

# Toxicology Research Laboratory

---

**UIC** The University of Illinois  
at Chicago

Department of Pharmacology (M/C 868)  
1940 W. Taylor St.  
Chicago, Illinois 60612-7353

20161005002

## REPORT DOCUMENTATION PAGE

**DRAFT**  
 Form Approved  
 OMB No. 0704-0188

1a. REPORT SECURITY CLASSIFICATION		1b. RESTRICTIVE MARKINGS	
2a. SECURITY CLASSIFICATION AUTHORITY Unclassified		3. DISTRIBUTION/AVAILABILITY OF REPORT  Unlimited	
2b. DECLASSIFICATION/DOWNGRADING SCHEDULE			
4. PERFORMING ORGANIZATION REPORT NUMBER(S)  UIC-5A; (UIC/TRL Study No. 097)		5. MONITORING ORGANIZATION REPORT NUMBER(S)	
6a. NAME OF PERFORMING ORGANIZATION Toxicology Research Laboratory University of Illinois at Chicago	6b. OFFICE SYMBOL (if applicable)	7a. NAME OF MONITORING ORGANIZATION U.S. Army Medical Research Acquisition Activity	
6c. ADDRESS (City, State, and ZIP Code) Department of Pharmacology (M/C 868) 1940 W. Taylor Street Chicago, IL 60612-7353		7b. ADDRESS (City, State, and ZIP Code) ATTN: SGRD-RMA-RCD Fort Detrick Frederick, MD 21702	
8a. NAME OF FUNDING/SPONSORING ORGANIZATION U.S. Army Medical Materiel Development Activity	8b. OFFICE SYMBOL (if applicable) SGRD-UMP	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER DAMD17-92-C-2001	
8c. ADDRESS (City, State, and ZIP Code) Fort Detrick Frederick, MD 21702-5009		10. SOURCE OF FUNDING NUMBERS	
		PROGRAM ELEMENT NO. 63807A	PROJECT NO. 30463807
		TASK NO. QC	WORK UNIT ACCESSION NO. 073
11. TITLE (Include Security Classification)			
12. PERSONAL AUTHOR(S) Levine, Barry S.; Tomlinson, Michael J. (Pathology Associates, Inc.)			
13a. TYPE OF REPORT Draft	13b. TIME COVERED FROM _____ TO _____	14. DATE OF REPORT (Year, Month, Day)	15. PAGE COUNT
16. SUPPLEMENTARY NOTATION THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS			
17. COSATI CODES		18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)	
FIELD	GROUP	SUB-GROUP	
19. ABSTRACT (Continue on reverse if necessary and identify by block number)			
<p>This study evaluated the toxicity of WR238605 in dogs following thirteen weeks of daily oral (gavage) administration. A thirteen week recovery period was included for all groups. Dose levels studied were 0 (vehicle control), 0.1, 2.0 and 6.0 mg base/kg/day. The primary toxic effects of WR238605 were seen in the lungs and RBCs. Drug treatment was associated with hemolytic anemia which was supported by reticulocytosis, bone marrow hypercellularity, decrease in bone marrow M/E ratio, splenomegaly, extramedullary hematopoiesis, and hemosiderosis in the liver and spleen. Mild hepatotoxicity as evidenced by hepatocyte necrosis (high dose males) was supported by altered clinical chemistry values. Possibly, secondary to the hematologic alterations, congestion of retinal vessels was seen in one high dose female, which was no longer evident by the end of the recovery period. Generalized or secondary toxic effects related to the stress produced by the anemic and/or methemoglobinemic state included decreases in weight gain; neutrophilic and monocytic leukocytosis; and depletion of thymic lymphocytes. Methemoglobinemia was manifested by clinical signs of cyanosis (blue gums, tongue, and sclera). Lung lesions induced by WR238605 included alveolar proteinosis and subacute inflammation. Also, chronic inflammation of the alveolar and bronchiolar epithelium developed in the recovery period. This was deemed to be part of the process of resolution of alveolar proteinosis and as such a secondary lesion to a direct treatment-related effect. All of the above described toxic effects were generally seen at the high and mid dose levels. Hemosiderosis and subacute inflammation of the liver (minimal severity), secondary to hemolytic anemia, and bone marrow hypercellularity (minimal severity) were also seen in low dose animals. However, these findings in low dose animals were not supported by alterations in clinical pathology parameters. WR238605 toxicity was essentially reversible, except for the lung lesions (subacute inflammation) and the microscopic changes secondary to the observed hemolytic anemia (hepatic hemosiderosis). Based upon the these findings, the no observed effect level (NOEL) in this study was equivocal, but was considered to be near the low dose level of 0.1 mg base/kg/day.</p>			
20. DISTRIBUTION/AVAILABILITY OF ABSTRACT <input type="checkbox"/> UNCLASSIFIED/UNLIMITED <input checked="" type="checkbox"/> SAME AS RPT. <input type="checkbox"/> DTIC USERS		21. ABSTRACT SECURITY CLASSIFICATION Unclassified	
22a. NAME OF RESPONSIBLE INDIVIDUAL Barry S. Levine	22b. TELEPHONE (Include Area Code) (312) 996-5543	22c. OFFICE SYMBOL N/A	

DRAFT

Title Page

Volume 3 of 3

Revised Draft Report for Task Order No. UIC-5A

THIRTEEN WEEK ORAL TOXICITY STUDY OF  
WR238605 WITH A THIRTEEN WEEK  
RECOVERY PERIOD IN DOGS

Sponsor: US Army Medical Materiel  
Development Activity

Test Article: WR238605

Contract No.: DAMD17-92-C-2001

Study Director

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

In-Life Phase Completed On

June 11, 1993

Performing Laboratory

TOXICOLOGY RESEARCH LABORATORY (TRL)  
University of Illinois at Chicago (UIC)  
Department of Pharmacology  
1940 W. Taylor St.  
Chicago, IL 60612-7353

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.

DRAFT

VOLUME 3

APPENDICES (contd.)

7	Individual Hematology Data .....	7-1
8	Individual Urinalysis Data .....	8-1
9	Cardiology Report .....	9-1
10	Ophthalmology Report .....	10-1
11	Individual Organ Weights .....	11-1
12	Pathology Report .....	12-1
13	Protocol and Protocol Amendments .....	13-1
14	Study Deviations .....	14-1

DRAFT

APPENDIX 7  
Individual Hematology Data

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Erythrocytes

STUDY ID: 097  
STUDY NO: 097  
ABBR: RBC

SEX: MALE

UNITS: 10<sup>6</sup>/cmm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1M:0 mg base/kg/day								
7531	6.61	7.33	7.07	6.63	6.06	6.04	7.48	7.41
7532	5.85	5.54	5.81	6.26	6.06	6.13	6.93	6.87
7512	6.25	6.26	6.02	5.91	5.92	6.00	6.35	7.29
7515	6.05	6.30	5.85	6.73	6.40	6.22	6.88	7.43
7521	6.52	6.29	6.38	6.63	6.30	7.09	--	--
7533	5.68	5.43	5.44	5.62	6.50	5.95	--	--
7520	6.64	6.95	6.82	6.38	6.21	7.00	--	--
7505	5.50	6.40	5.54	6.00	6.07	6.26	--	--
MEAN	6.14	6.31	6.12	6.27	6.19	6.34	6.91	7.25
SD	0.438	0.636	0.590	0.398	0.198	0.450	0.462	0.261
N	8	8	8	8	8	8	4	4
GROUP: 2M:0.1 mg base/kg/day								
7527	6.42	6.35	6.22	6.30	6.59	7.19	6.87	7.52
7519	6.02	6.00	5.86	6.23	5.95	6.54	6.73	7.47
7529	5.80	5.95	5.83	6.23	6.56	6.14	6.49	6.43
7536	6.50	6.15	6.65	5.77	5.58	5.79	6.42	6.49
7503	6.27	6.35	6.26	6.41	6.69	7.84	--	--
7523	6.59	6.48	6.97	6.66	6.54	5.97	--	--
7517	6.75	6.78	6.59	6.43	7.15	6.82	--	--
7528	6.43	6.26	5.58	6.41	6.65	6.80	--	--
MEAN	6.35	6.29	6.25	6.31	6.46	6.64	6.63	6.98
SD	0.309	0.268	0.474	0.257	0.483	0.679	0.209	0.598
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Erythrocytes

STUDY ID: 097  
STUDY NO: 097  
ABBR: RBC

SEX: MALE

UNITS: 10<sup>6</sup>/cmm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3M:2.0 mg base/kg/day								
7538	7.05	6.73	6.23	5.99	6.62	6.44	7.43	7.29
7516	6.41	6.18	6.42	5.33	5.92	6.88	6.63	7.59
7522	6.55	7.28	7.26	6.36	7.44	7.20	8.57	8.22
7510	6.97	6.93	6.64	5.93	6.25	5.72	7.78	7.07
7576	5.87	5.68	5.81	5.04	5.80	5.55	--	--
7506	6.38	5.81	6.00	5.55	6.61	5.86	--	--
7502	7.02	6.32	6.95	6.34	6.23	6.76	--	--
7514	6.19	5.73	6.01	5.23	5.68	5.85	--	--
MEAN	6.56	6.33	6.42	5.72	6.32	6.28	7.60	7.54
SD	0.429	0.597	0.505	0.506	0.571	0.618	0.805	0.499
N	8	8	8	8	8	8	4	4

GROUP: 4M:6.0 mg base/kg/day								
7535	6.65	6.99	6.95	6.11	6.78	6.56	7.00	7.68
7511	7.26	6.82	6.42	5.50	6.82	7.62	7.27	7.77
7530	6.29	6.55	6.20	5.38	6.47	5.52	5.77	7.28
7507	5.90	6.55	5.54	4.83	6.47	5.94	6.84	7.12
7508	5.76	5.90	5.94	5.02	5.75	5.11	--	--
7509	6.13	6.66	6.27	5.44	6.19	5.51	--	--
7518	6.34	6.14	5.95	5.26	5.71	6.05	--	--
7524	7.11	6.61	6.68	5.94	6.64	6.56	--	--
MEAN	6.43	6.53	6.24	5.44	6.35	6.11	6.72	7.46
SD	0.541	0.352	0.447	0.429	0.433	0.795	0.658	0.312
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Hemoglobin

STUDY ID: 097  
STUDY NO: 097  
ABBR: THGB

SEX: MALE

UNITS: g/dL

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1M:0 mg base/kg/day								
7531	15.9	17.7	17.1	16.0	15.8	14.9	18.3	18.1
7532	14.3	13.4	14.0	15.4	15.7	15.2	17.5	17.5
7512	15.2	15.2	14.7	14.6	14.6	15.0	15.5	17.8
7515	14.6	15.3	13.8	16.3	15.4	15.1	16.6	18.0
7521	16.5	15.7	16.2	17.0	16.3	18.2	--	--
7533	13.7	13.3	13.6	14.1	14.5	15.2	--	--
7520	16.3	17.4	16.9	15.8	16.5	17.6	--	--
7505	13.2	15.3	13.2	14.7	15.7	15.3	--	--
MEAN	15.0	15.4	14.9	15.5	15.6	15.8	17.0	17.9
SD	1.22	1.60	1.57	0.97	0.72	1.30	1.20	0.26
N	8	8	8	8	8	8	4	4

GROUP: 2M:0.1 mg base/kg/day								
7527	15.1	15.1	14.6	14.7	16.5	17.1	16.4	17.8
7519	14.8	14.7	14.5	15.6	15.3	16.8	17.0	18.8
7529	13.5	14.0	13.9	15.4	16.9	15.2	16.2	15.5
7536	16.2	15.3	16.3	14.2	14.8	14.3	16.0	16.3
7503	15.0	15.2	15.0	15.5	17.1	19.1	--	--
7523	16.6	16.4	17.8	17.0	16.7	15.5	--	--
7517	16.0	16.4	16.1	15.8	17.4	16.6	--	--
7528	15.3	15.2	13.3	15.5	15.8	16.7	--	--
MEAN	15.3	15.3	15.2	15.5	16.3	16.4	16.4	17.1
SD	0.97	0.80	1.46	0.82	0.92	1.45	0.43	1.48
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Hemoglobin

STUDY ID: 097  
STUDY NO: 097  
ABBR: THGB

SEX: MALE

UNITS: g/dL

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3M:2.0 mg base/kg/day								
7538	15.9	15.5	14.9	14.4	16.4	15.0	17.4	17.6
7516	16.0	15.4	16.1	13.1	14.4	16.7	16.4	18.7
7522	15.4	17.2	17.4	15.4	17.6	16.8	20.1	19.2
7510	15.7	15.7	14.9	13.9	14.0	13.1	17.6	15.9
7576	14.8	14.3	14.6	13.0	15.7	14.2	--	--
7506	15.7	14.5	15.0	14.0	16.5	14.7	--	--
7502	16.7	15.3	16.6	15.6	16.5	17.0	--	--
7514	14.3	13.2	14.4	12.5	14.8	13.8	--	--
MEAN	15.6	15.1	15.5	14.0	15.7	15.2	17.9	17.9
SD	0.74	1.17	1.08	1.12	1.24	1.50	1.57	1.46
N	8	8	8	8	8	8	4	4
GROUP: 4M:6.0 mg base/kg/day								
7535	16.7	17.6	17.9	16.0	18.2	16.2	17.3	19.0
7511	16.6	15.7	15.3	13.2	16.3	16.7	16.1	17.4
7530	14.4	15.5	14.5	12.3	15.5	12.7	13.1	16.6
7507	15.2	16.5	14.0	12.1	16.1	15.2	17.4	17.8
7508	14.9	15.5	15.5	13.1	14.5	13.4	--	--
7509	15.0	16.3	15.4	13.3	14.5	13.2	--	--
7518	15.6	15.0	14.6	12.9	13.7	14.4	--	--
7524	17.3	16.4	16.9	15.1	16.4	17.0	--	--
MEAN	15.7	16.1	15.5	13.5	15.7	14.9	16.0	17.7
SD	1.03	0.81	1.30	1.36	1.42	1.68	2.01	1.00
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Hematocrit

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
STUDY ID: 097 <span style="float: right;">SEX: MALE</span>								
STUDY NO: 097								
ABBR: HCT <span style="float: right;">UNITS: %</span>								
GROUP: 1M:0 mg base/kg/day								
7531	46.2	50.7	48.5	46.3	42.7	42.5	51.7	51.1
7532	41.8	39.1	40.7	44.4	43.1	44.0	48.9	48.8
7512	44.6	44.4	42.1	41.6	41.7	43.0	44.2	50.7
7515	42.7	44.2	40.8	46.3	44.7	43.4	47.5	51.6
7521	47.3	45.3	46.2	47.7	45.5	51.4	--	--
7533	41.5	39.4	39.7	40.6	42.2	42.8	--	--
7520	48.0	49.3	47.9	44.9	44.0	49.1	--	--
7505	39.0	45.1	39.1	42.2	42.3	43.2	--	--
MEAN	43.9	44.7	43.1	44.3	43.3	44.9	48.1	50.6
SD	3.16	4.10	3.81	2.54	1.33	3.37	3.12	1.22
N	8	8	8	8	8	8	4	4
GROUP: 2M:0.1 mg base/kg/day								
7527	43.5	42.9	41.4	42.1	44.0	48.0	45.8	49.5
7519	44.4	43.5	42.8	45.0	42.6	47.7	48.3	53.6
7529	40.0	41.1	40.5	43.2	45.2	42.7	44.6	43.9
7536	46.0	43.4	46.1	40.7	39.4	40.8	44.4	45.5
7503	43.9	43.9	43.8	44.7	46.4	54.3	--	--
7523	48.8	47.5	49.9	47.6	46.8	43.5	--	--
7517	47.9	47.5	46.3	45.1	50.0	47.2	--	--
7528	44.7	43.5	38.1	44.0	45.7	46.6	--	--
MEAN	44.9	44.2	43.6	44.1	45.0	46.4	45.8	48.1
SD	2.74	2.23	3.75	2.10	3.14	4.15	1.79	4.34
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

D R A F T

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Hematocrit

STUDY ID: 097  
STUDY NO: 097  
ABBR: HCT

SEX: MALE

UNITS: %

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3M:2.0 mg base/kg/day								
7538	46.5	45.1	42.6	42.4	45.7	43.7	50.1	48.8
7516	47.0	45.1	46.0	39.6	42.5	48.8	46.3	51.5
7522	44.7	49.2	48.4	43.9	50.3	47.6	56.3	52.9
7510	46.8	45.7	43.4	40.1	42.7	39.2	51.7	45.6
7576	43.1	41.4	42.4	38.2	43.4	41.1	--	--
7506	46.3	41.4	43.0	40.8	47.8	41.6	--	--
7502	50.1	44.7	48.8	46.7	45.6	49.1	--	--
7514	41.8	38.2	40.0	36.6	39.1	39.3	--	--
MEAN	45.8	43.9	44.3	41.0	44.6	43.8	51.1	49.7
SD	2.57	3.38	3.10	3.23	3.48	4.16	4.14	3.22
N	8	8	8	8	8	8	4	4

GROUP: 4M:6.0 mg base/kg/day								
7535	47.3	49.9	49.3	45.2	48.1	45.5	48.9	52.1
7511	48.0	45.0	42.2	37.7	44.3	47.2	44.9	48.1
7530	42.4	44.1	41.2	37.1	42.4	36.2	38.3	46.2
7507	43.3	47.7	40.6	36.8	47.9	44.6	50.3	49.1
7508	43.4	44.1	44.8	39.1	42.2	38.4	--	--
7509	44.3	47.2	44.1	39.1	42.2	38.5	--	--
7518	44.8	43.0	41.5	37.9	40.3	41.9	--	--
7524	50.1	46.5	48.4	44.5	46.9	45.5	--	--
MEAN	45.5	45.9	44.0	39.7	44.3	42.2	45.6	48.9
SD	2.71	2.30	3.32	3.30	2.99	4.08	5.38	2.46
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Mean Corpuscular Volume

STUDY ID: 097  
STUDY NO: 097  
ABBR: MCV

SEX: MALE

UNITS: fL

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1M:0 mg base/kg/day								
7531	69.9	69.2	68.6	69.8	70.5	70.4	69.1	69.0
7532	71.5	70.6	70.1	70.9	71.1	71.8	70.6	71.0
7512	71.4	70.9	69.9	70.4	70.4	71.7	69.6	69.5
7515	70.6	70.2	69.7	68.8	69.8	69.8	69.0	69.4
7521	72.5	72.0	72.4	71.9	72.2	72.5	--	--
7533	73.1	72.6	73.0	72.2	68.8	71.9	--	--
7520	72.3	70.9	70.2	70.4	70.9	70.1	--	--
7505	70.9	70.5	70.6	70.3	69.7	69.0	--	--
MEAN	71.5	70.9	70.6	70.6	70.4	70.9	69.6	69.7
SD	1.06	1.05	1.45	1.09	1.03	1.24	0.73	0.88
N	8	8	8	8	8	8	4	4

GROUP: 2M:0.1 mg base/kg/day								
7527	67.8	67.6	66.6	66.8	66.8	66.8	66.7	65.8
7519	73.8	72.5	73.0	72.2	71.6	72.9	71.8	71.8
7529	69.0	69.1	69.5	69.3	68.9	69.5	68.7	68.3
7536	70.8	70.6	69.3	70.5	70.6	70.5	69.2	70.1
7503	70.0	69.1	70.0	69.7	69.4	69.3	--	--
7523	74.1	73.3	71.6	71.5	71.6	72.9	--	--
7517	71.0	70.1	70.3	70.1	69.9	69.2	--	--
7528	69.5	69.5	68.3	68.6	68.7	68.5	--	--
MEAN	70.8	70.2	69.8	69.8	69.7	70.0	69.1	69.0
SD	2.22	1.88	1.95	1.69	1.61	2.10	2.10	2.57
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Mean Corpuscular Volume

STUDY ID: 097  
STUDY NO: 097  
ABBR: MCV

SEX: MALE

UNITS: fL

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3M:2.0 mg base/kg/day								
7538	66.0	67.0	68.4	70.5	69.0	67.9	67.4	66.9
7516	73.3	73.0	71.7	74.3	71.8	70.9	69.8	67.9
7522	68.2	67.6	66.7	69.0	67.6	66.1	65.7	64.4
7510	67.1	65.9	65.4	67.6	68.3	68.5	66.5	64.5
7576	73.4	72.9	73.0	75.8	74.8	74.1	--	--
7506	72.6	71.3	71.7	73.5	72.3	71.0	--	--
7502	71.4	70.7	70.2	73.7	73.2	72.6	--	--
7514	67.5	66.7	66.6	70.0	68.8	67.2	--	--
MEAN	69.9	69.4	69.2	71.8	70.7	69.8	67.4	65.9
SD	3.05	2.90	2.83	2.91	2.64	2.80	1.77	1.75
N	8	8	8	8	8	8	4	4

GROUP: 4M:6.0 mg base/kg/day								
7535	71.1	71.4	70.9	74.0	70.9	69.4	69.9	67.8
7511	66.1	66.0	65.7	68.5	65.0	61.9	61.8	61.9
7530	67.4	67.2	66.5	69.0	65.5	65.6	66.4	63.5
7507	73.4	72.8	73.3	76.2	74.0	75.1	73.5	69.0
7508	75.3	74.7	75.4	77.9	68.8	75.1	--	--
7509	72.3	70.9	70.3	71.9	68.8	69.9	--	--
7518	70.7	70.0	69.7	72.1	70.6	69.3	--	--
7524	70.5	70.3	72.5	74.9	70.6	69.4	--	--
MEAN	70.9	70.4	70.5	73.1	69.3	69.5	67.9	65.6
SD	3.00	2.81	3.29	3.32	2.96	4.41	4.99	3.39
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Mean Corpuscular Hemoglobin

STUDY ID: 097  
STUDY NO: 097  
ABBR: TMCH

SEX: MALE

UNITS: pg

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1M:0 mg base/kg/day								
7531	24.1	24.1	24.2	24.1	26.1	24.7	24.5	24.4
7532	24.4	24.2	24.1	24.6	25.9	24.8	25.3	25.5
7512	24.3	24.3	24.4	24.7	24.7	25.0	24.4	24.4
7515	24.1	24.3	23.6	24.2	24.1	24.3	24.1	24.2
7521	25.3	25.0	25.4	25.6	25.9	25.7	--	--
7533	24.1	24.5	25.0	25.1	23.7	25.5	--	--
7520	24.5	25.0	24.8	24.8	26.6	25.1	--	--
7505	24.0	23.9	23.8	24.5	25.9	24.4	--	--
MEAN	24.4	24.4	24.4	24.7	25.4	24.9	24.6	24.6
SD	0.42	0.40	0.62	0.48	1.05	0.49	0.51	0.59
N	8	8	8	8	8	8	4	4

GROUP: 2M:0.1 mg base/kg/day								
7527	23.5	23.8	23.5	23.3	25.0	23.8	23.9	23.7
7519	24.6	24.5	24.7	25.0	25.7	25.7	25.3	25.2
7529	23.3	23.5	23.8	24.7	25.8	24.8	25.0	24.1
7536	24.9	24.9	24.5	24.6	26.5	24.7	24.9	25.1
7503	23.9	23.9	24.0	24.2	25.6	24.4	--	--
7523	25.2	25.3	25.5	25.5	25.5	26.0	--	--
7517	23.7	24.2	24.4	24.6	24.3	24.3	--	--
7528	23.8	24.3	23.8	24.2	23.8	24.6	--	--
MEAN	24.1	24.3	24.3	24.5	25.3	24.8	24.8	24.5
SD	0.70	0.59	0.64	0.65	0.87	0.73	0.61	0.74
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Mean Corpuscular Hemoglobin

STUDY ID: 097  
STUDY NO: 097  
ABBR: TMCH

SEX: MALE

UNITS: pg

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3M:2.0 mg base/kg/day								
7538	22.6	23.0	23.9	24.0	24.8	23.3	23.4	24.1
7516	25.0	24.9	25.1	24.6	24.3	24.3	24.7	24.6
7522	23.5	23.6	24.0	24.2	23.7	23.3	23.5	23.4
7510	22.5	22.7	22.4	23.4	22.4	22.9	22.6	22.5
7576	25.2	25.2	25.1	25.8	27.1	25.6	--	--
7506	24.6	25.0	25.0	25.2	25.0	25.1	--	--
7502	23.8	24.2	23.9	24.6	26.5	25.1	--	--
7514	23.1	23.0	24.0	23.9	26.1	23.6	--	--
MEAN	23.8	24.0	24.2	24.5	25.0	24.2	23.6	23.7
SD	1.05	1.01	0.91	0.77	1.55	1.02	0.87	0.91
N	8	8	8	8	8	8	4	4
GROUP: 4M:6.0 mg base/kg/day								
7535	25.1	25.2	25.8	26.2	26.8	24.7	24.7	24.7
7511	22.9	23.0	23.8	24.0	23.9	21.9	22.1	22.4
7530	22.9	26.3	23.4	22.9	24.0	23.0	22.7	22.8
7507	25.8	25.2	25.3	25.1	24.9	25.6	25.4	25.0
7508	25.9	26.3	26.1	26.1	23.7	26.2	--	--
7509	24.5	24.5	24.6	24.4	23.7	24.0	--	--
7518	24.6	24.4	24.5	24.5	24.0	23.8	--	--
7524	24.3	24.8	25.3	25.4	24.7	24.7	--	--
MEAN	24.5	25.0	24.9	24.8	24.5	24.2	23.7	23.7
SD	1.15	1.08	0.95	1.11	1.04	1.38	1.58	1.31
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Mean Copuscular Hemo. Conc.

STUDY ID: 097  
STUDY NO: 097  
ABBR: TMCHC

SEX: MALE

UNITS: g/dL

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1M:0 mg base/kg/day								
7531	34.4	34.9	35.3	34.6	37.0	35.1	35.4	35.4
7532	34.2	34.3	34.4	34.7	36.4	34.5	35.8	35.9
7512	34.1	34.2	34.9	35.1	35.0	34.9	35.1	35.1
7515	34.2	34.6	33.8	35.2	34.5	34.8	34.9	34.9
7521	34.9	34.7	35.1	35.6	35.8	35.4	--	--
7533	33.0	33.8	34.3	34.7	34.4	35.5	--	--
7520	34.0	35.3	35.3	35.2	37.5	35.8	--	--
7505	33.8	33.9	33.8	34.8	37.1	35.4	--	--
MEAN	34.1	34.5	34.6	35.0	36.0	35.2	35.3	35.3
SD	0.54	0.51	0.62	0.34	1.22	0.43	0.39	0.43
N	8	8	8	8	8	8	4	4

GROUP: 2M:0.1 mg base/kg/day								
7527	34.7	35.2	35.3	34.9	37.5	35.6	35.8	36.0
7519	33.3	33.8	33.9	34.7	35.9	35.2	35.2	35.1
7529	33.7	34.1	34.3	35.6	37.4	35.6	36.3	35.3
7536	35.2	35.3	35.4	34.9	37.6	35.0	36.0	35.8
7503	34.2	34.6	34.2	34.7	36.9	35.2	--	--
7523	34.0	34.5	35.7	35.7	35.7	35.6	--	--
7517	33.4	34.5	34.8	35.0	34.8	35.2	--	--
7528	34.2	34.9	34.9	35.2	34.6	35.8	--	--
MEAN	34.1	34.6	34.8	35.1	36.3	35.4	35.8	35.6
SD	0.64	0.51	0.64	0.38	1.22	0.28	0.46	0.42
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Mean Copuscular Hemo. Conc.

