individual shall be identified.

All recorded data shall be reviewed, signed, and dated by a knowledgeable person, other than the person making the entry, to assure adherence to procedures and to verify observations.

Upon completion of the study and submission of the final report, all raw data, documentation, specimens, test article reserves and other materials necessary to reconstruct the study will be stored in the TRL archives maintained by Quality Assurance, unless specified by the Sponsor.

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All changes or revisions, and reasons therefore, to this protocol once it is approved shall be documented, signed by the Study Director and Sponsor, dated and maintained with the protocol.

10.0 REGULATORY REQUIREMENTS:

This study will be performed in compliance with the UIC/TRL Quality Assurance Program designed to conform with FDA Good Laboratory Practice Regulations and EPA Good Laboratory Practice Standards.

Will this study be submitted to a regulatory agency? Yes
If so, to which agency(ies)? U.S. Food and Drug Administration
Does the Sponsor request that test article samples be returned to the Sponsor? Yes
Does the Sponsor request that samples of the test article/carrier mixture(s) be sent to the Sponsor? No

11.0 PROTOCOL APPROVAL:

STUDY DIRECTOR:	Barry S. Levine, D.Sc., D.A.B.T.	5/15/95 Date
TOXICOLOGIST:	Clyde W. Wheeler, Ph.D.	5/15/95 Date
QUALITY ASSURANCE:	Ronald Schoenbeck	5/15/95 Date
SPONSOR APPROVAL:	George Schieferstein, Ph.D. Contracting Officer's Representative (COR)	5/16/95 Date

COMMENTS FROM THE COR:

UIC The University of Illinois at Chicago

Office of the Vice Chancellor for Research (M/C 672)
310 Administrative Office Building
1737 West Polk Street
Chicago, Illinois 60612-7227
(312) 996-4995

Contract No.: DAMD17-92-C-2001
Task Order No.: UIC-15B
UIC/TRL Study No.: 152

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Appendix 1

May 15, 1995

Barry S. Levine
Med-Pharmacology
312 BGRC, M/C 868

Dear Dr. Levine:

The modifications requested in your correspondence of May 10, 1995 pertaining to your approved protocol ACC: #93-031-22: "Six Month Oral Toxicity Study of WR238605 Succinate in Rats" have been reviewed in accordance with the Animal Care and Use Policies of the University of Illinois at Chicago. You will be pleased to know that the modifications were approved on May 12, 1995 and consequently the records of Animal Care Committee will be revised to reflect these changes.

Thank you for complying with the Animal Care Policies and Procedures of UIC.

Sincerely yours.

Michael W. Levine, Ph.D.
Chair, Animal Care Committee

MWL:st
xc: BRL

PROTOCOL AMENDMENT DRAFT

Study No.: 152

Title: Six Month Oral Toxicity Study of WR238605 Succinate in Rats

1. Page 1 Section 4.0

Add the study dates as follows:

4.1	Proposed Initiation of Dosing:	08/02/95
4.2	Proposed Necropsy Dates:	01/31/96 - 2/2/96
4.3	Proposed Study Completion Date (Draft Study Report):	5/3/96

Reason: The study dates have been finalized.

2. Page 2 Section 6.0

A. Change Barry S. Levine, D.Sc., D.A.B.T. from "Study Director" to "Principal Investigator".
B. Change Clyde W. Wheeler, Ph.D. from "Toxicologist" to "Study Director".
C. Indicate Teresa O'Neill as the Lead Technician.

Reason: Clarification of the study personnel.

3. Page 3 Section 7.5

Change the approximate body weight range in males to "225 - 275 g" from "200 - 250 g".

Reason: Mistake in the protocol.

4. Page 3 Section 7.10

Remove the two references to "Toxicologist" in the paragraph.

Reason: Because Dr. Wheeler became the Study Director, there is no longer anyone identified as "Toxicologist" in the study

5. Page 5 Section 8.2

A. Indicate that dosing initiation will start on "day 1" instead of on "day 0".
B. Indicate the days of scheduled necropsies as "days 183, 184 and 185" instead of "days 182, 183 and 184".

Reason: Day 1 is now defined as the first day of dosing.

6. Page 5 Section 8.6

Replace the first sentence with the following: "Dosing formulation calculations of the test article will be adjusted for the purity of the test article. The control materials will be assumed to be 100% pure for dosing calculations."

Reason: Sponsor requested change in the protocol.

7. Page 7 Section 8.7.8

Indicate that blood will be collected for the determination of plasma drug levels "≈ 24 hours after the first day of dosing" instead of "≈ 24 hours after dosing on day 0".

Reason: Clarification of the protocol. Day 0 is no longer defined as the start of dosing initiation.

8. Page 7 Section 8.7.8

Add the following two sentences to indicate that plasma samples will be sent to a Sponsor-directed laboratory for drug level analysis. "The plasma samples will be stored at -65° to -70°C. and sent in at least two shipments as directed by the Sponsor to Dr. Emil Lin, University of California at San Francisco (UCSF) for measurement of drug levels. The UCSF-generated report may be included in the UIC-generated final study report at the discretion of the Sponsor."

Reason: Sponsor requested that plasma samples be sent to Dr. Lin at UCSF for drug level analysis.

9. Page 8 Section 8.7.9

Change the days of scheduled necropsies to "days 183 - 185" from "days 182 - 184"

Reason: Because dosing initiation is now defined as day 1 instead of day 0, the scheduled necropsy days are shifted by one day.