STUDY ID: 097  
STUDY NO: 097  
ABBR: TMCHC

SEX: MALE

UNITS: g/dL

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3M:2.0 mg base/kg/day								
7538	34.2	34.4	35.0	34.1	35.9	34.3	34.7	36.1
7516	34.0	34.1	35.0	33.1	33.9	34.2	35.4	36.3
7522	34.5	35.0	36.0	35.1	35.0	35.3	35.7	36.3
7510	33.5	34.4	34.3	34.7	32.8	33.4	34.0	34.9
7576	34.3	34.5	34.4	34.0	36.2	34.5	--	--
7506	33.9	35.0	34.9	34.3	34.5	35.3	--	--
7502	33.3	34.2	34.0	33.4	36.2	34.6	--	--
7514	34.2	34.6	36.0	34.2	37.9	35.1	--	--
MEAN	34.0	34.5	35.0	34.1	35.3	34.6	35.0	35.9
SD	0.41	0.33	0.74	0.64	1.59	0.65	0.76	0.67
N	8	8	8	8	8	8	4	4

GROUP: 4M:6.0 mg base/kg/day								
7535	35.3	35.3	36.3	35.4	37.8	35.6	35.4	36.5
7511	34.6	34.9	36.3	35.0	36.8	35.4	35.9	36.2
7530	34.0	35.1	35.2	33.2	36.6	35.1	34.2	35.9
7507	35.1	34.6	34.5	32.9	33.6	34.1	34.6	36.3
7508	34.3	35.1	34.6	33.5	34.4	34.9	--	--
7509	33.9	34.5	34.9	34.0	34.4	34.3	--	--
7518	34.8	34.9	35.2	34.0	34.0	34.4	--	--
7524	34.5	35.3	34.9	33.9	35.0	35.6	--	--
MEAN	34.6	35.0	35.2	34.0	35.3	34.9	35.0	36.2
SD	0.50	0.30	0.70	0.85	1.53	0.60	0.77	0.25
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Reticulocytes (%RBCs)

STUDY ID: 097  
STUDY NO: 097  
ABBR: RETICS

SEX: MALE

UNITS: % RBCs

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1M:0 mg base/kg/day								
7531	0.2	0.3	0.6	0.5	0.1	0.2	0.4	0.2
7532	0.3	0.3	0.1	0.7	0.8	0.5	0.3	0.2
7512	0.6	0.0	0.1	0.0	0.5	0.5	0.4	0.5
7515	0.3	0.0	0.1	0.2	0.1	0.0	0.7	0.2
7521	0.1	0.0	0.0	0.2	0.1	0.3	--	--
7533	0.5	0.4	0.2	0.3	0.0	0.1	--	--
7520	0.7	0.1	0.0	0.1	0.0	0.2	--	--
7505	0.4	0.1	0.0	0.3	0.1	0.3	--	--
MEAN	0.4	0.2	0.1	0.3	0.2	0.3	0.5	0.3
SD	0.20	0.16	0.20	0.22	0.29	0.18	0.17	0.15
N	8	8	8	8	8	8	4	4

GROUP: 2M:0.1 mg base/kg/day								
7527	0.1	0.0	0.0	0.0	0.1	0.1	0.5	0.2
7519	0.4	0.1	0.2	0.0	0.6	0.8	0.9	0.8
7529	0.3	0.0	0.0	0.0	0.2	0.1	0.1	0.2
7536	0.0	0.1	0.1	0.2	0.4	0.1	0.7	0.3
7503	0.8	0.1	0.4	0.6	0.4	0.9	--	--
7523	0.2	0.0	0.2	0.1	0.3	0.0	--	--
7517	1.2	0.2	0.4	0.1	0.3	0.2	--	--
7528	0.2	0.0	0.0	0.0	0.2	0.5	--	--
MEAN	0.4	0.1	0.2	0.1	0.3	0.3	0.6	0.4
SD	0.40	0.07	0.17	0.21	0.16	0.35	0.34	0.29
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Reticulocytes (%RBCs)

STUDY ID: 097  
STUDY NO: 097  
ABBR: RETICS

SEX: MALE

UNITS: % RBCs

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3M:2.0 mg base/kg/day								
7538	0.1	0.2	0.8	0.8	0.6	0.6	0.4	0.9
7516	0.3	0.3	0.4	0.6	0.6	1.1	0.7	0.3
7522	0.8	0.0	0.3	0.6	0.7	1.2	0.5	0.3
7510	1.2	0.1	0.4	0.3	1.2	0.9	0.6	0.1
7576	0.5	0.0	0.0	0.7	0.6	0.9	--	--
7506	0.4	0.2	0.3	0.4	0.7	0.3	--	--
7502	0.3	0.0	0.4	0.7	0.5	0.3	--	--
7514	0.5	0.3	0.2	0.8	0.4	0.8	--	--
MEAN	0.5	0.1	0.4	0.6	0.7	0.8	0.6	0.4
SD	0.34	0.13	0.23	0.18	0.24	0.34	0.13	0.35
N	8	8	8	8	8	8	4	4

GROUP: 4M:6.0 mg base/kg/day								
7535	0.1	0.0	0.2	1.2	0.6	0.9	0.6	0.3
7511	0.1	0.0	0.2	0.5	0.6	1.0	0.5	0.1
7530	0.1	0.0	0.3	1.5	1.6	1.1	0.7	0.8
7507	0.3	0.1	0.3	2.0	1.4	1.2	1.2	0.2
7508	0.4	0.0	0.5	0.8	0.0	1.0	--	--
7509	0.3	0.2	0.5	1.0	0.0	2.1	--	--
7518	0.3	0.1	0.0	0.7	1.9	1.2	--	--
7524	0.5	0.1	0.5	1.0	0.9	0.9	--	--
MEAN	0.3	0.1	0.3	1.1	0.9	1.2	0.8	0.4
SD	0.15	0.07	0.18	0.48	0.71	0.39	0.31	0.31
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Nucleated Red Cells

STUDY ID: 097  
STUDY NO: 097  
ABBR: NRBC

SEX: MALE

UNITS: COUNT

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1M:0 mg base/kg/day								
7531	0	0	0	0	0	0	0	0
7532	0	0	0	0	1	1	0	0
7512	0	0	1	1	2	0	0	5
7515	1	0	0	0	0	0	4	1
7521	0	0	1	0	0	0	--	--
7533	0	0	0	0	0	2	--	--
7520	0	0	0	0	0	0	--	--
7505	0	0	0	0	0	1	--	--
MEAN	0	0	0	0	0	1	1	2
SD	0.4	0.0	0.5	0.4	0.7	0.8	2.0	2.4
N	8	8	8	8	8	8	4	4

GROUP: 2M:0.1 mg base/kg/day								
7527	0	0	1	3	0	0	0	1
7519	0	0	0	0	2	0	3	0
7529	0	0	0	0	0	1	0	0
7536	0	0	0	1	0	7	0	0
7503	1	0	1	3	2	0	--	--
7523	0	0	0	0	3	2	--	--
7517	0	0	0	0	0	1	--	--
7528	0	0	0	0	0	0	--	--
MEAN	0	0	0	1	1	1	1	0
SD	0.4	0.0	0.5	1.4	1.2	2.4	1.5	0.5
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Nucleated Red Cells

STUDY ID: 097  
STUDY NO: 097  
ABBR: NRBC

SEX: MALE

UNITS: COUNT

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3M:2.0 mg base/kg/day								
7538	0	0	0	1	1	1	0	11
7516	0	0	0	1	1	0	2	0
7522	0	1	0	0	0	0	0	1
7510	0	0	0	2	0	1	0	2
7576	0	0	1	1	2	0	--	--
7506	1	0	0	2	0	1	--	--
7502	2	0	0	0	0	1	--	--
7514	0	0	0	0	0	0	--	--
MEAN	0	0	0	1	1	1	1	4
SD	0.7	0.4	0.4	0.8	0.8	0.5	1.0	5.1
N	8	8	8	8	8	8	4	4

GROUP: 4M:6.0 mg base/kg/day								
7535	0	0	0	0	0	1	0	0
7511	0	0	0	5	0	0	0	1
7530	0	0	4	3	0	0	0	1
7507	0	0	3	8	2	4	0	0
7508	0	0	0	4	0	0	--	--
7509	0	0	0	9	9	2	--	--
7518	1	0	2	5	1	1	--	--
7524	0	0	0	2	0	0	--	--
MEAN	0	0	1	5	2	1	0	1
SD	0.4	0.0	1.6	3.0	3.1	1.4	0.0	0.6
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Heinz Bodies

STUDY IO: 097  
STUDY NO: 097  
ABBR: HB

SEX: MALE

UNITS: %

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1M:0 mg base/kg/day								
7531	0.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7532	0.5	0.0	0.0	0.0	0.3	0.0	0.0	0.0
7512	0.5	0.0	0.0	0.0	0.2	0.1	0.0	0.0
7515	0.1	0.0	0.0	0.0	0.1	0.0	0.0	0.0
7521	0.0	0.0	0.0	0.0	0.0	0.3	--	--
7533	0.0	0.0	0.0	0.0	0.0	0.0	--	--
7520	0.0	0.0	0.0	0.0	0.0	1.0	--	--
7505	0.2	0.1	0.0	0.0	0.1	0.6	--	--
MEAN	0.2	0.0	0.0	0.0	0.1	0.3	0.0	0.0
SD	0.26	0.04	0.00	0.00	0.11	0.37	0.00	0.00
N	8	8	8	8	8	8	4	4

GROUP: 2M:0.1 mg base/kg/day								
7527	0.0	0.0	0.0	0.0	0.0	0.6	0.0	0.0
7519	0.0	0.0	0.0	0.0	0.0	0.3	0.0	0.0
7529	0.1	0.0	0.0	0.2	0.2	0.3	0.0	0.0
7536	0.0	0.0	0.0	0.0	0.1	0.4	0.1	0.1
7503	0.0	0.0	0.0	0.0	0.1	1.1	--	--
7523	0.0	0.1	0.0	0.0	0.0	0.1	--	--
7517	0.2	0.0	0.1	0.0	0.0	0.1	--	--
7528	0.0	0.0	0.0	0.0	0.0	0.0	--	--
MEAN	0.0	0.0	0.0	0.0	0.1	0.4	0.0	0.0
SD	0.07	0.04	0.04	0.07	0.08	0.35	0.05	0.05
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Heinz Bodies

STUDY ID: 097  
STUDY NO: 097  
ABBR: HB

SEX: MALE

UNITS: %

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3M:2.0 mg base/kg/day								
7538	0.0	0.0	0.4	0.0	0.0	0.3	0.0	0.0
7516	0.1	0.0	0.0	0.0	0.2	0.1	0.0	0.0
7522	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.0
7510	0.8	0.1	0.0	0.2	0.2	0.1	0.0	0.0
7576	0.0	0.0	0.0	0.3	0.1	0.0	--	--
7506	0.0	0.0	0.0	0.0	0.1	0.0	--	--
7502	0.1	0.0	0.0	0.0	0.1	0.1	--	--
7514	0.3	0.1	0.0	0.0	0.0	0.0	--	--
MEAN	0.2	0.0	0.1	0.1	0.1	0.1	0.0	0.0
SD	0.28	0.05	0.14	0.12	0.08	0.10	0.05	0.00
N	8	8	8	8	8	8	4	4

GROUP: 4M:6.0 mg base/kg/day								
7535	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0
7511	0.0	0.0	0.0	0.3	0.0	0.2	0.0	0.0
7530	0.0	0.1	0.0	0.0	0.0	0.1	0.0	0.0
7507	0.0	0.0	0.1	0.0	0.1	0.0	0.0	0.0
7508	0.1	0.1	0.0	0.0	0.3	0.0	--	--
7509	0.0	0.1	0.0	0.0	0.0	0.5	--	--
7518	0.2	0.0	0.0	0.0	0.2	0.0	--	--
7524	0.0	0.0	0.1	0.0	0.2	0.0	--	--
MEAN	0.0	0.0	0.0	0.0	0.1	0.1	0.0	0.0
SD	0.07	0.05	0.05	0.11	0.11	0.18	0.00	0.00
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: % Methemoglobin

STUDY ID: 097  
STUDY NO: 097  
ABBR: %METHGB

SEX: MALE  
UNITS: %

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1M:0 mg base/kg/day								
7531	1.3	0.9	0.6	0.7	1.0	0.7	0.8	0.5
7532	1.2	0.9	0.8	0.7	0.8	0.9	0.6	0.5
7512	3.9	2.2	1.0	0.9	1.3	1.1	0.6	0.8
7515	1.2	1.3	0.8	0.6	0.7	0.7	0.8	0.8
7521	1.5	1.0	1.1	0.7	1.5	0.6	--	--
7533	2.4	1.5	1.2	1.2	0.9	1.2	--	--
7520	1.6	1.0	0.7	1.1	0.7	0.6	--	--
7505	2.0	1.3	0.9	0.9	0.7	0.6	--	--
MEAN	1.9	1.3	0.9	0.9	1.0	0.8	0.7	0.7
SD	0.91	0.44	0.20	0.21	0.30	0.24	0.12	0.17
N	8	8	8	8	8	8	4	4

GROUP: 2M:0.1 mg base/kg/day								
7527	2.2	1.3	1.2	1.1	1.1	1.1	0.8	0.8
7519	4.4	2.8	2.2	1.7	0.7	2.7	0.8	0.9
7529	2.5	1.9	1.2	1.4	1.0	1.1	0.7	0.9
7536	1.4	1.0	0.9	1.2	0.9	1.0	0.5	0.8
7503	1.2	1.1	1.0	1.0	1.1	1.0	--	--
7523	1.5	1.0	0.9	0.8	0.9	0.7	--	--
7517	1.6	1.0	0.9	0.9	0.7	1.0	--	--
7528	2.2	1.3	1.0	1.0	0.8	0.8	--	--
MEAN	2.1	1.4	1.2	1.1	0.9	1.2	0.7	0.9
SD	1.03	0.63	0.44	0.29	0.16	0.63	0.14	0.06
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: % Methemoglobin

STUDY ID: 097  
STUDY NO: 097  
ABBR: %METHGB

SEX: MALE

UNITS: %

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3M:2.0 mg base/kg/day								
7538	2.3	2.1	16.1	21.0	21.6	19.2	1.4	1.0
7516	1.3	0.7	10.1	10.9	9.9	9.2	0.6	0.8
7522	3.3	2.8	19.8	18.8	17.8	17.4	0.8	0.7
7510	1.9	1.3	9.4	11.2	9.5	8.3	0.5	0.7
7576	0.9	0.9	10.7	12.0	10.9	10.9	--	--
7506	2.2	1.7	11.0	14.8	11.5	10.8	--	--
7502	1.4	1.1	12.3	13.4	12.8	11.8	--	--
7514	2.3	1.9	14.6	16.2	15.0	15.2	--	--
MEAN	2.0	1.6	13.0	14.8	13.6	12.9	0.8	0.8
SD	0.75	0.70	3.58	3.67	4.25	3.96	0.40	0.14
N	8	8	8	8	8	8	4	4

GROUP: 4M:6.0 mg base/kg/day								
7535	1.9	1.0	14.3	14.9	16.3	14.4	3.8	0.7
7511	1.4	0.9	10.1	13.1	14.4	11.0	1.9	1.0
7530	1.9	1.6	23.1	21.7	22.8	19.2	5.3	0.9
7507	2.3	2.8	22.2	22.3	23.1	25.5	4.0	0.8
7508	1.6	1.0	9.2	10.0	11.5	11.5	--	--
7509	1.3	0.8	16.8	17.0	17.0	11.4	--	--
7518	1.6	1.8	13.0	16.6	20.0	22.4	--	--
7524	2.7	1.8	25.7	24.4	25.1	27.3	--	--
MEAN	1.8	1.5	16.8	17.5	18.8	17.8	3.8	0.9
SD	0.47	0.68	6.23	4.95	4.75	6.67	1.40	0.13
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Platelets

STUDY ID: 097  
STUDY NO: 097  
ABBR: PLT

SEX: MALE

UNITS: 10<sup>3</sup>/ccm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1M:0 mg base/kg/day								
7531	347	290	248	308	284	255	284	259
7532	242	206	179	197	143	183	214	199
7512	421	322	295	274	275	259	295	294
7515	310	244	226	218	246	221	248	251
7521	363	309	184	228	235	262	--	--
7533	481	437	352	369	291	330	--	--
7520	380	302	256	244	244	230	--	--
7505	303	271	231	212	204	185	--	--
MEAN	356	298	246	256	240	241	260	251
SD	74.1	67.8	56.9	58.0	48.6	47.7	36.8	39.2
N	8	8	8	8	8	8	4	4

GROUP: 2M:0.1 mg base/kg/day								
7527	381	365	216	285	276	267	334	281
7519	447	363	306	296	286	278	297	345
7529	350	324	231	263	243	257	310	317
7536	381	323	340	336	285	304	319	305
7503	352	337	321	274	284	272	--	--
7523	302	256	202	194	175	231	--	--
7517	392	340	290	267	263	296	--	--
7528	493	379	318	377	319	340	--	--
MEAN	387	336	278	287	266	281	315	312
SD	59.5	38.1	53.5	54.0	42.8	32.9	15.6	26.6
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Platelets

STUDY ID: 097  
STUDY NO: 097  
ABBR: PLT

SEX: MALE

UNITS: 10<sup>3</sup>/ccm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3M:2.0 mg base/kg/day								
7538	373	340	245	111	177	223	342	302
7516	401	361	223	124	154	186	416	394
7522	406	346	124	115	175	187	346	258
7510	485	447	133	82	61	61	266	199
7576	369	317	108	39	63	82	--	--
7506	402	379	115	185	299	355	--	--
7502	280	247	159	104	150	156	--	--
7514	608	439	67	142	192	229	--	--
MEAN	416	360	147	113	159	185	343	288
SD	96.1	64.8	60.0	42.5	75.8	91.9	61.3	82.2
N	8	8	8	8	8	8	4	4

GROUP: 4M:6.0 mg base/kg/day								
7535	246	297	91	95	177	166	299	306
7511	391	376	121	132	403	569	518	310
7530	334	234	92	144	215	270	217	264
7507	438	344	97	62	86	110	221	264
7508	389	234	97	52	291	100	--	--
7509	449	401	93	72	291	195	--	--
7518	449	361	120	54	115	202	--	--
7524	271	279	75	126	155	166	--	--
MEAN	371	316	98	92	217	222	314	286
SD	79.6	64.2	15.4	37.4	105.9	150.0	141.3	25.5
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Prothrombin Time

STUDY ID: 097  
STUDY NO: 097  
ABBR: PT

SEX: MALE

UNITS: sec

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1M:0 mg base/kg/day								
7531	6.9	7.2	6.9	7.2	7.2	7.0	7.1	7.5
7532	7.0	7.2	7.3	7.0	7.0	7.2	6.9	7.1
7512	7.3	7.0	7.2	7.0	7.5	7.2	7.1	7.3
7515	8.2	8.0	8.3	7.9	7.1	8.0	7.8	8.3
7521	7.2	7.0	7.3	6.9	7.1	7.2	--	--
7533	7.1	7.2	7.4	7.0	7.1	7.3	--	--
7520	7.0	7.0	7.2	7.0	7.1	7.1	--	--
7505	7.2	7.7	7.5	7.4	7.4	7.3	--	--
MEAN	7.2	7.3	7.4	7.2	7.2	7.3	7.2	7.6
SD	0.41	0.37	0.41	0.33	0.17	0.30	0.39	0.53
N	8	8	8	8	8	8	4	4

GROUP: 2M:0.1 mg base/kg/day								
7527	6.9	7.0	7.1	7.1	7.5	7.1	7.1	7.3
7519	7.1	7.0	7.3	7.1	7.0	7.0	7.0	7.3
7529	7.8	8.0	8.0	7.6	7.7	7.8	7.9	7.9
7536	7.5	7.4	7.4	7.3	7.3	7.3	7.5	7.8
7503	7.3	7.4	7.6	7.4	7.5	7.6	--	--
7523	7.2	7.1	7.5	7.1	7.3	7.3	--	--
7517	7.4	7.2	7.4	7.1	7.5	7.1	--	--
7528	7.3	7.3	7.3	7.1	8.0	7.2	--	--
MEAN	7.3	7.3	7.5	7.2	7.5	7.3	7.4	7.6
SD	0.27	0.33	0.27	0.19	0.30	0.27	0.41	0.32
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Prothrombin Time

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
STUDY ID: 097 <span style="float: right;">SEX: MALE</span>								
STUDY NO: 097								
ABBR: PT <span style="float: right;">UNITS: sec</span>								
GROUP: 3M:2.0 mg base/kg/day								
7538	7.3	7.2	7.3	6.9	7.1	7.2	7.3	7.4
7516	7.6	7.3	7.4	7.1	7.3	7.2	7.5	7.6
7522	7.3	7.3	7.1	6.8	7.2	7.1	7.3	7.4
7510	7.6	7.2	7.4	6.8	7.1	6.9	7.4	7.4
7576	7.1	7.2	7.0	6.9	7.0	7.0	--	--
7506	7.1	7.0	7.1	6.8	7.0	6.9	--	--
7502	7.3	7.2	7.1	6.8	7.2	7.2	--	--
7514	7.3	7.0	7.0	6.9	6.9	6.9	--	--
MEAN	7.3	7.2	7.2	6.9	7.1	7.1	7.4	7.5
SD	0.19	0.12	0.17	0.10	0.13	0.14	0.10	0.10
N	8	8	8	8	8	8	4	4

GROUP: 4M:6.0 mg base/kg/day								
7535	7.2	7.0	7.0	6.7	8.0	7.0	7.2	7.5
7511	7.4	7.3	7.1	6.8	6.9	6.9	7.0	7.4
7530	7.2	7.1	7.1	6.9	6.9	7.0	7.1	7.3
7507	7.4	7.0	7.1	6.9	7.3	7.0	7.2	7.4
7508	7.3	7.2	7.1	6.9	7.1	7.1	--	--
7509	7.3	7.2	7.2	6.9	7.2	7.2	--	--
7518	7.3	7.2	7.1	6.8	7.0	6.9	--	--
7524	7.0	7.3	7.1	7.0	7.1	7.1	--	--
MEAN	7.3	7.2	7.1	6.9	7.2	7.0	7.1	7.4
SD	0.13	0.12	0.05	0.09	0.36	0.10	0.10	0.08
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

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

STUDY ID: 097  
STUDY NO: 097  
ABBR: APTT

SEX: MALE

UNITS: sec

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1M:0 mg base/kg/day								
7531	11.2	11.1	10.5	10.0	9.8	10.5	10.3	10.4
7532	12.4	11.6	10.9	10.8	9.2	10.9	11.1	11.1
7512	12.7	11.9	11.1	10.8	11.2	10.9	10.7	10.7
7515	12.6	12.3	11.5	10.9	11.9	10.8	10.9	11.1
7521	12.0	11.4	9.8	9.9	10.3	10.0	--	--
7533	12.3	11.6	10.6	11.1	10.7	10.0	--	--
7520	11.9	11.0	10.7	10.6	9.8	10.7	--	--
7505	11.8	11.1	11.2	10.6	10.8	11.0	--	--
MEAN	12.1	11.5	10.8	10.6	10.5	10.6	10.8	10.8
SD	0.49	0.45	0.52	0.43	0.87	0.40	0.34	0.34
N	8	8	8	8	8	8	4	4

GROUP: 2M:0.1 mg base/kg/day								
7527	11.9	11.7	11.5	10.7	11.2	10.3	10.8	11.3
7519	11.7	11.4	11.1	11.2	10.5	11.1	10.3	10.4
7529	11.0	10.8	10.5	9.9	10.1	10.1	10.2	12.3
7536	11.4	11.3	10.8	11.0	11.0	10.7	10.5	10.5
7503	13.4	11.8	11.2	10.3	10.4	10.0	--	--
7523	10.9	10.9	10.0	9.8	9.7	9.3	--	--
7517	13.7	13.0	12.9	13.0	12.3	12.4	--	--
7528	11.7	10.9	10.3	10.3	10.1	10.7	--	--
MEAN	12.0	11.5	11.0	10.8	10.7	10.6	10.5	11.1
SD	1.04	0.72	0.90	1.03	0.82	0.92	0.26	0.88
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

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

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
STUDY ID: 097								
STUDY NO: 097								
ABBR: APTT								
								SEX: MALE
								UNITS: sec
GROUP: 3M:2.0 mg base/kg/day								
7538	11.8	12.3	11.0	10.7	10.7	11.2	10.2	10.5
7516	11.9	12.4	10.9	10.9	10.4	10.5	10.3	10.3
7522	11.2	10.2	10.3	10.9	9.8	9.9	9.8	10.3
7510	11.3	11.6	10.5	10.4	10.5	10.5	10.4	10.4
7576	11.5	11.1	10.5	10.7	9.9	10.1	--	--
7506	10.9	10.8	10.1	10.3	10.0	10.2	--	--
7502	11.8	10.9	10.3	9.8	10.0	10.2	--	--
7514	11.6	10.9	10.6	10.4	10.5	10.2	--	--
MEAN	11.5	11.3	10.5	10.5	10.2	10.4	10.2	10.4
SD	0.35	0.77	0.31	0.37	0.34	0.40	0.26	0.10
N	8	8	8	8	8	8	4	4

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 4M:6.0 mg base/kg/day								
7535	12.3	12.0	11.2	11.4	10.6	10.8	10.6	10.7
7511	12.5	11.2	9.9	11.1	10.6	10.1	10.4	10.6
7530	11.8	12.0	10.8	11.0	10.2	11.0	10.8	10.5
7507	11.6	10.9	10.2	11.3	9.8	10.4	10.4	10.5
7508	11.9	12.3	11.2	11.2	10.7	10.8	--	--
7509	11.9	11.5	10.6	11.1	10.7	10.9	--	--
7518	10.9	10.9	10.5	11.0	10.3	11.9	--	--
7524	11.7	11.5	10.6	11.2	10.6	11.0	--	--
MEAN	11.8	11.5	10.6	11.2	10.4	10.9	10.6	10.6
SD	0.48	0.53	0.45	0.14	0.32	0.52	0.19	0.10
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Leukocytes

STUDY ID: 097  
STUDY NO: 097  
ABBR: WBC

SEX: MALE

UNITS: 10<sup>3</sup>/cmm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1M:0 mg base/kg/day								
7531	11.0	12.0	16.4	11.8	10.6	12.1	10.9	9.5
7532	8.5	7.6	7.9	7.7	8.9	6.9	8.6	10.7
7512	9.2	10.4	9.0	8.7	10.3	9.1	11.4	11.2
7515	6.9	6.9	6.5	6.7	6.4	7.0	6.9	7.7
7521	6.7	6.3	5.2	7.7	6.6	6.6	--	--
7533	10.1	8.9	10.3	12.9	8.8	9.5	--	--
7520	7.6	7.0	9.4	8.6	7.3	8.5	--	--
7505	8.5	6.8	7.4	8.8	7.8	7.6	--	--
MEAN	8.6	8.2	9.0	9.1	8.3	8.4	9.5	9.8
SD	1.51	2.03	3.40	2.14	1.59	1.83	2.09	1.56
N	8	8	8	8	8	8	4	4

GROUP: 2M:0.1 mg base/kg/day								
7527	8.6	8.1	11.9	10.3	11.3	9.3	10.4	10.6
7519	9.2	7.4	7.1	7.7	7.8	8.6	7.8	9.2
7529	7.3	12.6	6.9	6.5	7.6	6.6	9.2	11.0
7536	10.1	10.1	9.4	9.0	10.4	8.3	8.4	9.9
7503	8.2	8.6	8.3	6.9	8.4	9.4	--	--
7523	6.9	9.5	8.4	7.8	5.5	6.3	--	--
7517	14.9	12.4	13.1	11.7	10.8	11.0	--	--
7528	11.1	13.2	15.1	10.0	10.4	9.9	--	--
MEAN	9.5	10.2	10.0	8.7	9.0	8.7	9.0	10.2
SD	2.57	2.23	3.00	1.82	2.02	1.60	1.12	0.79
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Leukocytes

STUDY ID: 097  
STUDY NO: 097  
ABBR: WBC

SEX: MALE  
UNITS: 10<sup>3</sup>/cmm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3M:2.0 mg base/kg/day								
7538	7.6	8.6	10.0	9.0	10.6	9.9	7.9	8.9
7516	9.8	10.4	11.7	10.4	8.7	11.1	8.8	7.7
7522	7.3	7.3	9.8	9.4	8.7	9.2	5.4	7.6
7510	9.1	7.9	8.7	10.3	8.6	12.2	7.4	10.0
7576	9.9	6.0	8.6	11.0	10.3	11.6	--	--
7506	11.6	12.5	10.2	11.6	9.0	12.7	--	--
7502	7.9	8.2	8.5	9.4	11.3	12.2	--	--
7514	10.1	9.6	17.1	13.4	12.5	12.3	--	--
MEAN	9.2	8.8	10.6	10.6	10.0	11.4	7.4	8.6
SD	1.48	2.01	2.84	1.44	1.45	1.25	1.44	1.13
N	8	8	8	8	8	8	4	4

GROUP: 4M:6.0 mg base/kg/day								
7535	6.5	9.1	10.3	11.3	12.7	13.1	9.4	7.9
7511	8.1	8.5	7.2	7.6	11.7	10.5	8.5	8.2
7530	9.9	10.1	9.4	11.1	10.7	14.5	10.2	7.7
7507	7.8	10.7	8.3	8.2	9.6	10.0	10.0	8.9
7508	8.9	9.2	8.6	8.4	10.1	9.3	--	--
7509	10.0	10.1	9.4	11.2	13.6	15.3	--	--
7518	5.9	7.9	8.1	7.0	8.2	12.6	--	--
7524	11.2	11.2	10.0	12.5	14.1	18.3	--	--
MEAN	8.5	9.6	8.9	9.7	11.3	13.0	9.5	8.2
SD	1.81	1.12	1.05	2.08	2.05	3.04	0.76	0.53
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: M. Neutrophils

STUDY ID: 097  
STUDY NO: 097  
ABBR: M. Neutrop

SEX: MALE

UNITS:  $10^3/\text{cmm}$ 

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1M:0 mg base/kg/day								
7531	5.9	7.9	12.3	7.2	6.0	7.5	7.2	5.8
7532	4.8	4.7	5.5	4.5	6.2	4.4	5.8	7.3
7512	4.9	7.7	5.7	5.2	5.7	5.7	6.4	7.2
7515	3.4	4.3	4.0	4.2	4.4	5.0	4.6	5.2
7521	4.1	4.2	3.1	5.7	4.0	3.7	--	--
7533	5.5	5.2	6.3	9.0	5.4	5.2	--	--
7520	4.3	4.3	5.5	6.2	4.0	5.1	--	--
7505	5.7	3.5	4.2	6.6	4.7	4.5	--	--
MEAN	4.8	5.2	5.8	6.1	5.1	5.1	6.0	6.4
SD	0.86	1.66	2.82	1.56	0.89	1.13	1.10	1.04
N	8	8	8	8	8	8	4	4

GROUP: 2M:0.1 mg base/kg/day								
7527	5.9	5.0	7.0	6.0	7.6	5.4	6.7	8.0
7519	4.0	3.6	3.6	3.3	3.8	4.7	3.5	5.4
7529	4.5	10.6	4.0	3.1	3.7	3.4	5.7	8.4
7536	7.1	6.9	5.6	6.1	7.0	6.1	5.5	6.1
7503	5.2	4.8	4.6	3.4	5.1	5.3	--	--
7523	3.6	6.4	5.5	4.8	3.1	3.8	--	--
7517	8.8	7.4	8.4	6.4	5.8	6.3	--	--
7528	4.4	7.7	10.7	4.7	5.7	6.0	--	--
MEAN	5.4	6.6	6.2	4.7	5.2	5.1	5.4	7.0
SD	1.76	2.16	2.41	1.35	1.61	1.08	1.34	1.45
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or &gt; 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: M. Neutrophils

STUDY ID: 097 SEX: MALE  
 STUDY NO: 097  
 ABBR: M. Neutrop UNITS: 10<sup>3</sup>/cmm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3M:2.0 mg base/kg/day								
7538	4.3	5.1	5.7	4.8	7.0	6.9	5.0	6.0
7516	6.9	7.0	7.5	6.8	5.0	8.4	5.5	4.5
7522	4.6	4.3	7.4	5.9	5.6	6.0	2.8	4.8
7510	6.2	4.4	5.6	6.1	4.0	8.3	3.5	6.7
7576	5.7	3.8	5.8	8.1	7.1	8.1	--	--
7506	6.8	8.3	6.7	8.2	4.7	8.1	--	--
7502	3.6	4.4	5.3	5.9	7.0	7.7	--	--
7514	5.9	5.5	12.0	8.3	7.4	8.4	--	--
MEAN	5.5	5.4	7.0	6.8	6.0	7.7	4.2	5.5
SD	1.21	1.55	2.19	1.31	1.31	0.86	1.26	1.03
N	8	8	8	8	8	8	4	4

GROUP: 4M:6.0 mg base/kg/day								
7535	4.4	6.7	7.5	8.5	10.0	10.0	7.2	5.0
7511	3.9	4.9	2.7	4.0	6.2	7.5	5.7	4.1
7530	5.0	6.6	5.8	7.0	7.2	10.3	6.3	4.8
7507	4.4	6.3	5.2	4.4	5.9	5.7	5.2	6.0
7508	5.1	6.3	5.8	5.4	6.8	6.5	--	--
7509	6.1	4.9	6.3	7.2	9.8	11.2	--	--
7518	3.8	5.8	5.1	4.5	4.8	9.7	--	--
7524	6.4	5.7	5.2	8.8	10.2	12.4	--	--
MEAN	4.9	5.9	5.5	6.2	7.6	9.2	6.1	5.0
SD	0.96	0.71	1.36	1.90	2.10	2.35	0.86	0.78
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: I. Neutrophils

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
STUDY ID: 097								
STUDY NO: 097								
ABBR: I. Neutrop								
SEX: MALE								
UNITS: 10 <sup>3</sup> /cmm								
GROUP: 1M:0 mg base/kg/day								
7531	0.2	0.1	0.2	0.8	0.1	0.8	0.3	0.1
7532	0.0	0.2	0.1	0.2	0.3	0.3	0.0	0.1
7512	0.2	0.2	0.1	0.3	0.3	0.3	0.3	0.2
7515	0.0	0.1	0.4	0.3	0.2	0.4	0.2	0.3
7521	0.0	0.1	0.1	0.2	0.3	0.2	--	--
7533	0.0	0.2	0.6	0.8	0.5	0.5	--	--
7520	0.1	0.2	0.6	0.5	0.4	0.0	--	--
7505	0.0	0.1	0.3	0.3	0.2	0.2	--	--
MEAN	0.1	0.2	0.3	0.4	0.3	0.3	0.2	0.2
SD	0.09	0.05	0.21	0.25	0.12	0.24	0.14	0.10
N	8	8	8	8	8	8	4	4

GROUP: 2M:0.1 mg base/kg/day								
7527	0.0	0.2	0.4	0.8	0.2	0.3	0.3	0.1
7519	0.1	0.0	0.3	0.3	0.2	0.1	0.1	0.4
7529	0.1	0.1	0.4	0.3	0.2	0.2	0.1	0.1
7536	0.0	0.2	0.4	0.4	0.2	0.2	0.4	0.3
7503	0.1	0.3	0.2	0.5	0.3	0.2	--	--
7523	0.0	0.1	0.3	0.2	0.1	0.2	--	--
7517	0.1	0.4	0.5	0.4	0.4	0.6	--	--
7528	0.1	0.4	0.5	0.5	0.4	0.1	--	--
MEAN	0.1	0.2	0.4	0.4	0.3	0.2	0.2	0.2
SD	0.05	0.15	0.10	0.18	0.11	0.16	0.15	0.15
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: I. Neutrophils

STUDY ID: 097  
STUDY NO: 097  
ABBR: I. Neutrop

SEX: MALE

UNITS: 10<sup>3</sup>/cmm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3M:2.0 mg base/kg/day								
7538	0.0	0.3	0.2	0.7	0.3	0.3	0.5	0.0
7516	0.1	0.2	0.1	0.9	0.4	0.1	0.4	0.4
7522	0.1	0.2	0.5	0.4	0.0	0.1	0.1	0.2
7510	0.0	0.5	0.5	0.9	0.9	0.1	0.7	0.0
7576	0.3	0.0	0.4	0.7	0.2	0.5	--	--
7506	0.2	0.1	0.2	1.2	0.5	0.9	--	--
7502	0.2	0.1	0.0	0.2	0.0	0.6	--	--
7514	0.0	0.1	0.9	0.7	0.5	0.0	--	--
MEAN	0.1	0.2	0.4	0.7	0.4	0.3	0.4	0.2
SD	0.11	0.16	0.29	0.31	0.30	0.32	0.25	0.19
N	8	8	8	8	8	8	4	4

GROUP: 4M:6.0 mg base/kg/day								
7535	0.1	0.2	0.3	0.6	0.3	0.3	0.1	0.3
7511	0.1	0.2	0.0	0.3	0.2	0.3	0.2	0.3
7530	0.2	0.0	0.4	0.7	0.5	0.7	0.1	0.2
7507	0.0	0.0	0.3	0.7	0.5	0.3	0.2	0.1
7508	0.1	0.1	0.2	0.3	0.5	0.2	--	--
7509	0.1	0.2	0.3	0.7	0.8	0.5	--	--
7518	0.0	0.1	0.2	0.4	0.8	0.1	--	--
7524	0.0	0.1	0.3	0.4	0.6	0.9	--	--
MEAN	0.1	0.1	0.3	0.5	0.5	0.4	0.2	0.2
SD	0.07	0.08	0.12	0.18	0.21	0.27	0.06	0.10
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Lymphocytes

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
STUDY ID: 097 <span style="float: right;">SEX: MALE</span>								
STUDY NO: 097								
ABBR: Lymphocyte <span style="float: right;">UNITS: 10<sup>3</sup>/cmm</span>								
GROUP: 1M:0 mg base/kg/day								
7531	4.1	3.1	2.8	3.1	3.7	3.1	2.8	2.8
7532	3.1	1.9	1.7	2.4	1.8	1.6	2.1	2.9
7512	3.3	1.9	2.8	2.9	3.7	2.5	3.3	2.6
7515	2.5	1.9	1.8	1.7	1.5	1.1	1.7	2.0
7521	2.4	1.7	1.5	1.2	1.7	2.0	--	--
7533	3.5	2.6	2.7	2.3	2.0	2.3	--	--
7520	2.8	2.0	2.4	1.4	2.3	2.3	--	--
7505	2.3	2.9	2.5	1.2	2.4	1.8	--	--
MEAN	3.0	2.3	2.3	2.0	2.4	2.1	2.5	2.6
SD	0.62	0.53	0.53	0.76	0.86	0.61	0.71	0.40
N	8	8	8	8	8	8	4	4

GROUP: 2M:0.1 mg base/kg/day								
7527	1.7	2.4	3.2	2.9	2.4	2.1	2.7	1.4
7519	4.3	3.6	2.4	3.2	3.1	2.7	3.4	2.7
7529	2.2	1.1	1.8	2.3	2.4	2.5	2.2	2.0
7536	2.4	2.3	2.7	1.5	2.5	1.6	2.1	2.4
7503	2.5	2.7	3.2	2.4	1.8	3.7	--	--
7523	2.6	2.6	2.0	2.2	1.4	1.7	--	--
7517	4.2	2.9	2.2	3.4	3.1	2.5	--	--
7528	4.4	2.9	2.6	3.5	3.5	2.5	--	--
MEAN	3.0	2.6	2.5	2.7	2.5	2.4	2.6	2.1
SD	1.08	0.71	0.52	0.69	0.70	0.66	0.59	0.56
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Lymphocytes

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
STUDY ID: 097								
STUDY NO: 097								
ABBR: Lymphocyte								
SEX: MALE								
UNITS: 10 <sup>3</sup> /cmm								
GROUP: 3M:2.0 mg base/kg/day								
7538	2.6	2.5	2.9	2.5	1.9	1.4	1.8	2.0
7516	2.5	2.8	2.8	2.0	2.4	1.9	2.2	2.5
7522	2.1	2.3	1.2	1.5	1.7	1.7	1.7	1.2
7510	1.9	1.9	1.7	2.2	2.3	2.6	2.4	2.5
7576	2.8	1.6	1.9	1.0	1.8	1.4	--	--
7506	3.8	3.5	2.2	1.3	3.1	2.9	--	--
7502	3.2	3.0	2.8	2.8	2.9	3.2	--	--
7514	3.1	2.9	3.1	3.4	3.6	2.3	--	--
MEAN	2.8	2.6	2.3	2.1	2.5	2.2	2.0	2.1
SD	0.62	0.62	0.68	0.81	0.68	0.68	0.33	0.61
N	8	8	8	8	8	8	4	4

GROUP: 4M:6.0 mg base/kg/day								
7535	1.6	1.7	1.9	1.1	1.5	1.8	1.0	1.9
7511	3.3	2.8	3.9	2.8	3.6	2.2	2.0	3.3
7530	3.7	2.3	1.8	1.3	1.7	1.9	1.9	1.8
7507	2.7	3.2	2.1	2.2	2.4	2.5	2.9	2.3
7508	3.4	2.1	2.0	1.9	1.2	1.6	--	--
7509	2.8	4.2	1.8	2.1	1.8	2.0	--	--
7518	1.7	1.7	2.1	1.5	1.8	1.3	--	--
7524	2.8	3.8	2.5	1.9	1.1	1.6	--	--
MEAN	2.8	2.7	2.3	1.9	1.9	1.9	2.0	2.3
SD	0.76	0.94	0.70	0.55	0.80	0.38	0.78	0.68
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Monocytes

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
STUDY ID: 097								
STUDY NO: 097								
ABBR: Monocytes								
SEX: MALE								
UNITS: 10 <sup>3</sup> /cmm								
GROUP: 1M:0 mg base/kg/day								
7531	0.6	0.5	0.7	0.2	0.3	0.4	0.2	0.6
7532	0.3	0.6	0.3	0.5	0.4	0.3	0.3	0.2
7512	0.6	0.6	0.5	0.3	0.4	0.4	1.1	0.8
7515	0.8	0.4	0.1	0.3	0.1	0.2	0.1	0.1
7521	0.1	0.2	0.2	0.3	0.2	0.4	--	--
7533	0.9	0.6	0.6	0.5	0.7	0.8	--	--
7520	0.3	0.3	0.7	0.5	0.3	0.9	--	--
7505	0.3	0.2	0.4	0.6	0.4	0.5	--	--
MEAN	0.5	0.4	0.4	0.4	0.4	0.5	0.4	0.4
SD	0.28	0.18	0.23	0.14	0.18	0.24	0.46	0.33
N	8	8	8	8	8	8	4	4

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 2M:0.1 mg base/kg/day								
7527	0.7	0.3	1.0	0.5	1.0	1.2	0.5	0.5
7519	0.4	0.2	0.6	0.7	0.3	0.4	0.5	0.3
7529	0.4	0.8	0.5	0.5	0.7	0.5	1.1	0.4
7536	0.6	0.7	0.2	0.7	0.3	0.2	0.2	0.6
7503	0.2	0.8	0.2	0.5	0.8	0.2	--	--
7523	0.5	0.4	0.5	0.6	0.5	0.4	--	--
7517	1.0	0.7	1.0	0.6	1.0	0.7	--	--
7528	2.0	2.2	1.4	1.0	0.2	0.9	--	--
MEAN	0.7	0.8	0.7	0.6	0.6	0.6	0.6	0.5
SD	0.57	0.63	0.42	0.17	0.32	0.35	0.38	0.13
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Monocytes

STUDY ID: 097  
STUDY NO: 097  
ABBR: Monocytes

SEX: MALE

UNITS: 10<sup>3</sup>/cmm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3M:2.0 mg base/kg/day								
7538	0.6	0.5	1.2	0.9	1.0	0.9	0.3	0.4
7516	0.3	0.3	1.2	0.5	0.7	0.6	0.5	0.3
7522	0.2	0.4	0.6	1.2	1.0	1.0	0.3	0.1
7510	0.5	0.7	0.4	0.8	0.7	0.7	0.3	0.4
7576	0.9	0.2	0.4	1.1	0.8	0.8	--	--
7506	0.5	0.3	0.7	0.2	0.4	0.8	--	--
7502	0.2	0.2	0.3	0.4	1.0	0.7	--	--
7514	0.8	1.0	1.2	0.9	0.8	1.4	--	--
MEAN	0.5	0.5	0.8	0.8	0.8	0.9	0.4	0.3
SD	0.26	0.28	0.39	0.35	0.21	0.25	0.10	0.14
N	8	8	8	8	8	8	4	4

GROUP: 4M:6.0 mg base/kg/day								
7535	0.4	0.5	0.5	1.0	0.6	0.9	0.6	0.2
7511	0.6	0.4	0.5	0.5	1.2	0.5	0.3	0.3
7530	0.6	0.9	1.4	1.9	1.0	1.3	1.0	0.5
7507	0.3	0.6	0.6	0.8	0.6	0.8	0.9	0.2
7508	0.2	0.5	0.5	0.5	0.9	0.6	--	--
7509	0.4	0.4	0.4	0.9	0.7	0.9	--	--
7518	0.4	0.2	0.7	0.4	0.6	1.3	--	--
7524	1.1	0.6	0.8	1.4	1.4	2.0	--	--
MEAN	0.5	0.5	0.7	0.9	0.9	1.0	0.7	0.3
SD	0.28	0.20	0.32	0.51	0.31	0.48	0.32	0.14
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or &gt; 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Eosinophils

STUDY ID: 097 SEX: MALE  
STUDY NO: 097  
ABBR: Eosinophil UNITS: 10<sup>3</sup>/cmm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1M:0 mg base/kg/day								
7531	0.2	0.4	0.5	0.5	0.4	0.2	0.3	0.3
7532	0.3	0.2	0.4	0.1	0.2	0.2	0.4	0.2
7512	0.3	0.0	0.0	0.0	0.2	0.2	0.2	0.4
7515	0.3	0.1	0.3	0.1	0.2	0.3	0.3	0.2
7521	0.1	0.1	0.4	0.4	0.4	0.3	--	--
7533	0.2	0.4	0.1	0.3	0.2	0.8	--	--
7520	0.2	0.2	0.2	0.0	0.2	0.3	--	--
7505	0.3	0.1	0.0	0.1	0.2	0.5	--	--
MEAN	0.2	0.2	0.2	0.2	0.3	0.4	0.3	0.3
SD	0.07	0.15	0.19	0.19	0.09	0.21	0.08	0.10
N	8	8	8	8	8	8	4	4

GROUP: 2M:0.1 mg base/kg/day								
7527	0.3	0.2	0.4	0.1	0.1	0.3	0.2	0.6
7519	0.4	0.1	0.2	0.2	0.3	0.7	0.3	0.5
7529	0.1	0.0	0.2	0.3	0.6	0.1	0.1	0.1
7536	0.0	0.0	0.5	0.3	0.4	0.3	0.2	0.5
7503	0.2	0.1	0.2	0.1	0.4	0.1	--	--
7523	0.2	0.1	0.2	0.1	0.4	0.3	--	--
7517	0.7	1.0	0.9	0.9	0.4	1.0	--	--
7528	0.1	0.0	0.0	0.3	0.5	0.4	--	--
MEAN	0.3	0.2	0.3	0.3	0.4	0.4	0.2	0.4
SD	0.22	0.34	0.28	0.26	0.15	0.31	0.08	0.22
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Eosinophils

STUDY ID: 097  
STUDY NO: 097  
ABBR: Eosinophil

SEX: MALE

UNITS: 10<sup>3</sup>/cmm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3M:2.0 mg base/kg/day								
7538	0.2	0.3	0.0	0.1	0.4	0.4	0.3	0.6
7516	0.1	0.1	0.1	0.2	0.1	0.1	0.2	0.0
7522	0.2	0.1	0.1	0.4	0.4	0.4	0.5	1.4
7510	0.5	0.4	0.5	0.3	0.7	0.5	0.6	0.4
7576	0.2	0.3	0.1	0.1	0.4	0.8	--	--
7506	0.2	0.4	0.3	0.7	0.4	0.0	--	--
7502	0.6	0.4	0.2	0.1	0.3	0.0	--	--
7514	0.3	0.2	0.0	0.1	0.3	0.2	--	--
MEAN	0.3	0.3	0.2	0.3	0.4	0.3	0.4	0.6
SD	0.17	0.13	0.17	0.21	0.17	0.28	0.18	0.59
N	8	8	8	8	8	8	4	4

GROUP: 4M:6.0 mg base/kg/day								
7535	0.0	0.0	0.1	0.1	0.3	0.1	0.5	0.5
7511	0.2	0.2	0.1	0.0	0.5	0.0	0.3	0.2
7530	0.5	0.3	0.0	0.2	0.3	0.3	0.8	0.3
7507	0.4	0.5	0.1	0.1	0.3	0.7	0.8	0.4
7508	0.2	0.2	0.2	0.3	0.7	0.5	--	--
7509	0.6	0.3	0.7	0.3	0.5	0.8	--	--
7518	0.1	0.2	0.0	0.3	0.2	0.3	--	--
7524	0.9	1.0	1.2	0.1	0.8	1.3	--	--
MEAN	0.4	0.3	0.3	0.2	0.5	0.5	0.6	0.4
SD	0.30	0.30	0.43	0.12	0.21	0.42	0.24	0.13
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or &gt; 10



THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Basophils

STUDY ID: 097  
STUDY NO: 097  
ABBR: Basophils

SEX: MALE

UNITS: 10<sup>3</sup>/cmm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3M:2.0 mg base/kg/day								
7538	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7516	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7522	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7510	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7576	0.0	0.0	0.0	0.0	0.0	0.0	--	--
7506	0.0	0.0	0.0	0.0	0.0	0.0	--	--
7502	0.0	0.0	0.0	0.0	0.0	0.0	--	--
7514	0.0	0.0	0.0	0.0	0.0	0.0	--	--
MEAN	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
SD	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
N	8	8	8	8	8	8	4	4

GROUP: 4M:6.0 mg base/kg/day								
7535	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7511	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7530	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7507	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7508	0.0	0.0	0.0	0.0	0.0	0.0	--	--
7509	0.0	0.0	0.0	0.0	0.0	0.0	--	--
7518	0.0	0.0	0.0	0.0	0.0	0.0	--	--
7524	0.0	0.0	0.0	0.0	0.0	0.0	--	--
MEAN	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
SD	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

## RBC MORPHOLOGY OBSERVATIONS

STUDY ID: 097  
STUDY NO: 097

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

SEX: MALE

ANIMAL ID	Week -3	Week -1	Week 2	Week 4
7531	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight
7532	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight
7512	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight
7515	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight
7521	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Normal Red Blood Cells
7533	Normal Red Blood Cells	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight
7520	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight
7505	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Normal Red Blood Cells

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: 097  
STUDY NO: 097

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

SEX: MALE

ANIMAL ID	Week 8	Week 13	Week 18	Week 26
7531	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight
7532	Anisocytosis,Slight; Decreased Platelets, Slight	Anisocytosis,Slight	Anisocytosis,Slight; Macrocytes,Slight	Normal Red Blood Cells
7512	Normal Red Blood Cells	Anisocytosis,Slight	Anisocytosis,Slight	Poikilocytes,Slight; Anisocytosis, Moderate
7515	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Normal Red Blood Cells
7521	Anisocytosis,Slight	Anisocytosis,Slight	--	--
7533	Normal Red Blood Cells	Anisocytosis,Slight	--	--
7520	Anisocytosis,Slight	Anisocytosis,Slight	--	--
7505	Anisocytosis,Slight	Anisocytosis,Slight	--	--

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

## RBC MORPHOLOGY OBSERVATIONS

STUDY ID: 097  
STUDY NO: 097

GROUP: 2M : 0.1 mg base/kg/day

SEX: MALE

ANIMAL ID	Week -3	Week -1	Week 2	Week 4
7527	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Normal Red Blood Cells
7519	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight
7529	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight
7536	Normal Red Blood Cells	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight
7503	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight
7523	Anisocytosis,Slight	Normal Red Blood Cells	Anisocytosis,Slight	Anisocytosis,Slight
7517	Anisocytosis,Slight	Normal Red Blood Cells	Anisocytosis,Slight	Anisocytosis,Slight
7528	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: 097  
STUDY NO: 097

GROUP: 2M : 0.1 mg base/kg/day

SEX: MALE

ANIMAL ID	Week 8	Week 13	Week 18	Week 26
7527	Anisocytosis,Slight	Anisocytosis,Slight	Normal Red Blood Cells	Anisocytosis,Slight
7519	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight
7529	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight
7536	Anisocytosis,Slight	Normal Red Blood Cells	Anisocytosis,Slight	Anisocytosis,Slight; Clumped Platelets, Moderate
7503	Anisocytosis,Slight	Anisocytosis,Slight	--	--
7523	Anisocytosis,Slight	Anisocytosis,Slight	--	--
7517	Anisocytosis,Slight	Anisocytosis,Slight	--	--
7528	Anisocytosis,Slight	Anisocytosis,Slight; Macrocytes,Slight	--	--

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: 097  
STUDY NO: 097

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

SEX: MALE

ANIMAL ID	Week -3	Week -1	Week 2	Week 4
7538	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight; Decreased Platelets, Slight
7516	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight
7522	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked
7510	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked	Anisocytosis,Slight; Microcytes,Slight; Decreased Platelets, Mod. to Marked
7576	Anisocytosis,Slight	Normal Red Blood Cells	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked
7506	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight; Decreased Platelets, Slight	Anisocytosis, Moderate
7502	Hypossegmented Neutrophils,Moderate Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked;Large Platelets,Slight
7514	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked	Anisocytosis,Slight; Decreased Platelets, Slight

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: 097  
STUDY NO: 097

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

SEX: MALE

ANIMAL ID	Week 8	Week 13	Week 18	Week 26
7538	Normal Red Blood Cells	Anisocytosis,Slight	Anisocytosis,Slight	Normal Red Blood Cells
7516	Normal Red Blood Cells;Decreased Platelets,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight
7522	Anisocytosis,Slight; Decreased Platelets, Slight	Normal Red Blood Cells	Anisocytosis,Slight	Normal Red Blood Cells
7510	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked	Anisocytosis,Slight	Anisocytosis,Slight
7576	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked	Decreased Platelets, Moderate;Normal Red Blood Cells	--	--
7506	Anisocytosis,Slight	Anisocytosis,Slight	--	--
7502	Anisocytosis,Slight; Decreased Platelets, Slight	Anisocytosis,Slight	--	--
7514	Anisocytosis,Slight	Anisocytosis,Slight	--	--

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: 097  
STUDY NO: 097

GROUP: 4M : 6.0 mg base/kg/day

SEX: MALE

ANIMAL ID	Week -3	Week -1	Week 2	Week 4
7535	Normal Red Blood Cells	Normal Red Blood Cells	Anisocytosis,Slight; Large Platelets, Slight;Decreased Platelets,Mod. to Marked	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked
7511	Anisocytosis,Slight	Anisocytosis, Moderate	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked	Anisocytosis,Slight; Decreased Platelets, Slight
7530	Normal Red Blood Cells	Normal Red Blood Cells	Large Platelets, Slight;Decreased Platelets,Mod. to Marked;Anisocytosis, Moderate	Anisocytosis,Slight; Decreased Platelets, Slight
7507	Normal Red Blood Cells	Anisocytosis,Slight	Anisocytosis, Moderate;Decreased Platelets,Mod. to Marked	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked
7508	Normal Red Blood Cells	Anisocytosis,Slight	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked
7509	Normal Red Blood Cells	Anisocytosis,Slight	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked	Decreased Platelets, Mod. to Marked
7518	Anisocytosis,Slight	Normal Red Blood Cells	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked	Polychromasia,Slight Anisocytosis,Slight; Decreased Platelets, Mod. to Marked
7524	Anisocytosis,Slight	Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight; Large Platelets, Slight;Decreased Platelets,Mod. to Marked	Anisocytosis,Slight; Decreased Platelets, Slight

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: 097  
STUDY NO: 097

GROUP: 4M : 6.0 mg base/kg/day

SEX: MALE

ANIMAL ID	Week 8	Week 13	Week 18	Week 26
7535	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight; Macrocytes,Slight	Anisocytosis,Slight
7511	Anisocytosis,Slight	Anisocytosis,Slight; Increased Platelets, Slight	Anisocytosis,Slight; Increased Platelets, Slight	Anisocytosis,Slight; Clumped Platelets, Moderate
7530	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight; Macrocytes,Slight	Anisocytosis,Slight
7507	Anisocytosis,Slight; Decreased Platelets, Moderate	Anisocytosis,Slight; Decreased Platelets, Slight	Anisocytosis,Slight; Macrocytes,Slight	Normal Red Blood Cells
7508	Anisocytosis,Slight; Decreased Platelets, Moderate	Anisocytosis,Slight; Decreased Platelets, Slight	--	--
7509	Anisocytosis,Slight; Decreased Platelets, Moderate	Anisocytosis,Slight; Macrocytes,Slight	--	--
7518	Anisocytosis,Slight; Decreased Platelets, Moderate	Anisocytosis,Slight	--	--
7524	Anisocytosis,Slight	Anisocytosis,Slight	--	--

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Erythrocytes

STUDY ID: 097  
STUDY NO: 097  
ABBR: RBC

SEX: FEMALE

UNITS: 10<sup>6</sup>/cmm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1F:0 mg base/kg/day								
7557	6.97	7.11	6.29	6.40	6.16	6.25	7.35	6.70
7541	6.58	6.30	6.70	6.63	6.66	7.05	7.20	7.35
7566	6.37	6.26	6.63	6.61	6.26	6.59	6.75	7.26
7549	6.52	6.16	6.23	6.20	6.36	6.23	6.87	6.95
7555	6.07	5.93	6.38	6.15	6.75	6.88	--	--
7558	6.42	6.48	5.75	5.55	5.63	6.37	--	--
7573	5.90	5.99	6.65	6.26	6.84	6.91	--	--
7542	6.37	6.70	6.44	6.70	6.78	6.40	--	--
MEAN	6.40	6.37	6.38	6.31	6.43	6.59	7.04	7.07
SD	0.324	0.391	0.309	0.372	0.413	0.322	0.280	0.298
N	8	8	8	8	8	8	4	4

GROUP: 2F:0.1 mg base/kg/day								
7543	7.12	6.34	6.56	6.50	6.88	6.26	6.97	7.19
7553	6.66	6.58	6.86	6.52	6.72	7.13	6.94	5.48
7545	6.98	6.70	6.33	6.43	6.52	6.57	7.23	7.07
7552	5.98	6.00	6.70	6.21	6.47	6.58	7.11	7.02
7569	6.28	6.29	5.90	6.66	6.83	6.54	--	--
7560	6.65	6.83	6.00	6.61	6.78	6.91	--	--
7567	6.54	6.06	6.32	6.13	5.72	7.65	--	--
7550	6.09	6.15	6.20	6.06	5.92	6.38	--	--
MEAN	6.54	6.37	6.36	6.39	6.48	6.75	7.06	6.69
SD	0.404	0.305	0.333	0.227	0.435	0.457	0.134	0.810
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Erythrocytes

STUDY ID: 097  
STUDY NO: 097  
ABBR: RBC

SEX: FEMALE

UNITS: 10<sup>6</sup>/cmm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3F:2.0 mg base/kg/day								
7562	6.13	6.32	6.05	6.20	6.68	6.65	7.35	6.54
7548	6.66	6.33	6.28	5.99	6.00	6.00	6.29	7.00
7571	6.00	7.27	6.72	5.18	6.62	7.61	7.80	7.76
7561	7.13	7.07	7.09	6.14	5.81	6.16	5.99	6.82
7564	6.54	6.11	6.14	5.81	5.99	6.07	--	--
7574	6.25	6.01	6.04	5.57	5.90	6.15	--	--
7556	6.44	6.59	6.63	6.08	7.13	6.76	--	--
7572	6.76	6.55	5.92	5.37	5.94	7.16	--	--
MEAN	6.49	6.53	6.36	5.79	6.26	6.57	6.86	7.03
SD	0.367	0.443	0.411	0.380	0.484	0.585	0.857	0.522
N	8	8	8	8	8	8	4	4

GROUP: 4F:6.0 mg base/kg/day								
7539	6.15	6.05	6.23	5.11	6.23	6.43	5.51	6.33
7563	6.42	5.98	5.73	6.26	6.66	6.65	7.54	7.80
7540	6.26	5.80	5.33	5.09	5.64	6.50	5.97	6.47
7554	6.37	6.56	5.85	4.64	6.16	6.12	5.36	7.18
7568	6.52	6.43	5.66	5.21	6.42	5.78	--	--
7544	6.16	5.12	5.56	5.26	6.00	6.72	--	--
7546	6.91	6.25	6.18	5.12	6.51	5.64	--	--
7551	5.99	6.73	6.16	5.58	6.00	5.50	--	--
MEAN	6.35	6.12	5.84	5.28	6.20	6.17	6.10	6.95
SD	0.283	0.508	0.328	0.471	0.328	0.477	0.998	0.681
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Hemoglobin

STUDY ID: 097  
STUDY NO: 097  
ABBR: THGB

SEX: FEMALE

UNITS: g/dL

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1F:0 mg base/kg/day								
7557	17.0	17.3	15.8	15.7	16.1	15.6	18.3	16.5
7541	16.6	15.2	16.9	17.0	17.9	17.8	18.4	19.3
7566	15.4	15.1	16.0	15.7	16.1	16.1	16.6	17.9
7549	15.5	14.6	14.9	14.9	15.6	15.3	16.9	17.3
7555	15.0	14.8	15.9	15.4	14.5	17.3	--	--
7558	16.2	15.9	14.5	14.3	14.4	16.5	--	--
7573	14.0	14.7	16.0	15.1	18.0	17.2	--	--
7542	15.6	16.3	15.8	16.6	14.5	16.2	--	--
MEAN	15.7	15.5	15.7	15.6	15.9	16.5	17.6	17.8
SD	0.95	0.94	0.73	0.88	1.45	0.87	0.93	1.18
N	8	8	8	8	8	8	4	4

GROUP: 2F:0.1 mg base/kg/day								
7543	16.7	14.5	15.1	15.2	16.4	15.1	16.8	17.2
7553	16.3	16.0	16.7	16.2	17.5	17.6	17.2	13.8
7545	17.0	16.9	15.7	16.0	17.4	16.8	18.5	17.7
7552	14.7	14.3	16.7	15.4	16.6	16.2	17.6	17.3
7569	15.6	15.5	13.7	16.6	17.5	16.2	--	--
7560	14.5	15.2	13.7	15.3	15.7	16.2	--	--
7567	15.6	14.5	15.1	14.5	13.6	18.6	--	--
7550	15.3	15.4	15.7	15.4	16.0	16.8	--	--
MEAN	15.7	15.3	15.3	15.6	16.3	16.7	17.5	16.5
SD	0.90	0.88	1.16	0.66	1.30	1.05	0.73	1.81
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Hemoglobin

STUDY ID: 097 SEX: FEMALE  
STUDY NO: 097  
ABBR: THGB UNITS: g/dL

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3F:2.0 mg base/kg/day								
7562	15.1	15.6	15.5	15.8	18.4	17.3	18.8	16.7
7548	16.3	15.7	15.4	15.2	14.9	14.7	15.8	17.3
7571	14.5	18.0	16.7	12.9	16.2	18.6	19.4	19.2
7561	17.1	17.3	17.1	15.4	15.0	14.7	14.6	16.5
7564	14.7	14.1	14.2	13.5	14.9	14.1	--	--
7574	15.5	14.9	15.1	14.2	15.6	15.8	--	--
7556	15.8	16.2	16.3	15.1	17.7	16.2	--	--
7572	15.9	15.9	14.3	13.1	14.3	16.9	--	--
MEAN	15.6	16.0	15.6	14.4	15.9	16.0	17.2	17.4
SD	0.86	1.24	1.06	1.13	1.47	1.53	2.32	1.23
N	8	8	8	8	8	8	4	4

GROUP: 4F:6.0 mg base/kg/day								
7539	15.4	15.2	15.7	13.1	15.7	16.7	14.3	16.2
7563	16.5	15.7	15.1	14.5	16.7	16.7	18.9	19.7
7540	16.1	14.9	13.5	13.1	13.9	16.4	15.3	16.0
7554	15.6	16.1	14.5	11.5	15.8	15.5	13.5	17.7
7568	16.8	16.2	14.4	13.3	16.8	14.2	--	--
7544	15.0	12.4	13.8	13.0	14.7	15.7	--	--
7546	15.7	14.8	14.2	11.9	14.5	13.3	--	--
7551	15.3	17.2	16.0	14.6	14.9	14.3	--	--
MEAN	15.8	15.3	14.7	13.1	15.4	15.4	15.5	17.4
SD	0.62	1.42	0.88	1.09	1.05	1.28	2.38	1.71
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Hematocrit

STUDY ID: 097  
STUDY NO: 097  
ABBR: HCT

SEX: FEMALE

UNITS: %

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1F:0 mg base/kg/day								
7557	49.3	49.6	43.5	44.4	42.9	43.3	51.5	46.1
7541	48.4	45.8	49.2	48.4	47.6	50.3	51.8	53.7
7566	45.6	43.8	46.1	46.3	43.6	45.8	46.6	51.0
7549	46.0	43.1	43.2	43.0	44.6	43.5	47.8	48.6
7555	43.5	42.0	45.0	43.1	42.2	48.1	--	--
7558	47.0	46.5	41.5	40.5	40.7	45.9	--	--
7573	41.2	41.6	45.4	43.5	46.9	47.3	--	--
7542	45.5	46.8	44.2	46.6	46.6	45.4	--	--
MEAN	45.8	44.9	44.8	44.5	44.4	46.2	49.4	49.9
SD	2.59	2.75	2.30	2.51	2.47	2.34	2.62	3.25
N	8	8	8	8	8	8	4	4