PROTOCOL AMENDMENT

DRAFT

Study No.: 152

Title: Six Month Oral Toxicity Study of WR238605 Succinate in Rats

10. Page 10 Section 11.0

Make the following changes in the protocol approval:

A. Indicate that Barry S. Levine, D.Sc., D.A.B.T. is the "Principal Investigator" instead of the "Study Director".
B. Change Clyde W. Wheeler, Ph.D. from "Toxicologist" to "Study Director".
C. Remove "Toxicologist" as a position identified in the study protocol.

Reason: Clarification of the study personnel.

Approvals:

FORMER STUDY DIRECTOR: Barry S. Levine, D.Sc., D.A.B.T. — Date: 8/1/95

CURRENT STUDY DIRECTOR: Clyde W. Wheeler, Ph.D. — Date: 8/01/95

SPONSOR APPROVAL: George J. Schieferstein, Ph.D. Contracting Officer's Representative (COR) — Date: 8/4/95

PROTOCOL AMENDMENT DRAFT

Study No.: 152

Title: Six Month Oral Toxicity Study of WR238605 Succinate in Rats

11. Page 5 Section 8.6

A. In the first sentence, indicate that "Dosing formulation calculations of the test article will be adjusted for the purity of the test article and the base mole fraction."

B. Remove the fourth sentence which discusses adjustments for purity and base mole fraction in dosing calculations.

Reason: A. Clarification of the protocol. B. Mistake in the protocol. As stated above (Protocol Amendment 11A.), the dosing formulation calculations will be adjusted for both the test article purity and the base mole fraction.

Approvals:

STUDY DIRECTOR: Clyde W. Wheeler, Ph.D. — Date: 8/30/95

SPONSOR APPROVAL: George J. Schieferstein, Ph.D. Contracting Officer's Representative (COR) — Date: 9/7/95

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PROTOCOL AMENDMENT

Study No.: 152

Title: Six Month Oral Toxicity Study of WR238605 Succinate in Rats

12. Page 1 Section 3.3

Change the Study Director from "Clyde W. Wheeler, Ph.D." to "Barry S. Levine, D.Sc., D.A.B.T.".

Reason: Dr. Wheeler has resigned from UIC.

13. Page 2 Section 6.0

Change the Study Director from "Clyde W. Wheeler, Ph.D." to "Barry S. Levine, D.Sc., D.A.B.T.".

Reason: Dr. Wheeler has resigned from UIC.

14. Page 10 Section 11.0

Indicate that "Barry S. Levine, D.Sc., D.A.B.T." is the Study Director.

Reason: Clarification of the study personnel.

Approvals:

FORMER STUDY DIRECTOR: Clyde W. Wheeler, Ph.D. — Date: 10/6/95

CURRENT STUDY DIRECTOR: Barry S. Levine, D.Sc., D.A.B.T. — Date: 10/6/95

SPONSOR APPROVAL: George J. Schieferstein, Ph.D. Contracting Officer's Representative (COR) — Date: 10/10/95

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PROTOCOL AMENDMENT

Study No. 152

Title: Six Month Oral Toxicity Study of WR238605 Succinate in Rats

15. Page 7 Section 8.7.7

Activated partial thromboplastin time will only be measured in the same 10 rats/sex/group used for clinical chemistry and hematology measurements, not in all animals.

Reason: Clarification of procedures; mistake in protocol.

Approvals:

STUDY DIRECTOR: Barry S. Levine, D.Sc., D.A.B.T. — Date 6/6/96

SPONSOR APPROVAL: George J. Schieferstein, Ph.D. Contracting Officer's Representative (COR) — Date 6/10/96

PROTOCOL AMENDMENT DRAFT

Study No.: 152
Title: Six Month Oral Toxicity Study of WR238605 Succinate in Rats

16. Page 8 Section 8.7.9

In the second paragraph replace "....carbon dioxide asphyxiation " with "...carbon dioxide anesthesia followed by exsanguination".

Reason: To clarify the euthanasia procedure.

STUDY DIRECTOR: Barry S. Levine, D.Sc., D.A.B.T. 6/24/96 Date

QUALITY ASSURANCE: Ronald Schoenbeck 6/24/96 Date

SPONSOR APPROVAL: George J. Schieferstein, Ph.D. Contracting Officer's Representative (COR) 6/26/96 Date

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APPENDIX N

STUDY DEVIATIONS

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

Study Deviations*

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Deviation Type	Specific Deviation	Effect on Study
Protocol	The humidity was ≤2% out of range on 10/16/95, 10/17/95 and 01/31/96.	None. Deviations were minimal.
Protocol	Food consumption was not measured during the specified times for the following animals: Animal No. 470 (Day 15 - Day 22); Animal No. 476 (Day 148 - Day 155); Animal No. 500 (Day 99 - Day 106); Animal No. 580 (Day 71 - Day 78). For these animals, food was inadvertently dumped before weighing. Also, food consumption was not measured during the specified times for the following animals: Animal No. 476 (Day 155 - Day 162); Animal No. 482 (Day 155 - Day 162); Animal No. 579 (Day 127 - Day 134). For these animals the food became wet due to lix-it problems.	Negligible; only seven data points are missing from a total of 4160 total food consumption values.
Protocol	At scheduled necropsy, all rats were bled from the abdominal vena cava, instead of just the animals required for clinical pathology (activated partial thromboplastin time). All animals were bled so that there would be no discrepancies in organ weight between clinical pathology animals and the remaining animals.	None; all animals were exsanguinated at necropsy for the sake of consistency.

*The detailed "Deviation Reports" are contained in the raw data which are archive at the Toxicology Research Laboratory, University of Illinois at Chicago, Department of Pharmacology, 1940 W. Taylor St., Chicago, Illinois 60612.

The above deviations did not affect the integrity of the study.

Barry S. Levine, D.Sc., D.A.B.T.

Date