GROUP: 2F:0.1 mg base/kg/day								
7543	48.3	42.4	43.6	43.9	45.8	42.3	47.3	48.4
7553	47.2	46.3	47.8	45.4	46.8	49.7	48.3	38.3
7545	50.2	47.8	45.6	46.0	46.9	47.2	51.4	49.8
7552	42.6	42.2	46.6	43.2	44.5	48.0	49.1	47.7
7569	45.6	45.1	40.5	47.2	48.2	46.5	--	--
7560	44.2	45.1	40.1	44.1	44.7	45.0	--	--
7567	45.6	42.3	43.7	42.2	39.5	53.6	--	--
7550	43.8	43.6	43.6	42.7	42.2	45.1	--	--
MEAN	45.9	44.4	43.9	44.3	44.8	47.2	49.0	46.1
SD	2.52	2.07	2.72	1.73	2.83	3.41	1.75	5.24
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Hematocrit

STUDY ID: 097  
STUDY NO: 097  
ABBR: HCT

SEX: FEMALE

UNITS: %

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3F:2.0 mg base/kg/day								
7562	43.8	45.3	43.1	46.1	49.1	48.5	52.8	46.2
7548	47.1	44.3	43.4	42.9	42.5	41.6	43.3	47.8
7571	42.8	51.9	47.8	38.7	47.9	54.3	55.5	53.9
7561	51.7	49.8	49.9	44.1	40.7	41.6	41.1	46.1
7564	43.9	41.1	41.0	40.1	40.4	40.9	--	--
7574	44.4	42.9	43.5	41.8	43.1	44.9	--	--
7556	45.5	46.8	47.2	44.1	50.3	46.6	--	--
7572	46.7	45.9	41.7	38.9	42.1	49.4	--	--
MEAN	45.7	46.0	44.7	42.1	44.5	46.0	48.2	48.5
SD	2.83	3.52	3.19	2.69	3.95	4.68	7.04	3.68
N	8	8	8	8	8	8	4	4

GROUP: 4F:6.0 mg base/kg/day								
7539	45.7	44.5	44.7	39.7	46.7	48.0	40.9	46.1
7563	47.4	44.1	42.8	42.2	47.8	47.1	54.1	54.3
7540	45.8	41.6	38.6	37.8	39.9	46.3	43.3	45.2
7554	46.2	47.1	42.4	34.8	45.2	46.9	40.8	50.3
7568	47.7	46.3	41.0	38.7	45.7	40.8	--	--
7544	43.2	36.0	38.8	37.5	40.5	44.1	--	--
7546	46.6	41.5	41.3	36.6	42.2	39.2	--	--
7551	45.3	50.3	45.3	43.1	44.4	41.4	--	--
MEAN	46.0	43.9	41.9	38.8	44.1	44.2	44.8	49.0
SD	1.40	4.32	2.45	2.79	2.89	3.36	6.32	4.19
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Mean Corpuscular Volume

STUDY ID: 097  
STUDY NO: 097  
ABBR: MCV

SEX: FEMALE

UNITS: fl

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1F:0 mg base/kg/day								
7557	70.7	69.8	69.2	69.4	69.6	69.3	70.1	68.8
7541	73.6	72.7	73.4	73.0	71.5	71.3	71.9	73.1
7566	71.6	70.0	69.5	70.0	69.6	69.5	69.0	70.2
7549	70.6	70.0	69.3	69.4	70.1	69.8	69.6	69.9
7555	71.7	70.8	70.5	70.1	68.8	69.9	--	--
7558	73.2	71.8	72.2	73.0	72.3	72.1	--	--
7573	69.8	69.4	68.3	69.5	68.6	68.5	--	--
7542	71.4	69.9	68.6	69.6	68.8	70.9	--	--
MEAN	71.6	70.6	70.1	70.5	69.9	70.2	70.2	70.5
SD	1.29	1.14	1.80	1.56	1.34	1.18	1.25	1.83
N	8	8	8	8	8	8	4	4

GROUP: 2F:0.1 mg base/kg/day								
7543	67.8	66.9	66.5	67.5	66.6	67.6	67.9	67.3
7553	70.9	70.4	69.7	69.6	69.6	69.7	69.6	69.9
7545	71.9	71.3	72.0	71.5	71.9	71.8	71.1	70.4
7552	71.2	70.3	69.6	69.6	68.8	72.9	69.1	67.9
7569	72.6	71.7	71.1	70.9	70.6	71.1	--	--
7560	66.5	66.0	66.8	66.7	65.9	65.1	--	--
7567	69.7	69.8	69.1	68.8	69.1	70.1	--	--
7550	71.9	70.9	70.3	70.5	71.3	70.7	--	--
MEAN	70.3	69.7	69.4	69.4	69.2	69.9	69.4	68.9
SD	2.16	2.08	1.92	1.66	2.13	2.48	1.33	1.51
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Mean Corpuscular Volume

STUDY ID: 097 SEX: FEMALE  
STUDY NO: 097  
ABBR: MCV UNITS: fL

---

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3F:2.0 mg base/kg/day								
7562	71.5	71.7	71.2	74.4	73.5	72.9	71.8	70.6
7548	70.7	70.0	69.1	71.6	70.8	69.3	68.8	68.3
7571	71.3	71.4	71.1	74.7	72.4	71.4	71.2	69.5
7561	72.5	70.4	70.4	71.8	70.1	67.5	68.6	67.6
7564	67.1	67.3	66.8	69.0	67.4	67.4	--	--
7574	71.0	71.4	72.0	75.0	73.1	73.0	--	--
7556	70.7	71.0	71.2	72.5	70.5	68.9	--	--
7572	69.1	70.1	70.4	72.4	70.9	69.0	--	--
MEAN	70.5	70.4	70.3	72.7	71.1	69.9	70.1	69.0
SD	1.67	1.41	1.64	2.00	1.95	2.24	1.64	1.32
N	8	8	8	8	8	8	4	4

---

GROUP: 4F:6.0 mg base/kg/day								
7539	74.3	73.6	71.7	77.7	75.0	74.7	74.2	72.8
7563	73.8	73.7	74.7	68.8	71.8	70.8	71.8	69.6
7540	73.2	71.7	72.4	74.3	70.7	71.2	72.5	69.9
7554	72.5	71.8	72.5	75.0	73.4	76.6	76.1	70.1
7568	73.2	72.0	72.4	74.3	71.2	70.6	--	--
7544	70.1	70.3	69.8	71.3	67.5	65.6	--	--
7546	67.4	66.4	66.8	71.5	68.8	69.5	--	--
7551	75.6	74.7	73.5	77.2	74.0	75.3	--	--
MEAN	72.5	71.8	71.7	73.8	71.6	71.8	73.7	70.6
SD	2.60	2.58	2.43	3.05	2.57	3.59	1.92	1.48
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Mean Corpuscular Hemoglobin

STUDY ID: 097  
STUDY NO: 097  
ABBR: TMCH

SEX: FEMALE  
UNITS: pg

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1F:0 mg base/kg/day								
7557	24.4	24.3	25.1	24.5	26.1	25.0	24.9	24.6
7541	25.2	24.1	25.2	25.6	26.9	25.2	25.6	26.3
7566	24.2	24.1	24.1	23.8	25.7	24.4	24.6	24.7
7549	23.8	23.7	23.9	24.0	24.5	24.6	24.6	24.9
7555	24.7	25.0	24.9	25.0	23.7	25.1	--	--
7558	25.2	24.5	25.2	25.8	25.6	25.9	--	--
7573	23.7	24.5	24.1	24.1	26.3	24.9	--	--
7542	24.5	24.3	24.5	24.8	23.7	25.3	--	--
MEAN	24.5	24.3	24.6	24.7	25.3	25.1	24.9	25.1
SD	0.57	0.38	0.54	0.74	1.21	0.46	0.47	0.79
N	8	8	8	8	8	8	4	4

GROUP: 2F:0.1 mg base/kg/day								
7543	23.5	22.9	23.0	23.4	23.8	24.1	24.1	23.9
7553	24.5	24.3	24.3	24.8	26.0	24.7	24.8	25.2
7545	24.4	25.2	24.8	24.9	26.7	25.6	25.6	25.0
7552	24.6	23.8	24.9	24.8	25.7	24.6	24.8	24.6
7569	24.8	24.6	26.3	24.9	25.6	24.8	--	--
7560	21.8	22.3	22.8	23.1	23.2	23.4	--	--
7567	23.9	23.9	23.9	23.7	23.8	24.3	--	--
7550	25.1	25.0	25.3	25.4	27.0	26.3	--	--
MEAN	24.1	24.0	24.4	24.4	25.2	24.7	24.8	24.7
SD	1.05	1.00	1.17	0.84	1.44	0.89	0.61	0.57
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Mean Corpuscular Hemoglobin

STUDY ID: 097  
STUDY NO: 097  
ABBR: TMCH

SEX: FEMALE

UNITS: pg

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3F:2.0 mg base/kg/day								
7562	24.6	24.7	25.6	25.5	27.5	26.0	25.6	25.5
7548	24.5	24.8	24.5	25.4	24.8	24.5	25.1	24.7
7571	24.2	24.8	24.9	24.9	24.5	24.4	24.9	24.7
7561	24.0	24.5	24.1	25.1	25.8	23.9	24.4	24.2
7564	22.5	23.1	23.1	23.2	24.9	23.2	--	--
7574	24.8	24.8	25.0	25.5	26.4	25.7	--	--
7556	24.5	24.6	24.6	24.8	24.8	24.0	--	--
7572	23.5	24.3	24.2	24.4	24.1	23.6	--	--
MEAN	24.1	24.5	24.5	24.9	25.4	24.4	25.0	24.8
SD	0.76	0.57	0.74	0.77	1.14	0.98	0.50	0.54
N	8	8	8	8	8	8	4	4

GROUP: 4F:6.0 mg base/kg/day								
7539	25.0	25.1	25.2	25.6	25.2	26.0	26.0	25.6
7563	25.7	26.3	26.4	23.7	25.1	25.1	25.1	25.3
7540	25.7	25.7	25.3	25.7	24.6	25.2	25.6	24.7
7554	24.5	24.5	24.8	24.8	25.6	25.3	25.2	24.7
7568	25.8	25.2	25.4	25.5	26.2	24.6	--	--
7544	24.4	24.2	24.8	24.7	24.5	23.4	--	--
7546	22.7	23.7	23.0	23.2	23.7	23.6	--	--
7551	25.5	25.6	26.0	26.2	24.8	26.0	--	--
MEAN	24.9	25.0	25.1	24.9	25.0	24.9	25.5	25.1
SD	1.05	0.86	1.02	1.04	0.75	0.98	0.41	0.45
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Mean Copuscular Hemo. Conc.

STUDY ID: 097  
STUDY NO: 097  
ABBR: TMCHC

SEX: FEMALE

UNITS: g/dL

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1F:0 mg base/kg/day								
7557	34.5	34.9	36.3	35.4	37.5	36.0	35.5	35.8
7541	34.3	33.2	34.3	35.1	37.6	35.4	35.5	35.9
7566	33.8	34.5	34.7	33.9	36.9	35.2	35.6	35.1
7549	33.7	33.9	34.5	34.7	35.0	35.2	35.4	35.6
7555	34.5	35.2	35.3	35.7	34.4	36.0	--	--
7558	34.5	34.2	34.9	35.3	35.4	35.9	--	--
7573	34.0	35.3	35.2	34.7	38.4	36.4	--	--
7542	34.3	34.8	35.7	35.6	34.4	35.7	--	--
MEAN	34.2	34.5	35.1	35.1	36.2	35.7	35.5	35.6
SD	0.33	0.71	0.66	0.60	1.58	0.43	0.08	0.36
N	8	8	8	8	8	8	4	4

GROUP: 2F:0.1 mg base/kg/day								
7543	34.6	34.2	34.6	34.6	35.8	35.7	35.5	35.5
7553	34.5	34.6	34.9	35.7	37.4	35.4	35.6	36.0
7545	33.9	35.4	34.4	34.8	37.1	35.6	36.0	35.5
7552	34.5	33.9	35.8	35.6	37.3	33.8	35.8	36.3
7569	34.2	34.4	35.1	35.2	36.3	34.8	--	--
7560	32.8	33.7	34.2	34.7	35.1	36.0	--	--
7567	34.2	34.3	34.6	34.4	34.4	34.7	--	--
7550	34.9	35.3	36.0	36.1	37.9	37.3	--	--
MEAN	34.2	34.5	35.0	35.1	36.4	35.4	35.7	35.8
SD	0.64	0.61	0.65	0.61	1.23	1.04	0.22	0.39
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Mean Copuscular Hemo. Conc.

STUDY ID: 097  
STUDY NO: 097  
ABBR: TMCHC

SEX: FEMALE

UNITS: g/dL

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3F:2.0 mg base/kg/day								
7562	34.5	34.4	36.0	34.3	37.5	35.7	35.6	36.1
7548	34.6	35.4	35.5	35.4	35.1	35.3	36.5	36.2
7571	33.9	34.7	34.9	33.3	33.8	34.3	35.0	35.6
7561	33.1	34.7	34.3	34.9	36.9	35.3	35.5	35.8
7564	33.5	34.3	34.6	33.7	36.9	34.5	--	--
7574	34.9	34.7	34.7	34.0	36.2	35.2	--	--
7556	34.7	34.6	34.5	34.2	35.2	34.8	--	--
7572	34.0	34.6	34.3	33.7	34.0	34.2	--	--
MEAN	34.2	34.7	34.9	34.2	35.7	34.9	35.7	35.9
SD	0.63	0.33	0.60	0.69	1.39	0.54	0.62	0.28
N	8	8	8	8	8	8	4	4

GROUP: 4F:6.0 mg base/kg/day								
7539	33.7	34.2	35.1	33.0	33.6	34.8	35.0	35.1
7563	34.8	35.6	35.3	34.4	34.9	35.5	34.9	36.3
7540	35.2	35.8	35.0	34.7	34.8	35.4	35.3	35.4
7554	33.8	34.2	34.2	33.0	35.0	33.0	33.1	35.2
7568	35.2	35.0	35.1	34.4	36.8	34.8	--	--
7544	34.7	34.4	35.6	34.7	36.3	35.6	--	--
7546	33.7	35.7	34.4	32.5	34.4	33.9	--	--
7551	33.8	34.2	35.3	33.9	33.6	34.5	--	--
MEAN	34.4	34.9	35.0	33.8	34.9	34.7	34.6	35.5
SD	0.68	0.72	0.47	0.87	1.15	0.89	1.00	0.55
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Reticulocytes (%RBCs)

STUDY ID: 097  
STUDY NO: 097  
ABBR: RETICS

SEX: FEMALE

UNITS: % RBCs

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1F:0 mg base/kg/day								
7557	0.1	0.0	0.1	0.1	0.0	0.5	0.6	0.4
7541	0.2	0.0	0.1	0.0	0.0	0.2	0.7	0.6
7566	0.1	0.1	0.0	0.1	0.1	0.6	0.2	0.8
7549	0.5	0.0	0.0	0.2	0.1	0.1	0.1	0.4
7555	0.3	0.0	0.6	0.5	0.0	0.3	--	--
7558	0.3	0.3	0.1	0.2	0.2	0.4	--	--
7573	0.6	0.2	0.2	0.1	0.3	0.6	--	--
7542	0.6	0.3	0.1	0.1	0.0	0.4	--	--
MEAN	0.3	0.1	0.2	0.2	0.1	0.4	0.4	0.6
SD	0.21	0.14	0.19	0.15	0.11	0.18	0.29	0.19
N	8	8	8	8	8	8	4	4

GROUP: 2F:0.1 mg base/kg/day								
7543	0.4	0.0	0.2	0.2	0.1	0.1	0.2	0.9
7553	0.2	0.1	0.0	0.0	0.0	0.3	0.5	0.0
7545	0.4	0.1	0.3	0.0	0.0	0.5	0.2	0.3
7552	0.3	0.3	0.2	0.3	0.1	0.3	0.2	0.3
7569	0.2	0.1	0.2	0.4	0.4	0.2	--	--
7560	0.3	0.1	0.6	0.2	0.5	0.5	--	--
7567	0.2	0.0	0.0	0.0	0.1	0.1	--	--
7550	0.2	0.0	0.5	0.0	0.0	0.4	--	--
MEAN	0.3	0.1	0.3	0.1	0.2	0.3	0.3	0.4
SD	0.09	0.10	0.21	0.16	0.19	0.16	0.15	0.38
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Reticulocytes (%RBCs)

STUDY ID: 097  
STUDY NO: 097  
ABBR: RETICS

SEX: FEMALE

UNITS: % RBCs

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3F:2.0 mg base/kg/day								
7562	0.5	0.0	0.5	1.3	0.3	0.4	0.6	0.1
7548	0.1	0.1	0.0	0.6	0.7	0.0	0.2	0.2
7571	0.0	0.1	0.1	1.0	0.5	0.7	0.1	0.0
7561	0.0	0.1	0.7	1.0	1.3	0.7	1.0	0.5
7564	0.6	0.0	0.3	0.5	0.5	0.8	--	--
7574	0.3	0.0	0.3	0.8	0.5	0.1	--	--
7556	0.0	0.1	0.1	0.2	1.5	0.8	--	--
7572	0.1	0.1	0.3	0.4	0.9	1.0	--	--
MEAN	0.2	0.1	0.3	0.7	0.8	0.6	0.5	0.2
SD	0.24	0.05	0.23	0.37	0.43	0.36	0.41	0.22
N	8	8	8	8	8	8	4	4

GROUP: 4F:6.0 mg base/kg/day								
7539	0.3	0.0	0.0	1.0	1.1	1.0	0.0	0.1
7563	0.5	0.3	1.0	0.0	0.8	1.7	0.5	0.1
7540	0.3	0.5	0.5	0.9	1.0	0.8	0.7	0.2
7554	0.1	0.2	0.8	0.4	1.4	1.5	1.1	0.2
7568	0.4	0.0	0.5	1.2	0.9	1.5	--	--
7544	0.4	0.1	0.2	1.0	1.0	1.5	--	--
7546	0.9	0.2	1.2	0.9	0.0	1.0	--	--
7551	0.1	0.0	0.1	0.3	0.9	1.6	--	--
MEAN	0.4	0.2	0.5	0.7	0.9	1.3	0.6	0.2
SD	0.25	0.18	0.43	0.42	0.40	0.34	0.46	0.06
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Nucleated Red Cells

STUDY ID: 097  
STUDY NO: 097  
ABBR: NRBC

SEX: FEMALE

UNITS: COUNT

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1F:0 mg base/kg/day								
7557	0	0	0	0	2	1	0	0
7541	0	0	0	0	0	2	0	0
7566	0	1	0	0	0	1	1	0
7549	0	0	0	1	0	3	1	0
7555	0	0	0	0	0	2	--	--
7558	0	0	0	0	0	1	--	--
7573	0	0	0	0	0	0	--	--
7542	0	0	0	0	0	1	--	--
MEAN	0	0	0	0	0	1	1	0
SD	0.0	0.4	0.0	0.4	0.7	0.9	0.6	0.0
N	8	8	8	8	8	8	4	4

GROUP: 2F:0.1 mg base/kg/day								
7543	0	0	0	3	0	0	3	0
7553	0	0	0	0	0	0	1	0
7545	0	0	0	0	0	1	1	1
7552	0	0	0	0	2	0	0	0
7569	0	0	0	0	0	0	--	--
7560	1	0	0	0	0	0	--	--
7567	0	0	0	0	0	0	--	--
7550	0	0	0	0	0	0	--	--
MEAN	0	0	0	0	0	0	1	0
SD	0.4	0.0	0.0	1.1	0.7	0.4	1.3	0.5
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or &gt; 10

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Nucleated Red Cells

STUDY ID: 097  
STUDY NO: 097  
ABBR: NRBC

SEX: FEMALE

UNITS: COUNT

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3F:2.0 mg base/kg/day								
7562	0	0	0	0	0	0	0	2
7548	1	0	0	0	0	0	0	1
7571	0	0	4	3	0	0	0	0
7561	0	0	0	1	0	0	0	0
7564	0	0	0	4	3	0	--	--
7574	0	0	0	1	1	0	--	--
7556	1	2	0	3	0	1	--	--
7572	0	0	0	4	1	0	--	--
MEAN	0	0	1	2	1	0	0	1
SD	0.5	0.7	1.4	1.7	1.1	0.4	0.0	1.0
N	8	8	8	8	8	8	4	4

GROUP: 4F:6.0 mg base/kg/day								
7539	0	0	0	1	0	0	0	0
7563	0	0	0	0	0	2	0	0
7540	0	0	2	7	2	2	0	0
7554	1	0	0	7	1	5	1	0
7568	1	0	3	5	0	0	--	--
7544	0	0	1	0	3	0	--	--
7546	0	0	1	10	5	0	--	--
7551	0	0	2	6	0	8	--	--
MEAN	0	0	1	5	1	2	0	0
SD	0.5	0.0	1.1	3.7	1.8	2.9	0.5	0.0
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Heinz Bodies

STUDY ID: 097

SEX: FEMALE

STUDY NO: 097

ABBR: HB

UNITS: %

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1F:0 mg base/kg/day								
7557	0.2	0.0	0.0	0.0	0.2	0.3	0.0	0.0
7541	0.9	0.0	0.0	0.1	0.1	0.1	0.1	0.0
7566	0.0	0.0	0.0	0.0	0.4	0.2	0.0	0.0
7549	0.2	0.0	0.0	0.0	0.0	0.0	0.1	0.0
7555	0.2	0.0	0.0	0.0	0.0	0.0	--	--
7558	0.1	0.1	0.0	0.0	0.0	0.2	--	--
7573	0.0	0.0	0.0	0.0	0.0	0.2	--	--
7542	0.2	0.1	0.0	0.2	0.0	0.0	--	--
MEAN	0.2	0.0	0.0	0.0	0.1	0.1	0.1	0.0
SD	0.29	0.05	0.00	0.07	0.15	0.12	0.06	0.00
N	8	8	8	8	8	8	4	4

GROUP: 2F:0.1 mg base/kg/day								
7543	0.5	0.0	0.0	0.0	0.1	0.1	0.2	0.0
7553	0.5	0.0	0.0	0.0	0.3	0.5	0.1	0.0
7545	0.2	0.0	0.4	0.0	0.0	0.1	0.0	0.0
7552	0.2	0.0	0.0	0.0	0.1	0.8	0.0	0.2
7569	0.0	0.3	0.1	0.0	0.2	0.3	--	--
7560	0.1	0.1	0.0	0.0	0.0	0.2	--	--
7567	0.0	0.0	0.0	0.0	0.0	0.0	--	--
7550	0.2	0.1	0.0	0.0	0.2	0.1	--	--
MEAN	0.2	0.1	0.1	0.0	0.1	0.3	0.1	0.1
SD	0.20	0.11	0.14	0.00	0.11	0.27	0.10	0.10
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Heinz Bodies

STUDY ID: 097  
STUDY NO: 097  
ABBR: HB

SEX: FEMALE

UNITS: %

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3F:2.0 mg base/kg/day								
7562	0.1	0.0	0.0	0.1	0.1	0.0	0.0	0.0
7548	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7571	0.0	0.1	0.0	0.0	0.0	0.6	0.0	0.1
7561	0.1	0.0	0.0	0.0	0.0	0.3	0.0	0.0
7564	0.2	0.0	0.0	0.1	0.4	0.2	--	--
7574	0.0	0.1	0.0	0.0	0.1	0.1	--	--
7556	0.0	0.0	0.0	0.0	0.0	0.0	--	--
7572	0.0	0.1	0.0	0.0	0.8	0.0	--	--
MEAN	0.1	0.0	0.0	0.0	0.2	0.2	0.0	0.0
SD	0.11	0.05	0.00	0.05	0.29	0.21	0.00	0.05
N	8	8	8	8	8	8	4	4
GROUP: 4F:6.0 mg base/kg/day								
7539	0.2	0.0	0.0	0.0	0.1	0.5	0.0	0.0
7563	0.0	0.0	0.0	0.0	0.0	0.8	0.0	0.0
7540	0.1	0.0	0.3	0.1	0.0	0.0	0.0	0.0
7554	0.0	0.0	0.5	0.0	0.1	0.0	0.0	0.0
7568	0.0	0.0	0.0	0.0	0.1	0.4	--	--
7544	0.3	0.0	0.0	0.2	0.1	0.0	--	--
7546	0.4	0.0	0.0	0.0	0.0	0.0	--	--
7551	0.2	0.1	0.0	0.0	0.1	0.0	--	--
MEAN	0.2	0.0	0.1	0.0	0.1	0.2	0.0	0.0
SD	0.15	0.04	0.19	0.07	0.05	0.31	0.00	0.00
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: % Methemoglobin

STUDY ID: 097  
STUDY NO: 097  
ABBR: %METHGB

SEX: FEMALE

UNITS: %

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1F:0 mg base/kg/day								
7557	1.4	1.2	0.8	0.9	0.9	0.8	0.5	0.7
7541	1.6	1.3	0.8	0.8	0.8	1.0	0.6	0.8
7566	2.1	1.4	1.3	1.3	0.9	0.9	1.2	1.2
7549	1.0	0.9	0.8	0.7	0.7	0.8	0.6	0.9
7555	1.5	1.2	0.8	0.8	0.8	0.7	--	--
7558	1.9	0.9	1.0	0.8	0.9	0.7	--	--
7573	3.4	3.2	1.9	1.5	0.8	1.3	--	--
7542	1.5	0.8	0.9	2.0	0.7	0.9	--	--
MEAN	1.8	1.4	1.0	1.1	0.8	0.9	0.7	0.9
SD	0.73	0.77	0.39	0.46	0.08	0.20	0.32	0.22
N	8	8	8	8	8	8	4	4

GROUP: 2F:0.1 mg base/kg/day								
7543	2.0	1.4	1.2	0.8	0.8	1.1	0.7	0.9
7553	3.3	2.7	2.7	1.0	1.0	3.6	0.5	1.1
7545	0.9	0.9	0.7	0.8	1.2	1.1	0.9	0.9
7552	1.7	1.1	0.9	1.0	0.8	0.8	0.8	0.9
7569	1.1	1.0	1.1	1.0	0.8	0.9	--	--
7560	2.0	1.0	1.1	1.1	1.1	0.9	--	--
7567	4.3	4.4	2.3	1.4	1.4	3.6	--	--
7550	1.1	1.0	1.0	1.2	1.4	1.3	--	--
MEAN	2.1	1.7	1.4	1.0	1.1	1.7	0.7	1.0
SD	1.19	1.24	0.72	0.20	0.26	1.21	0.17	0.10
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: % Methemoglobin

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
STUDY ID: 097								
STUDY NO: 097								
ABBR: %METHGB								
								SEX: FEMALE
								UNITS: %
GROUP: 3F:2.0 mg base/kg/day								
7562	1.5	1.1	8.9	13.1	12.1	12.9	1.1	0.9
7548	4.0	2.6	13.6	17.4	12.4	14.3	1.2	0.9
7571	0.9	0.9	15.2	17.8	14.3	14.7	0.9	1.0
7561	3.9	2.6	15.6	14.5	12.5	14.0	0.7	1.1
7564	1.5	1.0	13.5	18.0	16.3	15.5	--	--
7574	1.8	1.4	13.4	13.5	12.2	12.5	--	--
7556	1.1	0.6	0.9	9.5	8.2	7.6	--	--
7572	1.1	0.9	12.7	13.6	11.9	11.8	--	--
MEAN	2.0	1.4	11.7	14.7	12.5	12.9	1.0	1.0
SD	1.25	0.78	4.82	2.93	2.29	2.47	0.22	0.10
N	8	8	8	8	8	8	4	4

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 4F:6.0 mg base/kg/day								
7539	1.6	1.8	18.9	18.2	20.9	23.8	6.8	1.0
7563	1.5	1.2	29.3	24.6	26.3	25.9	2.1	1.2
7540	1.0	0.7	29.3	26.7	29.7	33.1	4.2	1.2
7554	2.0	1.5	13.4	16.0	16.1	15.5	3.7	0.9
7568	1.2	0.9	17.7	19.3	21.3	21.1	--	--
7544	1.6	1.0	30.3	30.6	26.3	27.9	--	--
7546	0.7	0.6	27.8	22.6	22.2	23.5	--	--
7551	1.2	0.8	25.1	24.7	25.7	27.3	--	--
MEAN	1.4	1.1	24.0	22.8	23.6	24.8	4.2	1.1
SD	0.41	0.41	6.43	4.82	4.26	5.19	1.95	0.15
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Platelets

STUDY ID: 097  
STUDY NO: 097  
ABBR: PLT

SEX: FEMALE

UNITS: 10<sup>3</sup>/ccm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1F:0 mg base/kg/day								
7557	378	323	291	274	286	294	363	248
7541	367	164	334	257	288	278	325	300
7566	285	277	255	237	244	249	260	301
7549	314	285	235	251	247	248	322	295
7555	418	392	306	358	291	317	--	--
7558	453	389	192	357	294	325	--	--
7573	215	326	213	365	353	346	--	--
7542	537	378	334	279	291	365	--	--
MEAN	371	317	270	297	287	303	318	286
SD	101.1	76.2	54.4	53.6	33.6	43.1	42.6	25.5
N	8	8	8	8	8	8	4	4

GROUP: 2F:0.1 mg base/kg/day								
7543	326	320	253	347	294	277	310	211
7553	437	434	276	259	260	325	409	574
7545	175	159	212	155	206	231	240	231
7552	424	336	347	296	303	237	406	363
7569	260	142	234	198	282	299	--	--
7560	384	280	275	230	200	197	--	--
7567	411	459	366	291	235	291	--	--
7550	448	338	246	258	284	258	--	--
MEAN	358	309	276	254	258	264	341	345
SD	97.3	114.0	54.0	60.2	40.0	41.7	81.7	167.0
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Platelets

STUDY ID: 097  
STUDY NO: 097  
ABBR: PLT

SEX: FEMALE

UNITS: 10<sup>3</sup>/ccm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3F:2.0 mg base/kg/day								
7562	257	362	139	98	70	150	365	339
7548	362	282	178	156	229	280	318	243
7571	245	261	106	89	134	162	326	282
7561	470	412	276	200	337	362	479	418
7564	369	325	106	157	309	372	--	--
7574	359	329	106	143	154	204	--	--
7556	352	316	199	102	293	310	--	--
7572	351	373	129	77	151	252	--	--
MEAN	346	333	155	128	210	262	372	321
SD	70.2	49.0	60.0	42.6	96.5	85.1	74.2	76.0
N	8	8	8	8	8	8	4	4
GROUP: 4F:6.0 mg base/kg/day								
7539	329	320	84	68	153	285	247	229
7563	326	215	129	291	262	287	184	247
7540	556	452	78	150	314	391	334	429
7554	474	319	131	171	159	171	176	275
7568	318	292	82	110	143	256	--	--
7544	444	424	82	288	338	371	--	--
7546	379	347	42	68	291	125	--	--
7551	343	324	45	75	44	68	--	--
MEAN	396	337	84	153	213	244	235	295
SD	86.7	74.2	32.9	92.6	103.0	114.6	73.1	91.3
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Prothrombin Time

STUDY ID: 097  
STUDY NO: 097  
ABBR: PT

SEX: FEMALE

UNITS: sec

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1F:0 mg base/kg/day								
7557	7.0	7.4	7.5	7.0	7.0	7.2	7.3	7.0
7541	7.2	7.0	7.3	7.1	7.2	7.2	7.2	7.4
7566	7.4	7.3	7.6	7.3	7.3	7.4	7.4	7.6
7549	7.3	7.5	7.6	7.4	7.9	7.6	7.4	7.6
7555	7.0	7.3	7.0	7.1	7.1	7.2	--	--
7558	7.3	7.3	7.2	7.2	7.1	7.1	--	--
7573	7.1	7.3	7.0	7.2	7.0	6.9	--	--
7542	7.4	7.3	7.5	7.5	7.2	7.4	--	--
MEAN	7.2	7.3	7.3	7.2	7.2	7.3	7.3	7.4
SD	0.16	0.14	0.25	0.17	0.29	0.21	0.10	0.28
N	8	8	8	8	8	8	4	4

GROUP: 2F:0.1 mg base/kg/day								
7543	7.2	7.7	7.6	7.5	7.5	7.5	7.6	7.4
7553	7.2	7.1	7.3	7.1	7.1	7.2	7.0	7.4
7545	7.2	7.1	7.4	7.2	7.3	7.3	7.4	7.5
7552	6.9	7.1	7.2	7.0	7.9	7.0	7.0	7.3
7569	7.2	7.0	7.3	7.1	6.9	7.1	--	--
7560	7.6	7.4	7.9	7.4	7.7	7.7	--	--
7567	7.2	7.4	7.2	7.3	7.1	7.5	--	--
7550	7.4	7.3	7.5	7.4	7.2	7.1	--	--
MEAN	7.2	7.3	7.4	7.3	7.3	7.3	7.3	7.4
SD	0.20	0.23	0.24	0.18	0.34	0.24	0.30	0.08
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Prothrombin Time

STUDY ID: 097  
STUDY NO: 097  
ABBR: PT

SEX: FEMALE

UNITS: sec

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3F:2.0 mg base/kg/day								
7562	6.8	7.3	7.3	6.9	7.1	7.2	7.1	7.5
7548	7.3	7.4	7.2	7.0	7.1	7.0	7.4	7.2
7571	7.1	7.3	7.2	6.8	7.1	7.0	7.3	7.3
7561	7.2	7.0	7.1	6.8	7.3	6.9	6.9	7.5
7564	7.4	7.5	7.4	6.9	7.6	7.4	--	--
7574	7.2	7.4	7.0	6.8	7.1	7.0	--	--
7556	7.1	7.7	7.6	7.0	6.8	6.9	--	--
7572	7.2	7.3	7.1	6.8	7.1	7.0	--	--
MEAN	7.2	7.4	7.2	6.9	7.2	7.1	7.2	7.4
SD	0.18	0.20	0.19	0.09	0.23	0.17	0.22	0.15
N	8	8	8	8	8	8	4	4

GROUP: 4F:6.0 mg base/kg/day								
7539	7.1	7.5	6.9	6.8	7.5	7.0	7.3	7.5
7563	7.4	7.4	7.4	7.2	7.3	7.4	7.4	7.4
7540	7.1	7.0	6.9	6.7	7.5	6.9	7.1	7.2
7554	7.5	7.5	7.4	7.0	7.0	6.9	7.3	7.8
7568	7.1	7.2	7.0	6.8	7.1	7.0	--	--
7544	7.3	7.3	7.2	7.1	7.3	7.4	--	--
7546	7.2	7.2	7.2	6.9	7.0	7.1	--	--
7551	7.0	7.5	7.1	6.7	7.6	7.1	--	--
MEAN	7.2	7.3	7.1	6.9	7.3	7.1	7.3	7.5
SD	0.17	0.18	0.20	0.19	0.24	0.20	0.13	0.25
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

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

STUDY ID: 097  
STUDY NO: 097  
ABBR: APTT

SEX: FEMALE

UNITS: sec

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1F:0 mg base/kg/day								
7557	12.1	10.9	10.3	10.3	10.0	10.5	10.1	10.6
7541	11.5	13.3	11.1	10.4	10.4	10.6	10.2	10.9
7566	11.2	11.8	10.6	10.6	10.3	10.5	10.5	10.3
7549	11.5	11.3	10.7	10.8	10.5	10.4	10.2	11.0
7555	12.6	11.9	11.1	10.4	10.7	11.1	--	--
7558	12.8	13.2	12.9	11.7	11.5	11.6	--	--
7573	12.6	12.2	12.5	12.4	11.2	11.4	--	--
7542	12.0	12.6	11.6	11.5	10.7	10.4	--	--
MEAN	12.0	12.2	11.4	11.0	10.7	10.8	10.3	10.7
SD	0.60	0.85	0.93	0.77	0.49	0.48	0.17	0.32
N	8	8	8	8	8	8	4	4

GROUP: 2F:0.1 mg base/kg/day								
7543	10.9	10.4	10.1	10.1	10.1	10.1	10.2	10.2
7553	11.6	11.7	10.9	10.8	11.2	10.9	10.6	11.0
7545	12.2	11.7	11.7	11.4	11.0	11.6	10.8	11.3
7552	11.4	11.3	10.7	10.9	11.3	11.0	11.1	11.3
7569	12.0	12.5	12.3	10.6	11.0	10.4	--	--
7560	12.7	12.9	10.7	10.5	10.5	10.8	--	--
7567	12.8	12.6	11.9	10.9	11.6	10.7	--	--
7550	11.8	11.6	10.9	10.3	10.8	12.3	--	--
MEAN	11.9	11.8	11.2	10.7	10.9	11.0	10.7	11.0
SD	0.64	0.81	0.74	0.41	0.47	0.69	0.38	0.52
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

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

STUDY ID: 097  
STUDY NO: 097  
ABBR: APTT

SEX: FEMALE  
UNITS: sec

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3F:2.0 mg base/kg/day								
7562	12.1	10.8	10.7	10.3	9.7	10.5	10.2	10.4
7548	10.8	11.0	10.4	10.2	10.2	10.7	10.3	11.0
7571	11.8	12.1	10.9	11.5	10.8	10.9	11.1	11.5
7561	11.2	10.8	9.9	10.3	9.5	10.0	10.5	9.9
7564	11.6	11.9	11.3	11.7	10.8	11.1	--	--
7574	11.6	11.0	11.4	11.0	10.4	10.8	--	--
7556	12.7	12.0	11.6	11.7	11.2	11.5	--	--
7572	11.1	11.6	10.6	9.9	10.2	10.3	--	--
MEAN	11.6	11.4	10.9	10.8	10.4	10.7	10.5	10.7
SD	0.60	0.56	0.57	0.74	0.58	0.47	0.40	0.70
N	8	8	8	8	8	8	4	4

GROUP: 4F:6.0 mg base/kg/day								
7539	12.6	11.7	12.5	10.9	10.3	10.1	10.3	10.8
7563	11.2	12.2	10.4	10.7	10.1	10.7	10.1	10.6
7540	12.7	12.2	11.5	11.7	11.7	11.3	11.8	12.3
7554	12.2	13.1	11.8	12.1	11.0	14.5	12.5	11.8
7568	11.9	12.2	11.3	12.2	11.6	11.6	--	--
7544	11.5	11.1	11.0	12.5	10.9	10.9	--	--
7546	11.5	10.9	10.5	11.6	10.7	10.5	--	--
7551	11.9	12.7	10.9	11.9	10.4	9.0	--	--
MEAN	11.9	12.0	11.2	11.7	10.8	11.1	11.2	11.4
SD	0.54	0.75	0.70	0.63	0.59	1.60	1.16	0.81
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Leukocytes

STUDY ID: 097  
STUDY NO: 097  
ABBR: WBC

SEX: FEMALE  
UNITS: 10<sup>3</sup>/cmm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1F:0 mg base/kg/day								
7557	8.6	6.8	8.3	8.8	8.2	7.0	7.4	9.0
7541	6.8	7.1	7.9	6.5	7.1	7.1	6.0	7.0
7566	7.9	13.2	7.4	9.3	8.4	8.7	7.1	9.0
7549	10.6	6.6	5.8	5.6	6.3	6.9	4.9	6.1
7555	6.6	8.9	9.2	5.6	6.7	6.1	--	--
7558	7.6	6.9	9.8	7.5	7.0	8.2	--	--
7573	7.3	9.1	15.3	7.5	8.5	10.7	--	--
7542	10.4	11.1	12.6	9.8	8.6	12.8	--	--
MEAN	8.2	8.7	9.5	7.6	7.6	8.4	6.4	7.8
SD	1.54	2.39	3.06	1.62	0.92	2.27	1.14	1.46
N	8	8	8	8	8	8	4	4

GROUP: 2F:0.1 mg base/kg/day								
7543	9.3	8.6	10.7	13.2	10.0	11.1	9.8	9.0
7553	8.6	9.0	6.7	5.9	6.7	6.4	7.3	12.4
7545	6.7	10.0	10.5	7.5	7.0	8.4	5.9	6.3
7552	9.6	9.6	11.6	8.6	8.8	7.0	11.4	10.2
7569	6.5	6.3	6.8	7.5	8.7	6.7	--	--
7560	9.6	13.4	10.3	7.3	7.2	7.4	--	--
7567	8.6	9.4	8.6	7.2	6.6	8.4	--	--
7550	8.6	12.9	10.8	9.8	14.3	9.3	--	--
MEAN	8.4	9.9	9.5	8.4	8.7	8.1	8.6	9.5
SD	1.21	2.30	1.89	2.25	2.58	1.57	2.47	2.54
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Leukocytes

STUDY ID: 097  
STUDY NO: 097  
ABBR: WBC

SEX: FEMALE

UNITS: 10<sup>3</sup>/cmm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3F:2.0 mg base/kg/day								
7562	7.1	6.8	5.6	7.2	6.4	7.5	6.7	6.5
7548	7.6	7.0	10.7	9.0	9.2	10.4	7.8	12.9
7571	5.9	7.3	6.8	5.9	10.6	12.3	9.3	6.1
7561	10.2	10.3	9.5	11.0	11.3	10.4	11.7	9.9
7564	6.8	8.9	6.6	9.2	9.0	7.2	--	--
7574	6.5	8.2	8.9	13.0	13.8	19.5	--	--
7556	11.6	8.7	7.3	8.5	13.6	12.4	--	--
7572	6.5	13.0	8.9	8.1	8.4	10.0	--	--
MEAN	7.8	8.8	8.0	9.0	10.3	11.2	8.9	8.9
SD	2.03	2.06	1.72	2.20	2.56	3.85	2.16	3.19
N	8	8	8	8	8	8	4	4

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 4F:6.0 mg base/kg/day								
7539	6.6	7.4	11.2	6.9	8.6	12.5	5.5	7.8
7563	9.2	12.9	11.0	8.1	8.1	9.6	7.9	8.5
7540	7.3	10.0	6.3	9.4	8.2	12.6	7.1	9.3
7554	9.5	9.6	8.6	7.5	17.9	25.2	21.9	10.5
7568	7.3	6.6	6.9	8.2	7.6	10.4	--	--
7544	9.1	13.9	7.3	10.2	12.7	13.0	--	--
7546	10.3	10.1	7.6	8.5	11.2	17.8	--	--
7551	8.5	8.2	8.7	7.9	7.5	7.6	--	--
MEAN	8.5	9.8	8.5	8.3	10.2	13.6	10.6	9.0
SD	1.29	2.54	1.82	1.05	3.62	5.57	7.60	1.16
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: M. Neutrophils

STUDY ID: 097  
STUDY NO: 097  
ABBR: M. Neutrop

SEX: FEMALE

UNITS: 10<sup>3</sup>/cmm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1F:0 mg base/kg/day								
7557	4.4	3.9	5.0	5.1	4.8	3.9	2.9	5.4
7541	4.6	5.0	5.3	4.2	4.8	5.3	4.3	5.1
7566	4.3	9.1	3.8	6.0	5.1	4.4	3.3	5.2
7549	7.4	4.5	3.3	3.4	3.8	4.8	2.7	3.5
7555	4.2	7.5	6.6	3.5	4.5	3.4	--	--
7558	5.4	4.6	7.0	4.7	4.2	5.1	--	--
7573	4.4	5.9	11.5	4.3	5.4	7.2	--	--
7542	5.1	5.8	8.3	5.1	4.6	7.9	--	--
MEAN	5.0	5.8	6.4	4.5	4.7	5.3	3.3	4.8
SD	1.06	1.74	2.66	0.87	0.50	1.56	0.71	0.88
N	8	8	8	8	8	8	4	4

GROUP: 2F:0.1 mg base/kg/day								
7543	5.0	5.6	6.4	9.4	5.1	6.5	5.8	6.5
7553	4.8	5.0	4.0	2.8	3.6	3.9	4.2	8.1
7545	4.4	6.2	8.1	4.7	4.3	5.3	2.8	3.2
7552	6.6	6.0	8.0	5.0	5.2	4.1	8.3	7.0
7569	3.1	3.4	3.7	5.3	5.2	4.8	--	--
7560	4.8	8.3	5.3	3.1	2.9	4.3	--	--
7567	4.9	6.4	4.4	3.9	3.6	3.4	--	--
7550	5.6	9.3	7.5	5.5	9.3	5.3	--	--
MEAN	4.9	6.3	5.9	5.0	4.9	4.7	5.3	6.2
SD	0.99	1.84	1.82	2.05	1.98	0.99	2.36	2.11
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: M. Neutrophils

STUDY ID: 097  
STUDY NO: 097  
ABBR: M. Neutrop

SEX: FEMALE  
UNITS: 10<sup>3</sup>/cmm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3F:2.0 mg base/kg/day								
7562	5.1	4.0	3.1	4.0	3.8	5.1	3.6	3.9
7548	3.7	3.0	6.6	5.3	7.0	7.2	5.2	8.5
7571	2.8	4.2	4.4	3.2	7.1	10.1	6.1	3.8
7561	6.1	4.7	5.1	6.7	7.1	7.3	8.7	6.6
7564	3.8	5.4	3.5	5.5	5.9	4.3	--	--
7574	2.5	4.0	5.1	8.2	11.6	14.6	--	--
7556	6.4	4.3	4.4	4.9	8.8	9.3	--	--
7572	3.8	10.0	6.4	5.4	4.0	6.5	--	--
MEAN	4.3	5.0	4.8	5.4	6.9	8.1	5.9	5.7
SD	1.45	2.15	1.25	1.54	2.53	3.28	2.13	2.27
N	8	8	8	8	8	8	4	4

GROUP: 4F:6.0 mg base/kg/day								
7539	3.0	4.8	9.1	3.2	6.1	8.0	3.7	4.4
7563	6.3	10.6	7.4	5.5	6.2	6.5	5.8	5.8
7540	4.1	6.6	2.9	6.9	5.0	8.8	4.0	6.1
7554	4.6	4.7	5.2	4.0	15.0	14.1	13.4	5.0
7568	3.5	3.9	3.9	4.6	4.1	7.7	--	--
7544	5.8	10.0	4.1	6.9	9.4	10.1	--	--
7546	6.3	7.5	4.5	6.0	7.5	12.6	--	--
7551	5.3	5.9	5.9	5.5	4.3	4.8	--	--
MEAN	4.9	6.8	5.4	5.3	7.2	9.1	6.7	5.3
SD	1.26	2.47	2.03	1.32	3.60	3.09	4.55	0.77
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: I. Neutrophils

STUDY ID: 097

SEX: FEMALE

STUDY NO: 097

ABBR: I. Neutrop

UNITS: 10<sup>3</sup>/cmm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1F:0 mg base/kg/day								
7557	3.6	0.1	0.0	0.0	0.2	0.1	0.2	0.1
7541	0.0	0.1	0.2	0.2	0.1	0.0	0.1	0.0
7566	0.2	0.3	0.3	0.1	0.3	0.0	0.1	0.0
7549	0.0	0.1	0.2	0.0	0.3	0.1	0.2	0.0
7555	0.1	0.1	0.2	0.0	0.2	0.1	--	--
7558	0.0	0.0	0.2	0.3	0.1	0.0	--	--
7573	0.1	0.3	0.5	0.5	0.0	0.0	--	--
7542	0.0	0.0	0.1	0.4	0.2	0.3	--	--
MEAN	0.5	0.1	0.2	0.2	0.2	0.1	0.2	0.0
SD	1.25	0.12	0.15	0.20	0.10	0.10	0.06	0.05
N	8	8	8	8	8	8	4	4

GROUP: 2F:0.1 mg base/kg/day								
7543	0.0	0.3	0.1	0.0	0.2	0.3	0.2	0.2
7553	0.0	0.0	0.1	0.0	0.1	0.4	0.4	0.6
7545	0.0	0.0	0.1	0.3	0.0	0.5	0.1	0.0
7552	0.0	0.0	0.6	0.9	0.2	0.3	0.0	0.3
7569	0.1	0.1	0.1	0.3	0.3	0.1	--	--
7560	0.2	0.1	0.2	0.1	0.1	0.1	--	--
7567	0.2	0.2	0.2	0.4	0.1	0.2	--	--
7550	0.0	0.3	0.1	0.3	0.4	0.6	--	--
MEAN	0.1	0.1	0.2	0.3	0.2	0.3	0.2	0.3
SD	0.09	0.13	0.17	0.29	0.13	0.18	0.17	0.25
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: I. Neutrophils

STUDY ID: 097

SEX: FEMALE

STUDY NO: 097

ABBR: I. Neutrop

UNITS: 10<sup>3</sup>/cmm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3F:2.0 mg base/kg/day								
7562	0.1	0.1	0.1	0.3	0.1	0.1	0.1	0.1
7548	0.1	0.1	0.2	0.5	0.2	0.1	0.2	0.6
7571	0.0	0.1	0.3	0.6	0.8	0.1	0.3	0.2
7561	0.1	0.4	0.7	1.0	0.7	0.6	0.5	0.0
7564	0.1	0.4	0.2	0.5	0.4	0.1	--	--
7574	0.1	0.2	0.4	0.5	0.4	1.2	--	--
7556	0.2	0.1	0.3	0.1	1.6	0.2	--	--
7572	0.0	0.3	0.1	0.3	0.6	0.6	--	--
MEAN	0.1	0.2	0.3	0.5	0.6	0.4	0.3	0.2
SD	0.06	0.14	0.20	0.27	0.47	0.40	0.17	0.26
N	8	8	8	8	8	8	4	4

GROUP: 4F:6.0 mg base/kg/day								
7539	0.1	0.1	0.3	0.9	0.4	0.9	0.2	0.3
7563	0.0	0.3	1.3	0.4	0.0	0.2	0.2	0.1
7540	0.0	0.2	0.6	0.4	0.2	0.5	0.1	0.3
7554	0.2	0.2	0.7	0.7	0.2	4.5	2.6	0.2
7568	0.1	0.0	0.5	0.7	0.1	0.1	--	--
7544	0.1	0.3	0.2	0.2	0.3	0.4	--	--
7546	0.1	0.0	0.0	0.4	0.4	0.7	--	--
7551	0.0	0.0	0.0	0.5	0.4	0.2	--	--
MEAN	0.1	0.1	0.5	0.5	0.3	0.9	0.8	0.2
SD	0.07	0.13	0.43	0.23	0.15	1.46	1.22	0.10
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or &gt; 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Lymphocytes

STUDY ID: 097

SEX: FEMALE

STUDY NO: 097

ABBR: Lymphocyte

UNITS: 10<sup>3</sup>/cmm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1F:0 mg base/kg/day								
7557	0.1	2.3	2.8	3.2	3.0	2.6	3.8	3.2
7541	2.0	1.8	2.0	1.6	1.8	1.5	1.4	1.4
7566	2.4	2.5	2.2	2.0	2.1	3.0	3.5	2.4
7549	2.3	1.6	2.0	2.0	2.1	1.7	1.5	2.3
7555	1.8	1.0	1.7	2.0	1.6	1.9	--	--
7558	1.6	2.1	1.7	1.8	2.5	2.3	--	--
7573	2.7	2.5	2.6	2.3	2.6	3.3	--	--
7542	4.4	3.9	3.3	3.5	3.1	3.8	--	--
MEAN	2.2	2.2	2.3	2.3	2.4	2.5	2.6	2.3
SD	1.20	0.85	0.57	0.68	0.54	0.81	1.28	0.74
N	8	8	8	8	8	8	4	4

GROUP: 2F:0.1 mg base/kg/day								
7543	3.4	2.7	4.0	3.0	3.5	3.2	3.2	2.0
7553	2.7	3.1	2.0	2.2	2.5	1.9	2.0	1.9
7545	1.9	3.2	1.7	1.6	2.0	1.7	2.7	2.7
7552	2.9	3.2	2.8	2.3	3.2	2.2	2.2	1.7
7569	2.9	2.1	2.3	1.3	2.6	1.3	--	--
7560	3.7	3.9	2.9	3.1	3.4	2.4	--	--
7567	2.8	2.0	3.0	2.4	2.2	4.0	--	--
7550	2.8	2.7	2.8	3.5	3.6	2.9	--	--
MEAN	2.9	2.9	2.7	2.4	2.9	2.5	2.5	2.1
SD	0.53	0.63	0.71	0.75	0.63	0.88	0.54	0.43
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Lymphocytes

STUDY ID: 097

SEX: FEMALE

STUDY NO: 097

ABBR: Lymphocyte

UNITS: 10<sup>3</sup>/cmm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3F:2.0 mg base/kg/day								
7562	1.2	2.4	2.1	2.6	2.2	1.8	2.5	2.5
7548	3.4	3.4	3.0	2.1	1.6	2.2	2.0	2.8
7571	2.6	2.6	1.3	1.5	1.8	1.8	2.1	1.6
7561	3.6	3.7	3.5	2.4	2.8	1.5	1.9	2.5
7564	2.2	2.5	2.1	2.4	2.1	1.8	--	--
7574	3.4	3.6	2.9	3.0	1.1	2.1	--	--
7556	3.8	3.7	2.1	2.6	1.9	1.6	--	--
7572	2.3	2.3	2.0	1.6	2.5	2.0	--	--
MEAN	2.8	3.0	2.4	2.3	2.0	1.9	2.1	2.4
SD	0.89	0.63	0.70	0.51	0.53	0.24	0.26	0.52
N	8	8	8	8	8	8	4	4

GROUP: 4F:6.0 mg base/kg/day								
7539	2.4	1.6	1.2	1.7	1.1	1.9	0.8	2.3
7563	1.7	0.9	1.5	1.3	1.2	1.2	1.3	1.4
7540	2.6	2.3	2.3	0.9	1.9	2.4	2.3	2.3
7554	4.3	3.4	1.9	2.1	1.4	4.5	3.7	3.4
7568	3.1	2.1	2.0	2.5	2.8	0.7	--	--
7544	1.8	2.6	2.5	1.8	2.2	2.1	--	--
7546	3.0	2.0	2.1	1.1	2.4	3.6	--	--
7551	1.7	1.7	1.9	1.1	1.5	1.7	--	--
MEAN	2.6	2.1	1.9	1.6	1.8	2.3	2.0	2.4
SD	0.89	0.74	0.42	0.56	0.61	1.25	1.28	0.82
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Monocytes

STUDY ID: 097  
STUDY NO: 097  
ABBR: Monocytes

SEX: FEMALE

UNITS: 10<sup>3</sup>/cmm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1F:0 mg base/kg/day								
7557	0.4	0.4	0.4	0.5	0.2	0.2	0.1	0.3
7541	0.3	0.1	0.2	0.5	0.3	0.2	0.1	0.3
7566	0.9	1.2	0.4	0.6	0.4	0.5	0.1	0.5
7549	0.7	0.4	0.2	0.2	0.1	0.3	0.3	0.2
7555	0.4	0.2	0.6	0.0	0.4	0.5	--	--
7558	0.5	0.3	1.0	0.7	0.2	0.6	--	--
7573	0.1	0.1	0.8	0.2	0.2	0.2	--	--
7542	0.8	0.9	0.4	0.6	0.4	0.5	--	--
MEAN	0.5	0.5	0.5	0.4	0.3	0.4	0.2	0.3
SD	0.27	0.40	0.28	0.25	0.12	0.17	0.10	0.13
N	8	8	8	8	8	8	4	4

GROUP: 2F:0.1 mg base/kg/day								
7543	0.3	0.1	0.1	0.5	1.0	0.4	0.3	0.4
7553	0.6	0.5	0.3	0.3	0.1	0.1	0.4	0.4
7545	0.2	0.5	0.6	0.5	0.4	0.3	0.3	0.1
7552	0.0	0.0	0.2	0.4	0.2	0.4	0.6	0.6
7569	0.3	0.5	0.2	0.3	0.3	0.1	--	--
7560	0.4	0.7	1.0	0.3	0.5	0.1	--	--
7567	0.6	0.8	0.5	0.3	0.2	0.8	--	--
7550	0.2	0.3	0.3	0.1	0.6	0.3	--	--
MEAN	0.3	0.4	0.4	0.3	0.4	0.3	0.4	0.4
SD	0.21	0.28	0.29	0.13	0.29	0.24	0.14	0.21
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Monocytes

STUDY ID: 097  
STUDY NO: 097  
ABBR: Monocytes

SEX: FEMALE

UNITS: 10<sup>3</sup>/cmm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3F:2.0 mg base/kg/day								
7562	0.6	0.2	0.3	0.3	0.1	0.3	0.2	0.0
7548	0.2	0.2	0.6	0.8	0.5	0.6	0.3	0.6
7571	0.3	0.4	0.6	0.6	0.7	0.1	0.7	0.4
7561	0.2	1.1	0.2	0.9	0.3	1.0	0.6	0.7
7564	0.3	0.5	0.6	0.8	0.5	0.5	--	--
7574	0.3	0.2	0.5	1.2	0.7	1.4	--	--
7556	0.7	0.4	0.2	0.8	0.8	0.9	--	--
7572	0.4	0.1	0.4	0.5	0.8	0.6	--	--
MEAN	0.4	0.4	0.4	0.7	0.6	0.7	0.5	0.4
SD	0.18	0.32	0.18	0.27	0.25	0.41	0.24	0.31
N	8	8	8	8	8	8	4	4

GROUP: 4F:6.0 mg base/kg/day								
7539	0.7	0.7	0.3	0.8	0.8	1.6	0.5	0.7
7563	0.8	1.2	0.7	0.6	0.6	1.4	0.3	0.8
7540	0.5	0.8	0.6	1.2	0.9	0.8	0.5	0.1
7554	0.5	0.9	0.7	0.6	1.1	1.3	1.8	0.8
7568	0.5	0.5	0.3	0.4	0.4	1.7	--	--
7544	0.5	0.7	0.3	1.0	0.4	0.4	--	--
7546	0.9	0.6	1.0	0.9	0.6	0.7	--	--
7551	0.7	0.3	0.8	0.6	1.0	0.6	--	--
MEAN	0.6	0.7	0.6	0.8	0.7	1.1	0.8	0.6
SD	0.16	0.27	0.26	0.26	0.27	0.50	0.69	0.34
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Eosinophils

STUDY ID: 097  
STUDY NO: 097  
ABBR: Eosinophil

SEX: FEMALE

UNITS: 10<sup>3</sup>/cmm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1F:0 mg base/kg/day								
7557	0.1	0.1	0.1	0.0	0.1	0.1	0.3	0.1
7541	0.0	0.1	0.3	0.0	0.0	0.1	0.1	0.2
7566	0.2	0.1	0.6	0.6	0.4	0.7	0.1	0.8
7549	0.1	0.1	0.1	0.1	0.0	0.1	0.1	0.1
7555	0.1	0.2	0.1	0.2	0.0	0.2	--	--
7558	0.1	0.0	0.0	0.0	0.0	0.2	--	--
7573	0.0	0.3	0.0	0.2	0.3	0.0	--	--
7542	0.1	0.6	0.5	0.2	0.3	0.3	--	--
MEAN	0.1	0.2	0.2	0.2	0.1	0.2	0.2	0.3
SD	0.06	0.19	0.23	0.20	0.17	0.22	0.10	0.34
N	8	8	8	8	8	8	4	4
GROUP: 2F:0.1 mg base/kg/day								
7543	0.6	0.0	0.1	0.3	0.2	0.6	0.3	0.0
7553	0.5	0.5	0.3	0.6	0.3	0.1	0.4	1.5
7545	0.3	0.1	0.0	0.5	0.4	0.7	0.1	0.3
7552	0.1	0.4	0.0	0.0	0.0	0.0	0.3	0.5
7569	0.1	0.3	0.5	0.3	0.3	0.5	--	--
7560	0.5	0.4	0.9	0.7	0.4	0.4	--	--
7567	0.2	0.1	0.5	0.3	0.4	0.1	--	--
7550	0.1	0.4	0.1	0.4	0.4	0.3	--	--
MEAN	0.3	0.3	0.3	0.4	0.3	0.3	0.3	0.6
SD	0.21	0.18	0.32	0.22	0.14	0.26	0.13	0.65
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or &gt; 10

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Eosinophils

STUDY ID: 097  
STUDY NO: 097  
ABBR: Eosinophil

SEX: FEMALE

UNITS: 10<sup>3</sup>/cmm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3F:2.0 mg base/kg/day								
7562	0.1	0.1	0.1	0.0	0.1	0.2	0.3	0.1
7548	0.2	0.4	0.2	0.4	0.0	0.3	0.1	0.3
7571	0.2	0.0	0.2	0.0	0.1	0.1	0.1	0.0
7561	0.2	0.3	0.0	0.0	0.3	0.0	0.1	0.1
7564	0.3	0.0	0.2	0.0	0.2	0.4	--	--
7574	0.2	0.1	0.0	0.1	0.0	0.2	--	--
7556	0.5	0.2	0.3	0.2	0.4	0.4	--	--
7572	0.0	0.3	0.0	0.2	0.5	0.3	--	--
MEAN	0.2	0.2	0.1	0.1	0.2	0.2	0.2	0.1
SD	0.15	0.15	0.12	0.15	0.19	0.14	0.10	0.13
N	8	8	8	8	8	8	4	4

GROUP: 4F:6.0 mg base/kg/day								
7539	0.3	0.3	0.2	0.3	0.2	0.1	0.3	0.2
7563	0.3	0.0	0.1	0.2	0.2	0.2	0.3	0.5
7540	0.1	0.1	0.0	0.0	0.2	0.1	0.1	0.5
7554	0.0	0.5	0.1	0.2	0.2	0.8	0.4	1.1
7568	0.1	0.1	0.1	0.0	0.2	0.2	--	--
7544	0.8	0.3	0.2	0.2	0.5	0.0	--	--
7546	0.0	0.0	0.0	0.1	0.3	0.2	--	--
7551	0.9	0.2	0.1	0.2	0.4	0.4	--	--
MEAN	0.3	0.2	0.1	0.2	0.3	0.3	0.3	0.6
SD	0.35	0.17	0.08	0.11	0.12	0.25	0.13	0.38
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Basophils

STUDY ID: 097  
STUDY NO: 097  
ABBR: Basophils

SEX: FEMALE  
UNITS: 10<sup>3</sup>/cmm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 1F:0 mg base/kg/day								
7557	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7541	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7566	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7549	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7555	0.0	0.0	0.0	0.0	0.0	0.0	--	--
7558	0.0	0.0	0.0	0.0	0.0	0.0	--	--
7573	0.0	0.0	0.0	0.0	0.0	0.0	--	--
7542	0.0	0.0	0.0	0.0	0.0	0.0	--	--
MEAN	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
SD	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
N	8	8	8	8	8	8	4	4

GROUP: 2F:0.1 mg base/kg/day								
7543	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7553	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7545	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7552	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0
7569	0.0	0.0	0.0	0.0	0.0	0.0	--	--
7560	0.0	0.0	0.0	0.0	0.0	0.0	--	--
7567	0.0	0.0	0.0	0.0	0.0	0.0	--	--
7550	0.0	0.0	0.0	0.0	0.0	0.0	--	--
MEAN	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
SD	0.00	0.00	0.00	0.00	0.04	0.00	0.00	0.00
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Basophils

STUDY ID: 097  
STUDY NO: 097  
ABBR: Basophils

SEX: FEMALE

UNITS: 10<sup>3</sup>/cmm

ANIMAL ID	Week -3	Week -1	Week 2	Week 4	Week 8	Week 13	Week 18	Week 26
GROUP: 3F:2.0 mg base/kg/day								
7562	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7548	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7571	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7561	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7564	0.0	0.0	0.0	0.0	0.0	0.0	--	--
7574	0.0	0.0	0.0	0.0	0.0	0.0	--	--
7556	0.0	0.0	0.0	0.0	0.0	0.0	--	--
7572	0.0	0.0	0.0	0.0	0.0	0.0	--	--
MEAN	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
SD	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
N	8	8	8	8	8	8	4	4

GROUP: 4F:6.0 mg base/kg/day								
7539	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7563	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7540	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7554	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7568	0.0	0.0	0.0	0.0	0.0	0.0	--	--
7544	0.0	0.0	0.0	0.0	0.0	0.0	--	--
7546	0.0	0.0	0.0	0.0	0.0	0.0	--	--
7551	0.0	0.0	0.0	0.0	0.0	0.0	--	--
MEAN	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
SD	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
N	8	8	8	8	8	8	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: 097  
STUDY NO: 097

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

SEX: FEMALE

ANIMAL ID	Week -3	Week -1	Week 2	Week 4
7557	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Normal Red Blood Cells
7541	Anisocytosis,Slight	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked	Anisocytosis,Slight	Normal Red Blood Cells
7566	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight
7549	Normal Red Blood Cells	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight
7555	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight
7558	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight
7573	Normal Red Blood Cells	Anisocytosis,Slight	Anisocytosis,Slight	Normal Red Blood Cells
7542	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: 097  
STUDY NO: 097

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

SEX: FEMALE

ANIMAL ID	Week 8	Week 13	Week 18	Week 26
7557	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight; Macrocytes,Slight	Anisocytosis,Slight
7541	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight
7566	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight
7549	Anisocytosis,Slight	Anisocytosis,Slight; Macrocytes,Slight	Anisocytosis,Slight	Normal Red Blood Cells
7555	Normal Red Blood Cells	Anisocytosis,Slight	--	--
7558	Anisocytosis,Slight	Anisocytosis,Slight	--	--
7573	Anisocytosis,Slight	Anisocytosis,Slight; Macrocytes,Slight	--	--
7542	Anisocytosis,Slight	Anisocytosis,Slight	--	--

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: 097

SEX: FEMALE

STUDY NO: 097

GROUP: 2F : 0.1 mg base/kg/day

ANIMAL ID	Week -3	Week -1	Week 2	Week 4
7543	Anisocytosis,Slight	Anisocytosis, Moderate	Anisocytosis,Slight	Anisocytosis,Slight
7553	Normal Red Blood Cells	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight
7545	Anisocytosis,Slight	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked	Anisocytosis,Slight	Normal Red Blood Cells
7552	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight
7569	Normal Red Blood Cells	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked	Anisocytosis,Slight	Anisocytosis,Slight
7560	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight
7567	Normal Red Blood Cells	Anisocytosis, Moderate	Anisocytosis,Slight	Normal Red Blood Cells
7550	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: 097  
STUDY NO: 097

GROUP: 2F : 0.1 mg base/kg/day

SEX: FEMALE

ANIMAL ID	Week 8	Week 13	Week 18	Week 26
7543	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight
7553	Anisocytosis,Slight	Poikilocytes,Slight; Anisocytosis,Slight	Anisocytosis,Slight	Increased Platelets, Moderate; Anisocytosis,Slight
7545	Anisocytosis,Slight	Anisocytosis,Slight; Clumped Platelets, Mod. to Marked	Anisocytosis,Slight	Anisocytosis,Slight
7552	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight; Macrocytes,Slight	Anisocytosis,Slight
7569	Anisocytosis,Slight	Normal Red Blood Cells	--	--
7560	Anisocytosis,Slight	Anisocytosis,Slight	--	--
7567	Anisocytosis,Slight	Anisocytosis,Slight	--	--
7550	Anisocytosis,Slight	Anisocytosis,Slight	--	--

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: 097  
STUDY NO: 097

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

SEX: FEMALE

ANIMAL ID	Week -3	Week -1	Week 2	Week 4
7562	Normal Red Blood Cells	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked
7548	Normal Red Blood Cells	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked
7571	Normal Red Blood Cells	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight; Large Platelets, Slight;Decreased Platelets,Mod. to Marked
7561	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight; Macrocytes,Slight
7564	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked	Anisocytosis,Slight
7574	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked	Anisocytosis,Slight; Decreased Platelets, Slight
7556	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked
7572	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight; Decreased Platelets, Slight	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: 097  
STUDY NO: 097

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

SEX: FEMALE

ANIMAL ID	Week 8	Week 13	Week 18	Week 26
7562	Normal Red Blood Cells; Decreased Platelets, Mod. to Marked	Anisocytosis, Slight	Anisocytosis, Slight	Anisocytosis, Moderate
7548	Normal Red Blood Cells	Normal Red Blood Cells	Anisocytosis, Slight	Poikilocytes, Slight; Anisocytosis, Slight
7571	Normal Red Blood Cells; Decreased Platelets, Slight	Anisocytosis, Slight	Anisocytosis, Slight	Anisocytosis, Slight
7561	Anisocytosis, Slight	Anisocytosis, Slight	Anisocytosis, Slight	Normal Red Blood Cells
7564	Anisocytosis, Slight	Anisocytosis, Slight	--	--
7574	Anisocytosis, Slight	Anisocytosis, Slight	--	--
7556	Anisocytosis, Slight	Anisocytosis, Slight	--	--
7572	Anisocytosis, Slight	Anisocytosis, Slight	--	--

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: 097  
STUDY NO: 097

GROUP: 4F : 6.0 mg base/kg/day

SEX: FEMALE

ANIMAL ID	Week -3	Week -1	Week 2	Week 4
7539	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked	Anisocytosis, Moderate;Decreased Platelets,Mod. to Marked
7563	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight	Normal Red Blood Cells
7540	Anisocytosis,Slight	Anisocytosis,Slight	Polychromasia,Slight Anisocytosis, Moderate;Large Platelets,Slight; Decreased Platelets, Mod. to Marked	Normal Red Blood Cells
7554	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight; Decreased Platelets, Slight	Anisocytosis, Moderate
7568	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked	Anisocytosis,Slight; Decreased Platelets, Mod. to Marked
7544	Anisocytosis,Slight	Anisocytosis,Slight	Anisocytosis, Moderate;Decreased Platelets,Mod. to Marked	Anisocytosis,Slight; Macrocytes,Slight
7546	Anisocytosis,Slight	Anisocytosis,Slight	Large Platelets, Slight;Decreased Platelets,Mod. to Marked;Anisocytosis, Moderate	Anisocytosis, Moderate;Decreased Platelets,Mod. to Marked
7551	Normal Red Blood Cells	Anisocytosis,Slight	Anisocytosis, Moderate;Large Platelets,Slight; Decreased Platelets, Mod. to Marked	Anisocytosis, Moderate;Large Platelets,Slight; Decreased Platelets, Mod. to Marked

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: 097  
STUDY NO: 097

GROUP: 4F : 6.0 mg base/kg/day

SEX: FEMALE

ANIMAL ID	Week 8	Week 13	Week 18	Week 26
7539	Anisocytosis, Slight; Decreased Platelets, Slight	Anisocytosis, Slight	Anisocytosis, Slight	Normal Red Blood Cells
7563	Anisocytosis, Slight	Anisocytosis, Slight	Anisocytosis, Slight	Anisocytosis, Slight
7540	Anisocytosis, Slight	Anisocytosis, Slight; Macrocytes, Slight	Anisocytosis, Slight	Normal Red Blood Cells
7554	Anisocytosis, Slight	Anisocytosis, Slight	Anisocytosis, Slight	Anisocytosis, Slight
7568	Anisocytosis, Slight; Decreased Platelets, Slight	Anisocytosis, Slight; Macrocytes, Slight	--	--
7544	Anisocytosis, Slight	Anisocytosis, Slight	--	--
7546	Anisocytosis, Slight; Decreased Platelets, Moderate	Anisocytosis, Slight; Macrocytes, Slight	--	--
7551	Anisocytosis, Slight; Decreased Platelets, Marked	Anisocytosis, Slight; Decreased Platelets, Moderate	--	--

(--)-Data Unavailable

DRAFT

APPENDIX 8  
Individual Urinalysis Data

URINALYSIS INFORMATION

DRAFT

A. Abbreviations

APP = Appearance	DY = Dark Yellow
SG = Specific Gravity	PY = Pale Yellow
PRO = Protein	LY = Light Yellow
GLU = Glucose	BR = Brown
KET = Ketones	AM = Amber
BILI = Bilirubin	> = Greater than
BL = Blood	FAT = Fatty
URO = Urobilinogen	WH = White
LEU = Leukocytes	BY = Bright Yellow
NIT = Nitrite	CL = Colorless
EPI = Epithelial	E = Erythrocyte
SQ = Squamous	FG = Fine Granular
TRANS = Transitional	CG = Course Granular
NA = Not Applicable	HY = Hyaline
TP = Triple Phosphate	GR = Granular
QNS = Quantity Not Sufficient	S = Starch
Y = Yellow	RC = Red Cell
	WC = Waxy

B. Qualitative Evaluation

Protein:	Negative Trace 1+ (30 mg/dl) 2+ (100 mg/dl) 3+ (500 mg/dl)	Bilirubin:	Negative 1+ (slight) 2+ (moderate) 3+ (marked)
Glucose:	Normal Trace (1/20 g/dl) 1+ (1/10 g/dl) 2+ (1/4 g/dl) 3+ (1/2 g/dl) 4+ (1 g/dl)	Blood:	Negative 5-10 Ery/ul 50 Ery/ul 250 Ery/ul
Ketones:	Negative 1+ (slight amount) 2+ (moderate) 3+ (large)	Leukocytes:	Negative Trace 1+ (moderate) 2+ (marked)
Urobilinogen:	Normal 1+ (1 mg/dl) 2+ (4 mg/dl) 3+ (8 mg/dl) 4+ (12 mg/dl)	Nitrite:	Negative Positive

C. Microscopic Examination: Five fields are examined.

Casts:	av. #/10x field
RBC's:	av. #/45x field
WBC's:	av. #/45x field
Epithelial Cells - Squamous:	av. #/45x field
- Transitional:	av. #/45x field
- Renal:	av. #/45x field
Crystals; Bacteria; Sperm; Mucus -	0 = Negative
	1+ = Occasional
	2+ = Seen in every field
	3+ = Large amounts in every field
	4+ = Full fields

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

Male Urinalysis Data (Week -1)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	APP	SG	COLOR	NIT	LEU	pH	PROT	GLU g/dl	KET	URO	BILI	BLOOD Ery/ul
0	7505	HAZY	1.008	LY	POS	TRACE	7	TRACE	NOR	NEG	NOR	NEG	5-10
	7512	HAZY	1.078	DY	NEG	NEG	6	+	NOR	NEG	NOR	NEG	50
	7515	HAZY	1.040	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7520	HAZY	1.030	Y	NEG	+	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7521	HAZY	1.024	LY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	50
	7531	CLEAR	1.090	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7532	CLEAR	1.090	Y	NEG	NEG	5	TRACE	NOR	NEG	NOR	NEG	NEG
	7533	HAZY	1.066	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
0.1	7503	CLEAR	1.040	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7517	HAZY	1.024	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7519	HAZY	1.038	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7523	HAZY	1.070	Y	NEG	NEG	7	TRACE	NOR	NEG	NOR	NEG	NEG
	7527	CLOUDY	1.056	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7528	HAZY	1.075	AM	NEG	++	8	+	NOR	NEG	NOR	NEG	NEG
	7529	HAZY	1.126	Y	NEG	NEG	5	TRACE	NOR	NEG	NOR	NEG	50
	7536	HAZY	1.026	LY	NEG	+	6	TRACE	NOR	NEG	NOR	NEG	NEG
2.0	7502	CLOUDY	1.132	AM	NEG	NEG	6	+	NOR	NEG	NOR	NEG	50
	7506	CLOUDY	1.052	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	250
	7510	HAZY	1.052	DY	NEG	NEG	6	NEG	NOR	NEG	NOR	NEG	250
	7514	HAZY	1.066	Y	NEG	TRACE	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7516	HAZY	1.042	Y	NEG	NEG	7	TRACE	NOR	NEG	NOR	NEG	NEG
	7522	CLOUDY	1.081	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7538	*	1.018	LY	NEG	++	7	NEG	NOR	NEG	NOR	NEG	NEG
	7576	CLEAR	1.070	DY	NEG	NEG	5	TRACE	NOR	NEG	NOR	NEG	NEG
6.0	7507	CLEAR	1.052	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7508	CLOUDY	1.096	DY	NEG	+	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7509	CLOUDY	1.093	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7511	HAZY	1.040	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7518	CLOUDY	1.014	Y	POS	++	7	TRACE	NOR	NEG	NOR	NEG	250
	7524	CLEAR	1.017	Y	NEG	++	5	TRACE	NOR	NEG	NOR	NEG	50
	7530	HAZY	1.036	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	50
	7535	HAZY	1.034	Y	NEG	+	7	TRACE	NOR	NEG	NOR	NEG	5-10

\*Inadvertently not collected.

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

Male Urinalysis Data (Week -1)

DRAFT

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	CASTS	RBC	WBC	EPITHELIAL CELLS			CRYSTALS	BACTERIA	SPERM	MUCUS
					SQ	TRANS	RENAL				
0	7505	0	2	0	0	0	0	0	1+	0	0
	7512	1 FG 4 HY	0	1	2	0	0	1+ TP	1+	0	0
	7515	1 CG	0	0	1	0	0	1+ TP	1+	1+	0
	7520	1 HY	10	4	2	0	0	0	2+	0	0
	7521	1 FG	0	0	1	0	0	0	1+	1+	0
	7531	1 HY 1 FG	1	2	1	0	0	1+ TP	1+	0	0
	7532	3 HY	0	1	2	0	0	0	1+	0	0
	7533	2 CGH	3	10	1	0	0	0	1+	1+	0
0.1	7503	1 FG 2 HY	10	0	1	0	0	0	1+	0	0
	7517	3 HY	2	0	4	0	0	1+ TP	1+	0	0
	7519	4 HY	10	1	5	0	0	1+ TP	1+	0	0
	7523	1 CG	0	2	1	0	0	2+ TP	1+	1+	0
	7527	2 FG	15	3	2	0	0	0	1+	0	0
	7528	2 FG 1 CG	1	0	3	0	0	1+ TP	1+	0	0
	7529	1 FG	52	3	1	0	0	1+ TP	1+	0	0
	7536	1 FG	0	2	0	0	0	0	1+	1+	0
2.0	7502	4 HY 1 FG	20	2	3	0	0	1+ TP	1+	0	0
	7506	1 HY	4	0	2	0	0	2+ TP	2+	0	0
	7510	1 FG	20	14	1	0	0	0	1+	1+	0
	7514	1 FG	45	0	2	0	0	1+ TP	1+	1+	0
	7516	1 FG	0	16	0	0	0	1+ TP	1+	0	0
	7522	2 FG 4 HY	10	2	1	0	0	0	1+	1+	0
	7538	0	0	0	5	0	0	0	1+	1+	0
	7576	3 HY 3 FG	1	0	1	0	0	0	1+	0	0
6.0	7507	3 HY 1 FG	25	0	1	0	0	1+ TP	1+	0	0
	7508	0	0	0	0	0	0	2+ TP	1+	0	0
	7509	0	1	10	1	0	0	1+ TP	1+	1+	0
	7511	1 CG 1 FG	3	10	1	0	0	0	1+	0	0
	7518	2 HY	1	0	2	0	0	0	2+	0	0
	7524	3 FG 4 HY	3	0	2	0	0	0	1+	0	0
	7530	1 FG	0	12	4	0	0	1+ TP	1+	1+	0
	7535	1 FG	5	4	0	0	0	1+ TP	1+	1+	0

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

Female Urinalysis Data (Week -1)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	APP	SG	COLOR	NTT	LEU	pH	PROT	GLU g/dl	KET	URO	BILI	BLOOD Ery/ul
0	7541	HAZY	1.090	Y	NEG	NEG	5	NEG	NOR	NEG	NOR	NEG	5-10
	7542	HAZY	1.081	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	50
	7549	HAZY	1.084	DY	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7555	HAZY	1.093	Y	NEG	NEG	9	TRACE	NOR	NEG	NOR	NEG	NEG
	7557	CLEAR	1.075	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7558	CLOUDY	1.105	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7566	CLEAR	1.035	Y	NEG	NEG	8	TRACE	NOR	NEG	NOR	NEG	50
	7573	HAZY	1.042	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	5-10
0.1	7543	HAZY	1.048	Y	NEG	NEG	7	TRACE	NOR	NEG	NOR	NEG	NEG
	7545	HAZY	1.050	Y	POS	NEG	5	TRACE	NOR	NEG	NOR	NEG	5-10
	7550	HAZY	1.045	AM	POS	++	8	TRACE	NOR	NEG	NOR	NEG	50
	7552	HAZY	1.112	DY	NEG	NEG	5	TRACE	NOR	NEG	NOR	NEG	NEG
	7553	CLEAR	1.044	Y	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7560	CLOUDY	1.040	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	50
	7567	CLEAR	1.060	DY	NEG	TRACE	8	TRACE	NOR	NEG	NOR	NEG	50
	7569	HAZY	1.050	Y	NEG	NEG	6	NEG	NOR	NEG	NOR	NEG	NEG
2.0	7548	HAZY	1.044	LY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7556	HAZY	1.072	Y	NEG	NEG	7	TRACE	NOR	NEG	NOR	NEG	NEG
	7561	HAZY	1.036	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7562	CLEAR	1.044	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	250
	7564	HAZY	1.068	Y	NEG	NEG	5	TRACE	NOR	NEG	NOR	NEG	NEG
	7571	CLOUDY	1.015	Y	POS	2+	8	TRACE	NOR	NEG	NOR	NEG	250
	7572	HAZY	1.040	Y	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	50
	7574	HAZY	1.030	LY	NEG	NEG	8	TRACE	NOR	NEG	NOR	NEG	50
6.0	7539	CLEAR	1.044	Y	NEG	NEG	7	TRACE	NOR	NEG	NOR	NEG	NEG
	7540	CLOUDY	1.096	AM	NEG	NEG	5	TRACE	NOR	NEG	NOR	NEG	5-10
	7544	CLOUDY	1.020	Y	POS	NEG	8	1+	NOR	NEG	NOR	NEG	50
	7546	CLOUDY	1.072	Y	NEG	NEG	5	TRACE	NOR	NEG	NOR	NEG	NEG
	7551	CLEAR	1.064	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7554	HAZY	1.062	Y	NEG	NEG	8	TRACE	NOR	NEG	NOR	NEG	NEG
	7563	HAZY	1.120	Y	NEG	NEG	7	TRACE	NOR	NEG	NOR	NEG	NEG
	7568	HAZY	1.062	LY	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

DRAFT

## Female Urinalysis Data (Week -1)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	CASTS	RBC	WBC	EPITHELIAL CELLS			CRYSTALS	BACTERIA	SPERM	MUCUS
					SQ	TRANS	RENAL				
0	7541	1 FG	0	0	2	0	0	1+ TP	1+	0	0
	7542	1 FG	0	0	5	0	0	0	1+	0	0
	7549	1 GH 2 FG	1	5	0	0	0	2+ TP	1+	0	0
	7555	1 CG	0	0	1	0	0	2+ TP	1+	0	0
	7557	1 HY 3 FG	6	1	1	0	0	1+ TP	1+	0	0
	7558	7 FG 1 CG	0	10	0	0	0	1+ TP	1+	0	0
	7566	1 HY	3	1	1	0	0	2+ TP	2+	0	0
	7573	3 HY	4	0	1	0	0	0	1+	0	0
0.1	7543	2 FG	0	3	0	0	0	1+ TP	1+	0	0
	7545	4 HY 1 FG	4	1	5	1	0	1+ TP	2+	0	0
	7550	2 HY	1	0	2	0	0	3+ TP	2+	0	0
	7552	4 HY 1 FG	0	0	3	0	0	1+ TP	1+	0	0
	7553	2 HY	5	0	2	1	0	1+ TP	1+	0	0
	7560	1 CG	8	0	3	0	0	1+ TP	1+	0	0
	7567	2 HY 1 FG	0	2	1	0	0	2+ TP	1+	0	0
	7569	1 FG	0	0	0	0	0	1+ TP	1+	0	0
2.0	7548	1 HY 1 FG	7	0	1	1	0	1+ TP	1+	0	0
	7556	0	11	4	0	0	0	1+ TP	1+	0	0
	7561	3 HY 1 FG	2	0	2	1	0	1+ TP	1+	0	0
	7562	2 HY 1 FG	4	2	2	0	0	1+ TP	1+	0	0
	7564	1 FG	0	0	20	0	0	0	1+	0	0
	7571	1 HY	4	0	0	1	0	2+ TP	4+	0	0
	7572	0	0	3	2	1	0	0	1+	0	0
	7574	0	0	0	1	0	0	1+ TP	1+	0	0
6.0	7539	1 HY	2	1	1	0	0	1+ TP	2+	0	0
	7540	3 HY	4	2	4	1	0	2+ TP	1+	0	0
	7544	2 FG	4	0	3	1	0	1+ TP	1+	0	0
	7546	4 HY	0	0	0	0	0	1+ TP	1+	0	0
	7551	2 FG	2	5	1	0	0	0	1+	0	0
	7554	1 FG	0	0	5	0	0	1+ TP	1+	0	0
	7563	1 CG 1 FG	0	2	0	0	0	2+ TP	1+	0	0
	7568	1 CG	0	0	0	0	0	1+ TP	1+	0	0

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

Male Urinalysis Data (Week 2)

DRAFT

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	APP	SG	COLOR	NIT	LEU	pH	PROT	GLU g/dl	KET	URO	BILI	BLOOD Ery/tul
0	7505	CLEAR	1.040	LY	NEG	NEG	5	NEG	NOR	NEG	NOR	NEG	5-10
	7512	CLEAR	1.084	Y	NEG	++	7	+	NOR	NEG	NOR	NEG	5-10
	7515	HAZY	1.026	Y	NEG	+	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7520	CLOUDY	1.040	Y	POS	++	7	TRACE	NOR	NEG	NOR	NEG	5-10
	7521	HAZY	1.064	DY	NEG	NEG	6	NEG	NOR	NEG	NOR	NEG	NEG
	7531	CLEAR	1.116	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7532	CLOUDY	1.019	Y	POS	+	7	TRACE	NOR	NEG	NOR	NEG	50
	7533	CLOUDY	1.093	AM	POS	++	6	+	NOR	NEG	NOR	NEG	5-10
0.1	7503	CLOUDY	1.056	Y	NEG	+	6	TRACE	NOR	NEG	NOR	NEG	50
	7517	CLOUDY	1.075	DY	NEG	++	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7519	HAZY	1.075	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7523	CLEAR	1.048	Y	NEG	NEG	7	TRACE	NOR	NEG	NOR	NEG	NEG
	7527	CLEAR	1.042	LY	NEG	+	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7528	TURBID	1.042	AM	NEG	++	7	TRACE	NOR	NEG	NOR	NEG	250
	7529	HAZY	1.116	DY	NEG	NEG	5	TRACE	NOR	NEG	NOR	NEG	NEG
	7536	HAZY	1.099	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
2.0	7502	HAZY	1.066	AM	NEG	NEG	6	+	NOR	NEG	NOR	NEG	50
	7506	CLOUDY	1.081	DY	NEG	+	6	TRACE	NOR	NEG	NOR	NEG	50
	7510	CLOUDY	1.090	DY	NEG	++	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7514	CLOUDY	1.078	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7516	CLOUDY	1.064	DY	NEG	++	6	+	NOR	NEG	NOR	NEG	50
	7522	TURBID	1.165	BR	NEG	NEG	6	+	NOR	NEG	NOR	NEG	NEG
	7538	CLEAR	1.050	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7576	CLOUDY	1.087	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
6.0	7507	CLEAR	1.021	Y	NEG	NEG	7	NEG	NOR	NEG	NOR	NEG	NEG
	7508	TURBID	1.099	DY	NEG	+	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7509	CLOUDY	1.090	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7511	CLOUDY	1.075	DY	NEG	TRACE	6	TRACE	NOR	NEG	NOR	NEG	50
	7518	CLOUDY	1.084	AM	NEG	+	7	TRACE	NOR	NEG	NOR	NEG	5-10
	7524	TURBID	1.150	BR	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7530	CLOUDY	1.056	DY	NEG	++	6	TRACE	NOR	NEG	NOR	NEG	50
	7535	CLOUDY	1.066	DY	NEG	+	6	+	NOR	NEG	NOR	NEG	5-10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

Male Urinalysis Data (Week 2)

DRAFT

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	CASTS	RBC	WBC	EPITHELIAL CELLS			CRYSTALS	BACTERIA	SPERM	MUCUS
					SQ	TRANS	RENAL				
0	7505	2 HY	2	0	3	0	0	1+ TP	1+	0	0
	7512	2 HY	2	0	3	0	0	3+ TP	1+	0	0
	7515	4 HY	23	2	2	0	0	0	1+	0	0
	7520	3 HY	20	4	2	0	0	3+ TP	2+	1+	0
	7521	1 CG	20	3	2	1	0	1+ TP	1+	1+	0
	7531	1 HY	0	0	2	0	0	4+ TP	1+	0	0
	7532	0	0	0	0	0	0	1+ TP	2+	0	0
	7533	1 HY	6	0	1	0	0	1+ TP	1+	2+	0
0.1	7503	1 FG 2 HY	15	0	1	1	0	0	1+	0	0
	7517	1 HY	30	10	5	0	0	1+ TP	1+	1+	0
	7519	1 HY	10	0	3	1	0	0	1+	2+	0
	7523	1 HY	0	1	2	0	0	1+ TP	1+	1+	0
	7527	1 HY	4	0	2	0	0	0	3+	0	0
	7528	1 HY	15	0	1	0	0	1+ TP	1+	0	0
	7529	1 FG	0	50	1	0	0	1+ TP	1+	1+	0
	7536	2 FG 5 HY	3	1	3	0	0	1+ TP	2+	0	0
2.0	7502	3 FG	5	2	4	0	0	3+ TP	1+	0	0
	7506	1 CG	6	0	4	0	0	1+ TP	1+	0	0
	7510	1 HY 1 CG	6	0	4	0	0	2+ TP	1+	1+	0
	7514	5 FG 1 HY	4	2	1	0	0	1+ TP	1+	1+	0
	7516	2 FG	50	5	10	0	0	2+ TP	1+	0	0
	7522	1 FG	0	0	1	0	0	2+ TP	1+	1+	0
	7538	3 FG	0	0	2	0	0	2+ TP	1+	1+	0
	7576	1 HY	0	0	4	0	0	0	1+	0	0
6.0	7507	2 FG	15	0	1	0	0	1+ TP	1+	1+	0
	7508	1 HY	5	10	3	0	0	1+ TP	1+	0	0
	7509	1 FG	4	0	0	0	0	1+ TP	2+	0	0
	7511	2 HY 1 FG	4	0	4	0	0	1+ TP	2+	1+	0
	7518	3 HY	10	2	1	0	0	2+ TP	1+	0	0
	7524	1 FG	0	0	0	0	0	1+ TP	1+	0	0
	7530	1 FG 1 HY	10	0	3	0	0	1+ TP	1+	1+	0
	7535	1 FG	10	0	1	0	0	1+ TP	1+	0	0

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

Female Urinalysis Data (Week 2)

DRAFT

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	APP	SG	COLOR	NIT	LEU	pH	PROT	GLU g/dl	KET	URO	BILI	BLOOD Ery/ul
0	7541	HAZY	1.099	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7542	HAZY	1.070	Y	NEG	+	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7549	CLOUDY	1.040	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7555	CLOUDY	1.096	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	50
	7557	CLEAR	1.081	LY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7558	HAZY	1.093	AM	NEG	++	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7566	CLOUDY	1.052	DY	NEG	++	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7573	CLEAR	1.042	LY	NEG	NEG	7	+	NOR	NEG	NOR	NEG	5-10
0.1	7543	CLEAR	1.105	DY	NEG	NEG	9	TRACE	NOR	NEG	NOR	NEG	NEG
	7545	CLEAR	1.027	Y	POS	+	6	TRACE	NOR	NEG	NOR	NEG	50
	7550	CLOUDY	1.120	BR	NEG	NEG	6	+	NOR	NEG	NOR	NEG	50
	7552	TURBID	1.112	AM	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7553	HAZY	1.054	Y	NEG	++	7	TRACE	NOR	NEG	NOR	NEG	5-10
	7560	CLOUDY	1.042	DY	NEG	NEG	6	NEG	NOR	NEG	NOR	NEG	NEG
	7567	HAZY	1.078	DY	NEG	++	6	+	NOR	NEG	NOR	NEG	50
	7569	HAZY	1.044	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
2.0	7548	HAZY	1.050	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7556	HAZY	1.066	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7561	CLEAR	1.064	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7562	CLOUDY	1.081	DY	NEG	NEG	9	+	NOR	NEG	NOR	NEG	NEG
	7564	HAZY	1.120	AM	NEG	NEG	8	+	NOR	NEG	NOR	NEG	NEG
	7571	HAZY	1.046	Y	NEG	NEG	7	TRACE	NOR	NEG	NOR	NEG	NEG
	7572	CLOUDY	1.044	DY	POS	++	6	TRACE	NOR	NEG	NOR	NEG	50
	7574	CLEAR	1.078	DY	NEG	NEG	7	TRACE	NOR	NEG	NOR	NEG	NEG
6.0	7539	CLEAR	1.050	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7540	TURBID	1.090	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7544	CLOUDY	1.054	DY	NEG	NEG	7	TRACE	NOR	NEG	NOR	NEG	NEG
	7546	HAZY	1.112	BR	NEG	NEG	7	+	NOR	NEG	NOR	NEG	NEG
	7551	CLOUDY	1.069	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7554	HAZY	1.072	DY	POS	NEG	7	TRACE	NOR	NEG	NOR	NEG	50
	7563	HAZY	1.057	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7568	CLOUDY	1.075	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

Female Urinalysis Data (Week 2)

DRAFT

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	CASTS	RBC	WBC	EPITHELIAL CELLS			CRYSTALS	BACTERIA	SPERM	MUCUS
					SQ	TRANS	RENAL				
0	7541	1 HY	0	0	2	0	0	0	1+	0	0
	7542	2 HY	0	0	0	0	0	1+ TP	1+	0	0
	7549	1 HY 1 CG	50	10	7	0	0	2+ TP	1+	1+	0
	7555	2 HY	5	0	0	0	0	2+ TP	1+	0	0
	7557	1 HY	3	0	4	0	0	2+ TP	1+	0	0
	7558	1 HY	15	3	4	0	0	1+ TP	1+	0	0
	7566	1 FG	150	0	5	0	0	2+ TP	1+	0	0
7573	0	2	0	1	0	0	3+ TP	1+	0	0	
0.1	7543	0	10	1	2	1	0	2+ TP	2+	0	0
	7545	1 HY	10	1	5	1	0	0	1+	0	0
	7550	0	1	0	1	1	0	1+ TP	1+	0	0
	7552	1 FG	8	0	3	0	0	2+ TP	1+	0	0
	7553	2 HY	20	0	4	4	0	3+ TP	1+	0	0
	7560	1 CG 2 FG 1 HY	0	4	0	1	0	1+ TP	2+	0	0
	7567	1 FG	5	0	1	0	0	1+ TP	1+	1+	0
	7569	0	2	0	3	1	0	1+ TP	1+	0	0
2.0	7548	4 HY	10	2	8	3	0	2+ TP	1+	0	0
	7556	1 FG 3 HY	8	0	1	0	0	0	1+	0	0
	7561	1 FG	2	5	3	0	0	1+ TP	1+	0	0
	7562	2 HY	2	0	1	0	0	1+ TP	1+	0	0
	7564	4 HY	2	0	3	0	0	2+ TP	1+	0	0
	7571	5 HY	2	0	6	1	0	1+ TP	1+	0	0
	7572	10 HY	0	0	5	0	0	0	2+	0	0
	7574	0	0	0	2	0	0	1+ TP	1+	0	0
6.0	7539	3 HY	3	0	2	1	0	0	1+	0	0
	7540	1 FG	0	0	3	0	0	0	1+	0	0
	7544	4 CG	8	10	5	1	0	2+ TP	1+	0	0
	7546	2 HY	0	0	3	1	1	1+ TP	1+	0	0
	7551	3 HY 7 FG	0	0	8	1	0	1+ TP	1+	0	0
	7554	2 FG	3	0	2	0	0	2+ TP	1+	0	0
	7563	1 HY 1 FG	3	0	1	0	0	0	1+	0	0
	7568	1 FG	0	0	0	1	0	1+ TP	1+	0	0

## THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

### Male Urinalysis Data (Week 4)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	APP	SG	COLOR	NIT	LEU	pH	PROT	GLU g/dl	KET	URO	BILI	BLOOD Ery/ul
0	7505	CLEAR	1.038	Y	NEG	+	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7512	HAZY	1.093	Y	NEG	NEG	6	NEG	NOR	NEG	NOR	NEG	5-10
	7515	CLEAR	1.030	Y	NEG	+	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7520	CLOUDY	1.060	Y	NEG	+	6	TRACE	NOR	NEG	NOR	NEG	50
	7521	CLOUDY	1.0215	DY	POS	++	8	TRACE	NOR	NEG	NOR	NEG	250
	7531	CLEAR	1.046	Y	NEG	TRACE	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7532	TURBID	1.030	DY	NEG	TRACE	7	TRACE	NOR	NEG	NOR	NEG	50
	7533	HAZY	1.143	DY	NEG	TRACE	6	TRACE	NOR	NEG	NOR	NEG	NEG
0.1	7503	CLOUDY	1.035	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7517	CLOUDY	1.046	Y	NEG	+	8	TRACE	NOR	NEG	NOR	NEG	50
	7519	CLOUDY	1.066	Y	NEG	+	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7523	HAZY	1.048	Y	NEG	++	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7527	HAZY	1.084	Y	NEG	TRACE	5	TRACE	NOR	NEG	NOR	NEG	5-10
	7528	CLOUDY	1.030	DY	POS	++	7	+	1/20	NEG	NOR	NEG	250
	7529	CLOUDY	1.090	DY	NEG	+	6	TRACE	NOR	NEG	NOR	NEG	50
	7536	CLOUDY	1.090	DY	NEG	NEG	5	TRACE	NOR	NEG	NOR	NEG	50
2.0	7502	HAZY	1.046	DY	NEG	+	7	TRACE	NOR	NEG	NOR	+	5-10
	7506	CLOUDY	1.038	DY	NEG	+	6	TRACE	NOR	NEG	NOR	NEG	50
	7510	CLOUDY	1.056	DY	NEG	++	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7514	HAZY	1.062	DY	NEG	NEG	6	TRACE	NOR	NEG	*	NEG	5-10
	7516	HAZY	1.070	AM	NEG	++	6	TRACE	NOR	NEG	NOR	++	5-10
	7522	HAZY	1.058	AM	NEG	++	6	TRACE	NOR	NEG	NOR	NEG	50
	7538	HAZY	1.070	AM	NEG	NEG	6	TRACE	NOR	NEG	NOR	+	NEG
	7576	CLEAR	1.064	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
6.0	7507	CLEAR	1.068	DY	NEG	TRACE	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7508	CLOUDY	1.060	AM	POS	+	6	TRACE	NOR	NEG	NOR	NEG	50
	7509	CLEAR	1.084	DY	NEG	NEG	5	TRACE	NOR	NEG	NOR	++	5-10
	7511	HAZY	1.099	DY	NEG	TRACE	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7518	HAZY	1.016	Y	NEG	TRACE	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7524	CLOUDY	1.112	AM	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7530	CLEAR	1.155	AM	NEG	NEG	5	TRACE	NOR	NEG	NOR	NEG	5-10
	7535	CLOUDY	1.090	DY	POS	++	7	TRACE	NOR	NEG	NOR	NEG	NEG

\*Inadvertently not collected.

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

DRAFT

## Male Urinalysis Data (Week 4)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	CASTS	RBC	WBC	EPITHELIAL CELLS			CRYSTALS	BACTERIA	SPERM	MUCUS
					SQ	TRANS	RENAL				
0	7505	3 HY 1 FG	4	0	6	0	0	1+ TP	1+	1+	0
	7512	1 FG	15	0	2	1	0	1+ TP	1+	0	0
	7515*										
	7520	2 HY	50	10	5	1	0	2+ TP	1+	1+	0
	7521	3 HY	2	0	1	0	0	1+ TP	3+	0	0
	7531	3 HY	1	0	2	0	0	1+ TP	1+	0	0
	7532	1 HY	0	0	3	0	0	1+ TP	2+	0	0
	7533	1 HY	4	0	4	0	0	1+ TP	1+	0	0
0.1	7503*										
	7517	1 HY	1	0	2	0	0	2+ TP	1+	0	0
	7519	1 HY 1 FG	30	2	2	0	0	0	1+	1+	0
	7523	1 FG	58	1	1	1	0	0	1+	1+	0
	7527	1 FG	35	5	1	0	0	1+ TP	1+	0	0
	7528	2 HY	4	0	3	0	0	0	1+	0	0
	7529	1 FG	20	2	0	0	0	1+ TP	1+	1+	0
	7536	1 HY	70	1	1	0	0	0	1+	1+	0
2.0	7502	2 HY	20	0	2	0	0	1+ TP	1+	0	0
	7506	2 HY	1	0	2	0	0	0	3+	0	0
	7510	1 HY	20	0	3	0	0	1+ TP	1+	1+	0
	7514	4 FG 1 HY	50	0	0	0	0	0	1+	1+	0
	7516	1 HY	50	0	5	0	0	1+ TP	1+	0	0
	7522	1 FG 1 HY	8	2	4	0	0	1+ TP	1+	1+	0
	7538	2 FG	0	0	1	0	0	1+ TP	1+	2+	0
	7576	1 HY 2 FG	0	0	7	0	0	1+ TP	1+	1+	0
6.0	7507	1 HY 1 FG	10	0	0	1	0	0	1+	1+	0
	7508	2 FG 1 HY	0	0	4	0	0	1+ TP	1+	0	0
	7509	2 FG	25	0	0	1	0	0	1+	2+	0
	7511	1 CG 1 HY	12	1	1	0	0	1+ TP	1+	1+	0
	7518	0	4	0	1	0	0	1+ TP	1+	2+	0
	7524	2 FG	10	0	3	0	0	1+ TP	1+	1+	0
	7530	1 FG	0	2	2	0	0	1+ TP	1+	1+	0
	7535	1 HY	0	0	1	0	0	1+ TP	1+	0	0

\*Inadvertently not collected.

# DRAFT

UIC/TRL Study No. 097

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

Female Urinalysis Data (Week 4)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	APP	SG	COLOR	NIT	LEU	pH	PROT	GLU g/dl	KET	URO	BILI	BLOOD Ery/ul
0	7541	CLEAR	1.087	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7542	CLEAR	1.087	Y	NEG	NEG	5	NEG	NOR	NEG	NOR	NEG	NEG
	7549	HAZY	1.040	Y	NEG	NEG	5	TRACE	NOR	NEG	NOR	NEG	5-10
	7555	CLEAR	1.090	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7557	HAZY	1.068	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	250
	7558	CLEAR	1.052	Y	NEG	++	9	NEG	NOR	NEG	NOR	NEG	5-10
	7566	CLEAR	1.054	Y	POS	+	7	TRACE	NOR	NEG	NOR	NEG	5-10
	7573	CLOUDY	1.060	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	5-10
0.1	7543	CLEAR	1.056	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7545	CLEAR	1.018	PY	POS	NEG	6	NEG	NOR	NEG	NOR	NEG	NEG
	7550	CLEAR	1.050	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7552	*	1.081	*	NEG	NEG	5	TRACE	NOR	NEG	NOR	NEG	NEG
	7553	CLEAR	1.044	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7560	HAZY	1.019	Y	NEG	+	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7567	CLOUDY	1.052	LY	POS	NEG	7	TRACE	NOR	NEG	NOR	NEG	250
	7569	CLEAR	1.052	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
2.0	7548	HAZY	1.042	AM	NEG	+	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7556	CLEAR	1.058	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7561	HAZY	1.078	DY	NEG	NEG	6	NEG	NOR	NEG	NOR	NEG	5-10
	7562	HAZY	1.042	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7564	HAZY	1.090	Y	NEG	NEG	5	NEG	NOR	NEG	NOR	NEG	NEG
	7571	HAZY	1.052	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	250
	7572	CLOUDY	1.030	Y	POS	+	6	NEG	NOR	NEG	NOR	*	50
	7574	CLEAR	1.064	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
6.0	7539	CLEAR	1.044	DY	NEG	TRACE	8	TRACE	NOR	NEG	NOR	NEG	5-10
	7540	HAZY	1.050	AM	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7544	HAZY	1.040	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7546	CLEAR	1.054	AM	POS	TRACE	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7551	CLOUDY	1.084	BR	POS	NEG	7	TRACE	NOR	NEG	NOR	NEG	250
	7554	HAZY	1.060	DY	NEG	NEG	7	TRACE	NOR	NEG	NOR	NEG	5-10
	7563	HAZY	1.069	AM	NEG	NEG	7	TRACE	NOR	NEG	NOR	NEG	NEG
	7568	CLOUDY	1.084	BR	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG

\*Inadvertently not collected.

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

Female Urinalysis Data (Week 4)

DRAFT

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	CASTS	RBC	WBC	EPITHELIAL CELLS			CRYSTALS	BACTERIA *	SPERM	MUCUS
					SQ	TRANS	RENAL				
0	7541	1 FG	0	0	2	0	0	1+ TP	1+	0	0
	7542	2 HY	5	0	1	0	0	0	1+	0	0
	7549	2 HY 1 FG	10	5	6	0	0	1+ TP	1+	0	0
	7555	1 FG 1 HY	19	0	2	0	0	1+ TP	1+	0	0
	7557	1 HY 2 FG	55	0	7	0	0	1+ TP	1+	0	0
	7558	1 HY	5	1	2	0	0	1+ TP	1+	0	0
	7566	4 HY	30	0	5	1	0	4+ TP	2+	0	0
	7573	0	1	0	1	0	0	2+ TP	1+	0	0
0.1	7543	1 FG	7	0	9	0	0	1+ TP	1+	0	0
	7545*										
	7550	1 FG	20	0	2	1	0	0	1+	0	0
	7552	0	0	0	1	4	0	0	1+	0	0
	7553	2 FG	0	0	2	0	0	0	1+	0	0
	7560	1 FG	10	1	3	3	0	0	1+	0	0
	7567	1 FG	50	0	3	5	0	1+ TP	1+	0	0
	7569	1 FG	5	0	1	0	0	0	1+	0	0
2.0	7548	2 HY	20	1	2	3	0	0	1+	0	0
	7556	0	1	0	0	1	0	1+ TP	1+	0	0
	7561	1 FG	0	0	1	0	0	1+ TP	1+	0	0
	7562	3 HY 2 FG	0	0	4	0	0	0	1+	0	0
	7564	0	0	0	0	0	0	0	1+	0	0
	7571	1 FG	0	0	5	0	0	1+ TP	1+	0	0
	7572	0	50	0	2	0	0	0	2+	0	0
	7574	1 HY	0	0	1	0	0	1+ TP	1+	0	0
3.0	7539	1 HY	3	0	3	0	0	1+ TP	1+	0	0
	7540	1 HY	0	0	3	0	0	1+ TP	1+	0	0
	7544	1 FG	11	0	0	1	0	0	1+	0	0
	7546	1 HY 3 FG	1	0	3	2	0	0	1+	0	0
	7551	3 HY	1	0	6	0	0	2+ TP	1+	0	0
	7554	1 HY	10	0	2	0	0	2+ TP	1+	0	0
	7563	2 FG	2	1	3	0	0	1+ TP	1+	0	0
	7568	0	0	0	4	0	0	1+ TP	1+	0	0

\*Inadvertently not collected.

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

Male Urinalysis Data (Week 8)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	APP	SG	COLOR	NIT	LEU	pH	PROT	GLU g/dl	KET	URO	BILI	BLOOD Ery/ul
0	7505	HAZY	1.068	DY	NEG	+	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7512	HAZY	1.070	Y	NEG	++	6	+	NOR	NEG	NOR	NEG	NEG
	7515	HAZY	1.124	DY	NEG	++	5	TRACE	NOR	NEG	NOR	NEG	50
	7520	CLOUDY	1.052	Y	NEG	+	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7521	HAZY	1.022	DY	POS	++	7	TRACE	NOR	NEG	NOR	NEG	NEG
	7531	HAZY	1.093	Y	NEG	+	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7532	CLEAR	1.093	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7533	CLEAR	1.060	PY	NEG	+	6	TRACE	NOR	NEG	NOR	NEG	NEG
0.1	7503	CLEAR	1.175	Y	NEG	++	7	++	NOR	NEG	NOR	NEG	NEG
	7517	HAZY	1.081	Y	NEG	++	5	TRACE	NOR	NEG	NOR	NEG	5-10
	7519	HAZY	1.093	DY	NEG	++	7	++	NOR	NEG	NOR	NEG	NEG
	7523	HAZY	1.056	Y	NEG	++	6	TRACE	NOR	NEG	NOR	NEG	50
	7527	CLEAR	1.135	DY	NEG	NEG	5	NEG	NOR	NEG	NOR	NEG	NEG
	7528	CLEAR	1.078	Y	NEG	NEG	5	NEG	NOR	NEG	NOR	NEG	NEG
	7529	HAZY	1.140	Y	NEG	NEG	5	TRACE	NOR	NEG	NOR	NEG	NEG
	7536	HAZY	1.068	Y	POS	++	6	+	NOR	NEG	NOR	NEG	50
2.0	7502	CLEAR	1.105	DY	NEG	NEG	7	TRACE	NOR	NEG	NOR	NEG	NEG
	7506	HAZY	1.105	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7510	HAZY	1.081	Y	NEG	++	5	TRACE	NOR	NEG	NOR	NEG	5-10
	7514	CLEAR	1.056	LY	POS	++	6	+	NOR	NEG	NOR	NEG	NEG
	7516	HAZY	1.084	Y	NEG	+	5	TRACE	NOR	NEG	NOR	NEG	50
	7522	HAZY	1.100	BR	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	50
	7538	CLEAR	1.081	DY	NEG	NEG	8	+	NOR	NEG	NOR	NEG	NEG
	7576	HAZY	1.060	Y	NEG	++	6	+	NOR	NEG	NOR	NEG	NEG
6.0	7507	HAZY	1.081	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7508	HAZY	1.140	BR	NEG	+	5	TRACE	NOR	NEG	NOR	NEG	50
	7509	HAZY	1.096	Y	NEG	NEG	5	TRACE	NOR	NEG	NOR	NEG	5-10
	7511	HAZY	1.093	Y	NEG	++	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7518	HAZY	1.066	Y	NEG	+	5	TRACE	NOR	NEG	NOR	NEG	5-10
	7524	HAZY	1.096	DY	NEG	++	5	+	NOR	NEG	NOR	NEG	5-10
	7530	HAZY	1.072	Y	NEG	+	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7535	HAZY	1.062	DY	NEG	++	5	TRACE	NOR	NEG	NOR	NEG	50

DRAFT

Male Urinalysis Data (Week 8)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	CASTS	RBC	WBC	EPITHELIAL CELLS			CRYSTALS	BACTERIA	SPERM	MUCUS
					SQ	TRANS	RENAL				
0	7505	2 HY	10	5	6	1	0	0	1+	1+	0
	7512	6 HY	0	5	2	1	0	1+ TP	1+	0	0
	7515	2 FG	5	20	1	0	0	1+ TP	1+	1+	0
	7520	5 HY	7	12	0	0	0	1+ TP	1+	1+	0
	7521*	1 HY	0	5	1	0	0	2+ TP	1+	1+	0
	7531	2 HY 1 CG	5	10	1	0	0	1+ TP	1+	0	0
	7532	2 FG 4 HY	0	0	5	0	0	1+ TP	1+	1+	0
	7533	1 HCG 2 HY	0	25	1	2	0	0	1+	0	0
0.1	7503	4 HY	0	5	2	0	0	2+ TP	1+	1+	0
	7517	5 HY	15	10	4	0	0	1+ TP	1+	0	0
	7519	3 HY 2 CG	0	100	4	0	0	1+ TP	1+	0	0
	7523	2 HY 1 FG	20	24	3	0	0	1+ TP	2+	1+	0
	7527	2 HY	0	0	0	0	0	1+ TP	1+	0	0
	7528	1 FG 2 HY	3	0	1	1	0	1+ TP	1+	1+	0
	7529	1 FG 3 CG	0	0	0	0	0	1+ TP	1+	0	0
	7536	1 HY	20	5	1	0	0	1+ TP	2+	0	0
2.0	7502	1 HY	0	0	1	0	0	1+ TP	1+	1+	0
	7506	2 HY 1 FG	30	2	4	0	0	1+ TP	1+	1+	0
	7510	1 FG	15	50	2	4	0	0	1+	2+	0
	7514	1 FG	0	50	1	0	0	0	1+	1+	0
	7516	2 FG	150	20	4	3	0	1+ TP	1+	1+	0
	7522	2 CG 1 FG 1 HY	25	3	7	2	0	2+ TP	1+	0	0
	7538	1 HY	0	2	4	0	0	1+ TP	1+	1+	0
	7576	3 HY	10	100	7	2	0	1+ TP	1+	0	0
6.0	7507	1 HY 2 FG	25	2	3	1	0	2+ TP	1+	1+	0
	7508	3 HY 1 FG	12	15	2	1	0	1+ TP	1+	1+	0
	7509	4 HY 4 FG	15	0	2	0	0	1+ TP	1+	1+	0
	7511	1 HY 2 FG	10	30	2	0	0	1+ TP	1+	0	0
	7518	4 HY	12	15	4	1	0	0	1+	2++	0
	7524	1 FG 1 CG	10	20	2	0	0	1+ TP	1+	0	0
	7530	0	2	5	1	0	0	1+ TP	1+	2+	0
	7535	1 FG	15	50	3	1	0	0	1+	1+	0

# DRAFT

UIC/TRL Study No. 097

## THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

### Female Urinalysis Data (Week 8)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	APP	SG	COLOR	NTT	LEU	pH	PROT	GLU g/dl	KET	URO	BILI	BLOOD Ery/ul
0	7541	CLEAR	1.084	Y	NEG	NEG	5	2+	NOR	NEG	NOR	NEG	NEG
	7542	HAZY	1.087	DY	NEG	2+	5	TRACE	NOR	NEG	NOR	NEG	50
	7549	HAZY	1.084	DY	NEG	1+	6	1+	NOR	NEG	NOR	NEG	NEG
	7555	HAZY	1.084	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7557	HAZY	1.096	Y	NEG	2+	6	1+	NOR	NEG	NOR	NEG	50
	7558	HAZY	1.128	DY	NEG	2+	7	2+	NOR	NEG	NOR	NEG	NEG
	7566	CLOUDY	1.056	LY	NEG	2+	6	1+	NOR	NEG	NOR	NEG	NEG
	7573	HAZY	1.054	LY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	5-10
0.1	7543	CLEAR	1.128	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7545	HAZY	1.056	Y	NEG	2+	6	2+	NOR	NEG	NOR	NEG	250
	7550	HAZY	1.056	Y	POS	2+	5	TRACE	NOR	NEG	NOR	NEG	250
	7552	CLEAR	1.087	LY	NEG	TRACE	5	1+	NOR	NEG	NOR	NEG	NEG
	7553	HAZY	1.090	LY	NEG	NEG	7	TRACE	NOR	NEG	NOR	NEG	NEG
	7560	HAZY	1.060	Y	NEG	2+	6	1+	NOR	NEG	NOR	NEG	250
	7567	CLEAR	1.066	Y	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7569	CLEAR	1.056	Y	NEG	NEG	6	1+	NOR	NEG	NOR	NEG	NEG
2.0	7548	HAZY	1.068	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7556	CLEAR	1.060	DY	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7561	HAZY	1.062	LY	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7562	HAZY	1.068	Y	NEG	TRACE	6	+	NOR	NEG	NOR	NEG	NEG
	7564	CLEAR	1.090	Y	POS	NEG	5	NEG	NOR	NEG	NOR	NEG	NEG
	7571	HAZY	1.054	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	50
	7572	HAZY	1.048	Y	POS	++	6	+	NOR	NEG	NOR	NEG	250
	7574	CLEAR	1.140	AM	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
6.0	7539	HAZY	1.087	DY	NEG	NEG	8	+	NOR	NEG	NOR	NEG	NEG
	7540	HAZY	1.092	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7544	CLEAR	1.057	DY	NEG	NEG	6	++	NOR	NEG	NOR	NEG	NEG
	7546	HAZY	1.100	BR	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7551	CLOUDY	1.116	BR	POS	+	6	+	NOR	NEG	NOR	NEG	NEG
	7554	CLOUDY	1.075	DY	POS	+	6	++	NOR	NEG	NOR	NEG	250
	7563	HAZY	1.124	DY	NEG	NEG	8	TRACE	NOR	NEG	NOR	NEG	NEG
	7568	HAZY	1.099	DY	POS	++	6	+	NOR	NEG	NOR	NEG	50

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

Female Urinalysis Data (Week 8)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	CASTS	RBC	WBC	EPITHELIAL CELLS			CRYSTALS	BACTERIA	SPERM	MUCUS
					SQ	TRANS	RENAL				
0	7541	2 HY	0	0	4	1	0	1+ TP	1+	0	0
	7542	2 HY 2 CG	10	5	3	0	0	1+ TP	2+	0	0
	7549	1 FG	0	5	6	1	0	2+ TP	1+	0	0
	7555	2 HY 1 FG	10	0	7	2	0	2+ TP	1+	0	0
	7557	1 HY	10	16	3	0	0	0	1+	0	0
	7558	4 HY 1 CG	0	10	2	0	0	3+ TP	1+	0	0
	7566	1 HY 1 FG	0	50	30	3	0	0	1+	0	0
	7573	1 HY	3	0	0	0	0	0	2+	0	0
0.1	7543	1 FG	0	0	1	1	0	1+ TP	1+	0	0
	7545	1 FG	50	25	4	0	0	0	1+	0	0
	7550	1 CG 1 HY	50	20	20	4	0	2+ TP	1+	0	0
	7552*	1 HY	0	1	1	0	0	1+ TP	1+	0	0
	7553	2 HY	0	10	7	0	0	2+ TP	1+	0	0
	7560	1 HY	50	15	1	0	0	0	1+	0	0
	7567	1 HY 1 FG	2	2	3	10	0	1+ TP	1+	0	0
	7569	1 FG	0	0	1	0	0	2+ TP	1+	0	0
2.0	7548	1 FG	0	0	1	2	0	1+ TP	1+	1+	0
	7556	1 HY	5	0	1	0	0	1+ TP	1+	0	0
	7561*	2 CG	5	0	1	0	0	0	1+	0	0
	7562	2 HY 1 CG	0	5	2	1	0	2+ TP	1+	0	0
	7564	3 HY	0	0	1	0	0	0	1+	0	0
	7571	1 HY	10	0	2	0	0	1+ TP	1+	0	0
	7572	1 HY	15	10	1	0	0	1+ TP	3+	0	0
	7574	1 HY	0	0	1	0	0	1+ TP	1+	0	0
6.0	7539*	1 HY	0	0	1	2	0	2+ TP	1+	0	0
	7540	1 HY 1 FG	0	0	4	2	0	0	1+	0	0
	7544	1 FG	0	0	0	0	0	0	1+	0	0
	7546	2 HY	0	0	2	0	0	1+ TP	1+	0	0
	7551	4 CG	0	3	2	0	0	1+ TP	1+	0	0
	7554	1 HY	50	15	0	0	0	0	3+	0	0
	7563	2 CG 1 HY	0	0	2	0	0	1+ TP	1+	0	0
	7568	2 HY	20	15	100	10	0	1+ TP	1+	0	0

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

Male Urinalysis Data (Week 13)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	APP	SG	COLOR	NIT	LEU	pH	PROT	GLU g/dl	KET	URO	BILI	BLOOD Ery/ul
0	7505	CLOUDY	1.054	Y	POS	2+	6	1+	NOR	NEG	NOR	NEG	250
	7512	CLOUDY	1.078	Y	NEG	2+	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7515	CLEAR	1.064	LY	NEG	2+	5	1+	NOR	NEG	NOR	NEG	NEG
	7520	CLEAR	1.032	LY	NEG	2+	6	1+	NOR	NEG	NOR	NEG	NEG
	7521	CLEAR	1.003	CL	POS	2+	7	TRACE	NOR	NEG	NOR	NEG	50
	7531	CLEAR	1.087	Y	NEG	1+	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7532	HAZY	1.052	Y	POS	2+	6	1+	NOR	NEG	NOR	NEG	5-10
	7533	CLEAR	1.068	LY	NEG	2+	6	TRACE	NOR	NEG	NOR	NEG	NEG
0.1	7503	HAZY	1.0485	Y	NEG	NEG	6	1+	NOR	NEG	NOR	NEG	250
	7517	HAZY	1.024	DY	NEG	2+	6	1+	NOR	NEG	NOR	NEG	NEG
	7519	CLEAR	1.032	LY	NEG	2+	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7523	CLEAR	1.081	Y	NEG	2+	6	2+	NOR	NEG	NOR	NEG	NEG
	7527	CLOUDY	1.062	Y	NEG	2+	6	TRACE	NOR	NEG	NOR	NEG	50
	7528	CLEAR	1.056	Y	NEG	2+	5	TRACE	NOR	NEG	NOR	NEG	NEG
	7529	CLEAR	1.087	DY	NEG	NEG	5	1+	NOR	NEG	NOR	NEG	NEG
	7536	CLEAR	1.062	Y	NEG	TRACE	6	TRACE	NOR	NEG	NOR	NEG	NEG
2.0	7502	CLOUDY	1.058	DY	NEG	TRACE	6	2+	NOR	NEG	NOR	NEG	NEG
	7506	CLEAR	1.070	DY	NEG	NEG	6	2+	NOR	NEG	NOR	NEG	NEG
	7510	CLEAR	1.060	Y	NEG	2+	6	2+	NOR	NEG	NOR	NEG	NEG
	7514	CLEAR	1.056	Y	NEG	2+	5	TRACE	NOR	NEG	NOR	NEG	5-10
	7516	CLOUDY	1.051	DY	NEG	2+	6	TRACE	NOR	NEG	NOR	NEG	50
	7522	HAZY	1.096	AM	NEG	NEG	5	1+	NOR	NEG	NOR	NEG	NEG
	7538	CLOUDY	1.064	Y	POS	NEG	6	2+	NOR	NEG	NOR	NEG	NEG
	7576	CLEAR	1.022	Y	POS	2+	6	TRACE	NOR	NEG	NOR	NEG	NEG
6.0	7507	CLEAR	1.036	Y	POS	2+	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7508	CLOUDY	1.066	DY	POS	2+	6	2+	NOR	NEG	NOR	NEG	50
	7509	CLEAR	1.028	LY	POS	2+	6	TRACE	NOR	NEG	NOR	NEG	50
	7511	HAZY	1.064	DY	NEG	2+	5	1+	NOR	NEG	NOR	NEG	NEG
	7518	HAZY	1.092	AM	POS	TRACE	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7524	CLEAR	1.063	AM	NEG	NEG	5	NEG	NOR	NEG	NOR	NEG	NEG
	7530	CLOUDY	1.064	LY	POS	2+	6	TRACE	NOR	NEG	NOR	2+	5-10
	7535	CLOUDY	1.060	DY	POS	2+	6	2+	NOR	NEG	NOR	NEG	5-10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

DRAFT

## Male Urinalysis Data (Week 13)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	CASTS	RBC	WBC	EPITHELIAL CELLS			CRYSTALS	BACTERIA	SPER M	MUCUS	YEAST CELLS
					SQ	TRANS	RENAL					
0	7505	1 FR	100	20	1	0	0	0	1+	0	0	0
	7512	2 FG	5	15	6	0	0	3+ TP	1+	0	0	0
	7515	2 HY 1 FG	0	5	0	0	0	0	1+	0	0	0
	7520	5 HY	6	20	5	0	0	0	1+	0	0	0
	7521	1 HY	15	10	1	0	0	0	1+	1+	0	0
	7531	1 FG	10	10	2	0	0	0	1+	1+	0	0
	7532	1 FG	0	3	2	0	0	1+ TP	1+	1+	0	0
	7533	3 HY	0	25	5	0	0	0	1+	0	0	0
0.1	7503	2 HY	350	0	3	0	0	0	1+	1+	0	0
	7517	2 HY	0	10	2	0	0	0	1+	1+	0	0
	7519	2 FG	5	40	1	1	0	0	0	2+	0	0
	7523	1 CG	0	20	1	0	0	0	1+	2+	0	0
	7527	2 HY	20	10	0	0	0	0	1+	0	0	0
	7528	2 HY	0	0	5	3	0	0	1+	2+	0	0
	7529	1 HY	0	0	3	0	0	1+ TP	1+	0	0	0
	7536	1 HY 1 FG	0	5	0	0	0	0	1+	1+	0	0
2.0	7502	2 HY	0	0	3	0	0	3+ TP	1+	0	0	0
	7506	4 HY	1	3	1	0	0	0	1+	0	0	0
	7510	1 FG	0	50	3	0	0	0	1+	1+	0	0
	7514	2 FG	5	20	1	0	0	0	1+	1+	0	0
	7516	2 FG	5	30	7	0	0	0	1+	0	0	0
	7522	4 HY	0	0	2	0	0	1+ TP	1+	1+	0	0
	7538	2 HY	0	0	3	0	0	1+ TP	1+	1+	0	0
	7576	1 FG	0	6	1	0	0	0	1+	0	0	0
6.0	7507	2 HY	0	15	2	0	0	0	1+	0	0	0
	7508	1 HY	15	10	3	0	0	0	1+	0	0	0
	7509	1 FG	5	25	0	0	0	0	2+	0	0	0
	7511	2 HY	0	40	3	0	0	0	1+	1+	0	0
	7518	0	0	0	1	1	0	0	1+	1+	0	0
	7524	1 FG	0	10	2	0	0	0	1+	1+	0	0
	7530	1 HY	5	15	0	0	0	1+ TP	1+	0	0	0
	7535	1 HY	5	15	0	0	0	0	1+	0	0	0

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

Female Urinalysis Data (Week 13)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	APP	SG	COLOR	NTT	LEU	pH	PROT	GLU g/dl	KET	URO	BILI	BLOOD Ery/ul
0	7541	HAZY	1.075	Y	NEG	TRACE	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7542	*	1.087	*	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	250
	7549	CLEAR	1.056	LY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	50
	7555	CLEAR	1.023	PY	POS	NEG	6	NEG	NOR	NEG	NOR	NEG	NEG
	7557	CLEAR	1.078	DY	NEG	NEG	5	TRACE	NOR	NEG	NOR	NEG	NEG
	7558	CLEAR	1.050	Y	NEG	2+	6	1+	NOR	NEG	NOR	NEG	NEG
	7566	CLEAR	1.058	Y	NEG	2+	6	1+	NOR	NEG	NOR	NEG	NEG
	7573	CLOUDY	1.034	Y	POS	2+	7	1+	NOR	NEG	NOR	NEG	250
0.1	7543	CLEAR	1.105	DY	NEG	NEG	6	1+	NOR	NEG	NOR	NEG	NEG
	7545	CLEAR	1.051	Y	NEG	1+	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7550	CLOUDY	1.069	Y	NEG	2+	5	1+	NOR	NEG	NOR	NEG	5-10
	7552	CLEAR	1.072	Y	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7553	CLEAR	1.087	DY	POS	NEG	5	2+	NOR	NEG	NOR	NEG	NEG
	7560	CLEAR	1.057	Y	NEG	NEG	8	2+	NOR	NEG	NOR	NEG	NEG
	7567	HAZY	1.081	Y	NEG	NEG	6	1+	NOR	NEG	NOR	NEG	NEG
	7569	CLEAR	1.032	LY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
2.0	7548	HAZY	1.060	DY	NEG	1+	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7556	CLEAR	1.056	DY	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7561	CLEAR	1.028	PY	POS	1+	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7562	CLEAR	1.042	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7564	CLEAR	1.084	DY	POS	NEG	5	1+	NOR	NEG	NOR	NEG	NEG
	7571	CLEAR	1.056	Y	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7572	HAZY	1.064	AM	NEG	NEG	5	TRACE	NOR	NEG	NOR	NEG	50
	7574	HAZY	1.056	DY	NEG	2+	6	1+	NOR	NEG	NOR	NEG	NEG
6.0	7539	CLEAR	1.062	DY	NEG	TRACE	6	1+	NOR	NEG	NOR	NEG	250
	7540	CLEAR	1.063	DY	NEG	NEG	5	1+	NOR	NEG	NOR	NEG	NEG
	7544	CLEAR	1.052	AM	NEG	NEG	6	1+	NOR	NEG	NOR	NEG	NEG
	7546	HAZY	1.084	AM	POS	TRACE	5	TRACE	NOR	NEG	NOR	NEG	5-10
	7551	CLEAR	1.066	AM	NEG	NEG	6	2+	NOR	NEG	NOR	NEG	NEG
	7554	HAZY	1.084	BR	NEG	NEG	6	3+	NOR	NEG	NOR	NEG	NEG
	7563	HAZY	1.048	BR	NEG	TRACE	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7568	HAZY	1.045	DY	NEG	NEG	6	2+	NOR	NEG	NOR	NEG	NEG

\*Inadvertently not collected.

## THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

### Female Urinalysis Data (Week 13)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	CASTS	RBC	WBC	EPITHELIAL CELLS			CRYSTALS	BACTERIA	SPERM	MUCUS
					SQ	TRANS	RENAL				
0	7541	1 HY	0	0	5	0	0	1+ TP	1+	0	0
	7542*	1 HY 1 FG	10	0	0	0	0	1+ TP	1+	0	0
	7549	1 CG	15	0	10	0	0	0	1+	0	0
	7555	1 HY	0	3	1	0	0	0	1+	0	0
	7557	1 HY	0	0	3	0	0	1+ TP	1+	0	0
	7558	0	0	15	25	0	0	1+ TP	1+	0	0
	7566	3 FG	0	50	23	6	0	0	1+	0	0
	7573	1 HY	15	10	0	0	0	0	3+	0	0
0.1	7543	0	0	0	1	0	0	2+ TP	1+	0	0
	7545	1 HY	0	7	9	0	0	2+ TP	1+	0	0
	7550	1 FG	10	22	3	0	0	0	1+	0	0
	7552	1 FG 2 HY	0	0	4	1	0	0	1+	0	0
	7553	2 HY	0	0	0	0	0	0	1+	0	0
	7560	1 HY	0	0	1	0	0	1+ TP	1+	0	0
	7567	2 FG	0	0	5	0	0	1+ TP	1+	0	0
	7569	1 FG 1 HY	0	0	3	0	0	0	1+	0	0
2.0	7548	1 HY	0	10	5	0	0	3+ TP	1+	0	0
	7556	1 HY	0	0	4	0	0	1+ TP	1+	0	0
	7561	0	5	2	1	0	0	0	1+	0	0
	7562	2 CG	0	0	4	0	0	1+ TP	1+	0	0
	7564	2 HY	0	0	3	0	0	0	2+	0	0
	7571	2 HY 1 CG	0	0	1	1	0	0	1+	0	0
	7572	3 HY	10	0	5	0	0	0	1+	0	0
	7574	1 HY	0	50	10	0	0	1+ TP	1+	0	0
6.0	7539	3 HY	30	5	25	0	0	1+ TP	1+	0	0
	7540	3 HY 1 FG	0	0	3	0	0	0	1+	0	0
	7544	3 FG	0	0	6	0	0	0	1+	0	0
	7546	2 HY	0	7	3	0	0	1+ TP	1+	0	0
	7551	2 FG	0	0	5	0	0	0	1+	0	0
	7554	0	0	0	1	0	0	2+ TP	1+	0	0
	7563	1 HY 2 FG	0	5	3	0	0	0	1+	0	0
	7568	2 FG 1 CG	0	0	12	0	0	2+ TP	1+	0	0

\* Animal also has yeast cells 1+.

# DRAFT

UIC/TRL Study No. 097

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

Male Urinalysis Data (Week 18)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	APP	SG	COLOR	NIT	LEU	pH	PROT	GLU g/dl	KET	URO	BILI	BLOOD Ery/tl
0	7512	CLOUDY	1.060	DY	NEG	2+	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7515	HAZY	1.084	DY	NEG	TRACE	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7531	CLOUDY	1.084	DY	NEG	1+	6	NEG	NOR	NEG	NOR	NEG	5-10
	7532	HAZY	1.066	LY	NEG	TRACE	6	NEG	NOR	NEG	NOR	NEG	NEG
0.1	7519	CLEAR	1.050	Y	NEG	1+	6	NEG	NOR	NEG	NOR	NEG	5-10
	7527	CLEAR	1.104	Y	NEG	2+	5	TRACE	NOR	NEG	NOR	NEG	5-10
	7529	TURBID	1.072	DY	NEG	2+	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7536	CLEAR	1.078	Y	NEG	1+	6	NEG	NOR	NEG	NOR	NEG	5-10
2.0	7510	HAZY	1.084	Y	NEG	2+	5	1+	NOR	NEG	NOR	NEG	5-10
	7516	CLOUDY	1.100	BR	NEG	TRACE	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7522	CLEAR	1.105	DY	NEG	2+	6	NEG	NOR	NEG	NOR	NEG	5-10
	7538	CLEAR	1.078	Y	POS	TRACE	6	TRACE	NOR	NEG	NOR	NEG	NEG
6.0	7507	CLOUDY	1.093	DY	NEG	2+	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7511	TURBID	1.090	DY	POS	1+	6	1+	NOR	NEG	NOR	NEG	50
	7530	TURBID	1.062	DY	POS	2+	6	TRACE	NOR	NEG	NOR	NEG	250
	7535	TURBID	1.087	DY	POS	2+	6	TRACE	NOR	NEG	NOR	NEG	5-10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

Male Urinalysis Data (Week 18)

DRAFT

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	CASTS	RBC	WBC	EPITHELIAL CELLS			CRYSTALS	BACTERIA	SPERM	MUCUS
					SQ	TRANS	RENAL				
0	7512	3 FG 2 HY	0	14	1	0	0	1+ TP	1+	1+	0
	7515	1 HY 1 FG	12	5	4	0	0	1+ TP	0	1+	0
	7531	2 HY	20	23	1	0	0	1+ TP	1+	0	0
	7532	1 HY	0	5	2	0	0	1+ TP	1+	0	0
0.1	7519	1 FG 1 HY	12	10	2	0	0	1+ TP	2+	0	0
	7527	1 FG 1 HY	3	15	1	0	0	2+ TP	1+	1+	0
	7529	2 FG 4 HY	9	30	5	0	0	0	1+	0	0
	7536	3 FG 1 CG	10	20	1	0	0	0	1+	1+	0
2.0	7510	1 FG 1 HY	22	100	13	0	0	0	1+	1+	0
	7516	1 FG	10	0	4	0	0	2+ TP	1+	0	0
	7522	1 FG	10	15	2	0	0	2+ TP	1+	1+	0
	7538	1 HY 1 FG	0	3	2	0	0	1+ TP	1+	1+	0
6.0	7507	1 HY 2 FG	5	14	0	0	0	1+ TP	1+	0	0
	7511	3 FG	40	10	0	0	0	1+ TP	1+	0	0
	7530	1 HY	15	10	1	0	0	0	2+	0	0
	7535	4 HY	15	25	1	0	0	1+ TP	1+	1+	0

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

Female Urinalysis Data (Week 18)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	APP	SG	COLOR	NTT	LEU	pH	PROT	GLU g/dl	KET	URO	BILI	BLOOD Ery/ul
0	7541	HAZY	1.100	*	NEG	NEG	6	NEG	NOR	NEG	NOR	NEG	NEG
	7549	CLEAR	1.062	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7557	CLEAR	1.116	LY	NEG	NEG	5	1+	NOR	NEG	NOR	NEG	NEG
	7566	CLEAR	1.066	Y	NEG	2+	6	NEG	NOR	NEG	NOR	NEG	NEG
0.1	7543	CLEAR	1.108	DY	NEG	NEG	6	NEG	NOR	NEG	NOR	NEG	NEG
	7545	CLEAR	1.048	DY	NEG	NEG	7	NEG	NOR	NEG	NOR	NEG	NEG
	7552	CLOUDY	1.090	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	250
	7553	CLEAR	1.081	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
2.0	7548	TURBID	1.072	DY	NEG	NEG	6	NEG	NOR	NEG	NOR	NEG	NEG
	7561	CLOUDY	1.090	AM	NEG	2+	6	TRACE	NOR	NEG	NOR	NEG	250
	7562	CLEAR	1.090	DY	NEG	NEG	8	NEG	NOR	NEG	NOR	NEG	NEG
	7571	TURBID	1.062	DY	NEG	2+	6	2+	NOR	NEG	NOR	NEG	50
6.0	7539	TURBID	1.128	Y	NEG	NEG	6	NEG	NOR	NEG	NOR	NEG	NEG
	7540	CLEAR	1.026	Y	NEG	1+	6	NEG	NOR	NEG	NOR	NEG	5-10
	7554	CLEAR	1.034	Y	NEG	TRACE	6	NEG	NOR	NEG	NOR	NEG	NEG
	7563	CLEAR	1.124	Y	NEG	2+	7	TRACE	NOR	NEG	NOR	NEG	NEG

\*Inadvertently not collected.

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

## Female Urinalysis Data (Week 18)

DRAFT

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	CASTS	RBC	WBC	EPITHELIAL CELLS			CRYSTALS	BACTERIA	SPERM	MUCUS
					SQ	TRANS	RENAL				
0	7541	1 HY	0	0	6	0	0	2+ TP	1+	0	0
	7549	2 HY 1 FG	0	0	6	1	0	0	1+	0	0
	7557	1 FG	2	1	3	0	0	1+ TP	1+	0	0
	7566*	1 HY	0	14	20	0	0	3+ TP	1+	0	0
0.1	7543	1 HY	0	0	4	1	0	1+ TP	1+	0	0
	7545*	1 HY	0	0	3	0	0	1+ TP	2+	0	0
	7552	3 HY	25	0	1	0	0	0	1+	0	0
	7553	2 HY	0	0	2	0	0	0	1+	0	0
2.0	7548	2 HY	0	5	3	0	0	2+ TP	1+	0	0
	7561	0	10	15	0	0	0	1+ TP	2+	0	0
	7562	1 FG	0	0	4	0	0	1+ TP	1+	0	0
	7571	1 HY	15	20	1	0	0	1+ TP	2+	0	0
6.0	7539	1 HY	0	0	1	0	0	1+ TP	1+	0	0
	7540	2 HY	10	10	2	0	0	1+ TP	2+	0	0
	7554	1 FG	0	10	4	0	0	1+ TP	1+	0	0
	7563	1 HY	0	12	1	0	0	1+ TP	1+	0	0

\* Animal also had Yeast cells

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

Male Urinalysis Data (Week 26)

DRAFT

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	APP	SG	COLOR	NIT	LEU	pH	PROT	GLU g/dl	KET	URO	BILI	BLOOD Ery/ul
0	7512	HAZY	1.132	DY	POS	2+	6	1+	NOR	NEG	NOR	NEG	NEG
	7515	CLEAR	1.063	Y	POS	2+	6	1+	NOR	NEG	NOR	NEG	NEG
	7531	HAZY	1.072	DY	NEG	NEG	6	1+	NOR	NEG	NOR	NEG	NEG
	7532	CLEAR	1.069	Y	POS	NEG	8	1+	NOR	NEG	NOR	NEG	NEG
0.1	7519	HAZY	1.060	Y	NEG	1+	6	1+	NOR	NEG	NOR	2+	50
	7527	HAZY	1.075	DY	POS	2+	6	1+	NOR	NEG	NOR	NEG	50
	7529	CLEAR	1.014	PY	POS	1+	8	1+	NOR	NEG	NOR	NEG	5-10
	7536	HAZY	1.075	Y	NEG	2+	5	TRACE	NOR	NEG	NOR	NEG	NEG
2.0	7510	HAZY	1.075	Y	NEG	2+	5	1+	NOR	NEG	NOR	NEG	NEG
	7516	CLEAR	1.078	Y	POS	NEG	6	TRACE	NOR	NEG	1+	NEG	NEG
	7522	HAZY	1.165	A	POS	1+	8	1+	NOR	NEG	NOR	NEG	NEG
	7538	HAZY	1.066	DY	POS	NEG	6	2+	NOR	NEG	NOR	NEG	NEG
6.0	7507	CLOUDY	1.062	LY	POS	1+	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7511	CLEAR	1.046	Y	NEG	2+	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7530	HAZY	1.046	LY	POS	2+	6	TRACE	NOR	NEG	NOR	NEG	50
	7535	CLEAR	1.084	DY	POS	2+	7	2+	NOR	NEG	NOR	NEG	NEG

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

Male Urinalysis Data (Week 26)

DRAFT

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	CASTS	RBC	WBC	EPITHELIAL CELLS			CRYSTALS	BACTERIA	SPERM	MUCUS
					SQ	TRANS	RENAL				
0	7512	2 HY	0	10	3	0	0	1+ TP	1+	1+	0
	7515	3 HY 2 FG	0	25	0	0	0	1+ TP	1+	1+	0
	7531	1 FG	0	0	2	3	0	4+ TP	1+	1+	0
	7532	1 FG	0	0	2	0	0	1+ TP	2+	1+	0
0.1	7519	1 HY 1 FG	5	15	1	1	0	1+ TP	1+	1+	0
	7527	1 FG 2 HY	15	52	1	0	0	2+ TP	1+	0	0
	7529	1 HY	12	5	2	0	0	0	2+	0	0
	7536	2 FG 1 HY	0	23	2	7	0	0	1+	2+	0
2.0	7510	4 HY	0	20	2	0	0	0	1+	3+	0
	7516	1 CG 1 HY	0	0	6	0	0	1+ TP	1+	1+	0
	7522	2 HY	0	10	5	4	0	2+ TP	1+	0	0
	7538	2 FG	0	0	1	0	0	3+ TP	2+	3+	0
6.0	7507	1 HY	0	8	1	0	0	1+ TP	4+	0	0
	7511	1 WC 1 FG	0	50	4	2	0	0	1+	1+	0
	7530	1 HY	5	15	1	0	0	1+ TP	4+	0	0
	7535	3 HY	0	10	3	0	0	0	1+	2+	0

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

Female Urinalysis Data (Week 26)

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	APP	SG	COLOR	NIT	LEU	pH	PROT	GLU g/dl	KET	URO	BILI	BLOOD Ery/ul
0	7541	HAZY	1.078	Y	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7549	CLEAR	1.072	DY	POS	NEG	7	TRACE	NOR	NEG	NOR	NEG	NEG
	7557	CLEAR	1.075	Y	POS	2+	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7566	CLEAR	1.081	Y	POS	1+	6	1+	NOR	NEG	NOR	NEG	NEG
0.1	7543	CLEAR	1.081	Y	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	7545	CLEAR	1.034	PY	NEG	TRACE	6	1+	NOR	NEG	NOR	NEG	NEG
	7552	CLEAR	1.090	Y	POS	NEG	6	1+	NOR	NEG	NOR	NEG	NEG
	7553	CLEAR	1.064	Y	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
2.0	7548	HAZY	1.060	Y	POS	1+	8	2+	NOR	NEG	NOR	NEG	NEG
	7561	CLEAR	1.102	DY	POS	NEG	9	2+	NOR	NEG	NOR	NEG	NEG
	7562	CLEAR	1.036	LY	NEG	TRACE	6	1+	NOR	NEG	NOR	NEG	NEG
	7571	HAZY	1.060	Y	POS	TRACE	6	1+	NOR	NEG	NOR	NEG	NEG
6.0	7539	HAZY	1.078	DY	NEG	NEG	7	1+	NOR	NEG	NOR	NEG	NEG
	7540	CLEAR	1.063	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	5-10
	7554	CLEAR	1.060	Y	POS	TRACE	6	1+	NOR	NEG	NOR	NEG	250
	7563	HAZY	1.075	Y	POS	2+	7	2+	NOR	NEG	NOR	NEG	5-10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

Female Urinalysis Data (Week 26)

DRAFT

DOSE LEVEL (mg/kg/day)	ANIMAL NO.	CASTS	RBC	WBC	EPITHELIAL SQ	CELLS TRANS	RENAL	CRYSTALS	BACTERIA	SPERM	MUCUS
0	7541	2 FG 4 HY	0	0	3	2	0	0	1+	0	0
	7549	1 HY	0	0	2	0	0	1+ TP	2+	1+	0
	7557	1 HY 1 FG	0	7	3	12	0	0	1+	0	0
	7566	1 HY 1 FG	0	50	13	0	0	2+ TP	1+	0	0
0.1	7543	1 FG	0	0	3	1	0	1+ TP	1+	0	0
	7545	1 CG 1 FG	3	2	5	1	0	0	1+	0	0
	7552	1 FG	0	0	5	4	0	0	1+	0	0
	7553	1 HY	0	0	5	0	0	1+ TP	1+	0	0
2.0	7548	5 HY 2 FG	0	100	8	0	0	1+ TP	1+	0	0
	7561	1 HY	0	0	1	0	0	2+ TP	1+	0	0
	7562	3 HY 2 FG	0	3	4	2	0	0	1+	0	0
	7564	5 HY 1 CG	0	0	1	4	0	0	1+	0	0
6.0	7539	0	0	0	2	3	0	1+ TP	1+	0	0
	7540	4 HY 1 FG	10	0	12	3	0	1+ TP	1+	0	0
	7554	2 FG 1 HY	150	4	3	0	0	0	1+	1+	0
	7563	1 HY	0	250	4	1	0	1+ TP	1+	0	0

DRAFT

APPENDIX 9  
Cardiology Report

DRAFT

September 14, 1993

TO: Barry S. Levine, D.Sc.  
Director  
Toxicology Research Laboratory (M/C 868)  
The University of Illinois  
1940 W. Taylor St.  
Chicago, IL 60612-7353

FROM: Robert Hamlin, D.V.M., Ph.D.  
Diplomate ACVIM (Cardiology/Internal Medicine)  
1520 Grenoble Rd.  
Columbus, OH 43221



RE: ECG Analysis of Records from Beagles on Study No. 097 during the Pretest Period, in Week 13 (Last Week of Treatment), and in Week 26 (Last Week of Recovery Period)

All records are of good quality. At Week 13, one high dose male demonstrated a changed t-wave whereas a possible atrial premature beat was observed for a high dose female. These mild changes were not apparent in any other animals and were considered incidental findings. Although within normal limits, a number of drug-treated dogs showed other apparent T-wave alterations (increased amplitude in both a positive and negative direction when compared to the pretest recording) and alterations of ST (J-point) segments. These were typically seen at the end of the recovery period as opposed to during Week 13. As such, they were considered incidental findings. Other changes which were also considered within normal limits included a possible secondary atrial ventricular block for a high dose female (no. 7568) in Week 13, and for a high dose male (no. 7511) at the end of the recovery period, which was not seen in the Week 13 observation period.

The quantitative analysis of heart rate, PQ interval and QT duration showed no differences among the various groups.

Thus, at the doses administered and under the conditions of this study, the test compound produced no systematic changes in the electrocardiograms.

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

DRAFT

Electrocardiogram diagnosis

Dose	Sex	Animal Number	Pretest	Week 13	Week 26
0	M	7505	WNL	WNL	-
		7512	WNL	WNL	WNL
		7515	WNL	WNL	WNL
		7520	WNL	WNL	-
		7521	WNL	WNL	-
		7531	WNL	WNL	WNL
		7532	WNL	WNL	WNL
	7533	WNL (iRBBB)	WNL	-	
	F	7541	WNL	WNL	WNL
		7542	RAD	WNL (iRBBB)	-
		7549	WNL	WNL	WNL
		7555	WNL	WNL	-
		7557	WNL	WNL	WNL
		7558	LAD	PWNL (RVE)	-
7566		RAD	WNL	WNL	
7573	WNL	WNL	-		
0.1	M	7503	WNL	WNL	-
		7517	WNL	WNL	-
		7519	WNL (LAD)	LTW	WNL
		7523	WNL	LTW	-
		7527	WNL	WNL	WNL
		7528	WNL	WNL	-
		7529	WNL (iRBBB)	WNL	WNL
	7536	WNL	WNL	WNL	
	F	7543	WNL	WNL	WNL
		7545	WNL	WNL	WNL
		7550	WNL	WNL	-
		7552	PWNL (RVE)	WNL (LAD)	WNL/NC (iRBBB)
		7553	WNL (LAD)	WNL	WNL/NC (LAD)
		7560	WNL (LAD)	WNL	-
7567		WNL	WNL	-	
7569	WNL (iRBBB)	WNL (JPD)	-		
2.0	M	7502	WNL	WNL	-
		7506	WNL	WNL	-
		7510	WNL	WNL	WNL
		7514	WNL	WNL (iRBBB)	-
		7516	WNL	WNL	WNL
		7522	WNL	WNL	WNL
		7538	WNL	WNL	WNL (LTWDPT)
	7576	WNL (LAD)	WNL	-	
	F	7548	WNL	WNL	WNL (LTWDPT)
		7556	WNL	WNL	-
		7561	PWNL (RVE/LAD)	LAD (NCP)	WNL (LAD/LTWDPT)
		7562	WNL	WNL	WNL
		7564	WNL	WNL	-
		7571	WNL	WNL	WNL
7572		WNL	WNL	-	
7574	WNL	WNL	-		
6.0	M	7507	WNL (RAD)	WNL	WNL
		7508	WNL	WNL	-
		7509	WNL	WNL	-
		7511	WNL	WNL	WNL (P2°AVB/LTWDPT)
		7518	WNL	WNL	-
		7524	WNL	WNL	-
		7530	WNL	CTW	WNL (JPDDPT)
	7535	WNL	WNL	WNL	
	F	7539	WNL	WNL (TWDPT)	WNL
		7540	WNL	WNL	WNL (TWDPT)
		7544	WNL	WNL	-
		7546	WNL	WNL	-
		7551	WNL	PAPB	-
		7554	WNL	WNL	WNL (TWDPT)
7563		WNL	WNL	WNL (TWDPT)	
7568	WNL	WNL (P2°AVB)	-		

- |  |                              |
|--|------------------------------|
| RVE = Right Ventricle Enlarged                       | Dose = mg base/kg/day        |
| PWNL = Probably within normal limits                 | NCP = No change from pretest |
| - = Animal previously sacrificed                     | NC = No change               |
| LTWDPT = Large T-waves different from pretest        | LAD = Left axis deviation    |
| iRBBB = Incomplete right bundle branch block         | WNL = Within normal limits   |
| JPDDPT = J point depression different from pretest   | RAD = Right axis deviation   |
| P2°AVB = Possible secondary atrial ventricular block | LTW = Large T-wave           |
| PAPB = Possible atrial premature beat                | JPD = J-point depression     |
| TWDPT = T-waves different from pretest               | CTW = Changed T-wave         |

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

SUMMARY REPORT  
TEST: PR INTERVAL

STUDY ID: 097  
STUDY NO: 097ECG  
ABBR: PR

SEX: MALE

UNITS: sec

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

GROUP(s):	0	0.1	2.0	6.0	mg base/kg/day
Period: Pretest					
MEAN	0.101	0.113	0.105	0.106	
SD	0.0121	0.0221	0.0140	0.0176	
N	8	8	8	8	
Period: Week 13					
MEAN	0.100	0.109	0.099	0.098	
SD	0.0151	0.0123	0.0072	0.0072	
N	8	8	8	8	
Period: Week 26					
MEAN	0.101	0.109	0.099	0.103	
SD	0.0082	0.0214	0.0131	0.0125	
N	4	4	4	4	

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

SUMMARY REPORT  
TEST: PR INTERVAL

STUDY ID: 097  
STUDY NO: 097ECG  
ABBR: PR

SEX: FEMALE

UNITS: sec

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

GROUP(s):            0            0.1            2.0            6.0            mg base/kg/day

	0	0.1	2.0	6.0
Period: Pretest				
MEAN	0.105	0.107	0.107	0.110
SD	0.0139	0.0074	0.0125	0.0142
N	8	8	8	8
Period: Week 13				
MEAN	0.110	0.109	0.102	0.105
SD	0.0161	0.0040	0.0050	0.0121
N	8	8	8	8
Period: Week 26				
MEAN	0.121	0.104	0.108	0.106
SD	0.0143	0.0206	0.0073	0.0161
N	4	4	4	4

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

SUMMARY REPORT  
TEST: QT INTERVAL

STUDY ID: 097  
STUDY NO: 097ECG  
ABBR: QT

SEX: MALE

UNITS: sec

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

GROUP(s):	0	0.1	2.0	6.0	mg base/kg/day
Period: Pretest					
MEAN	0.198	0.201	0.197	0.188	
SD	0.0163	0.0165	0.0094	0.0247	
N	8	8	8	8	
Period: Week 13					
MEAN	0.186	0.192	0.191	0.187	
SD	0.0123	0.0142	0.0206	0.0112	
N	8	8	8	8	
Period: Week 26					
MEAN	0.180	0.180	0.184	0.185	
SD	0.0150	0.0114	0.0047	0.0099	
N	4	4	4	4	

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

SUMMARY REPORT  
TEST: QT INTERVAL

STUDY ID: 097  
STUDY NO: 097ECG  
ABBR: QT

SEX: FEMALE

UNITS: sec

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

GROUP(s):	0	0.1	2.0	6.0	mg base/kg/day
Period: Pretest					
MEAN	0.202	0.202	0.190	0.212	
SD	0.0180	0.0164	0.0140	0.0113	
N	8	8	8	8	
Period: Week 13					
MEAN	0.192	0.185	0.193	0.185	
SD	0.0234	0.0137	0.0178	0.0086	
N	8	8	8	8	
Period: Week 26					
MEAN	0.183	0.180	0.196	0.203	
SD	0.0089	0.0106	0.0296	0.0225	
N	4	4	4	4	

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

SUMMARY REPORT  
TEST: Heart Rate

STUDY ID: 097  
STUDY NO: 097ECG  
ABBR: HR

SEX: MALE

UNITS: bpm

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

GROUP(s):	0	0.1	2.0	6.0	mg base/kg/day
Period: Pretest					
MEAN	127	132	129	143	
SD	17.3	18.0	9.5	19.8	
N	8	8	8	8	
Period: Week 13					
MEAN	129	127	127	137	
SD	28.8	23.5	20.7	23.4	
N	8	8	8	8	
Period: Week 26					
MEAN	133	142	145	128	
SD	20.8	17.9	12.7	15.8	
N	4	4	4	4	

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

DRAFT

SUMMARY REPORT  
TEST: Heart Rate

STUDY ID: 097  
STUDY NO: 097ECG  
ABBR: HR

SEX: FEMALE

UNITS: bpm

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

GROUP(s):	0	0.1	2.0	6.0	mg base/kg/day
Period: Pretest					
MEAN	125	133	130	123	
SD	23.8	11.6	8.9	23.5	
N	8	8	8	8	
Period: Week 13					
MEAN	128	126	128	121	
SD	19.1	19.5	31.0	16.3	
N	8	8	8	8	
Period: Week 26					
MEAN	134	132	118	140	
SD	41.3	10.5	19.7	21.5	
N	4	4	4	4	

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: PR INTERVAL

STUDY ID: 097  
STUDY NO: 097ECG  
ABBR: PR

SEX: MALE

UNITS: sec

ANIMAL ID    Pretest        Week 13        Week 26

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

7531	0.096	0.094	0.108
7532	0.104	0.100	0.096
7512	0.092	0.084	0.092
7515	0.104	0.116	0.108
7521	0.110	0.112	--
7533	0.104	0.118	--
7520	0.078	0.076	--
7505	0.118	0.096	--
MEAN	0.101	0.100	0.101
SD	0.0121	0.0151	0.0082
N	8	8	4

GROUP: 2-M:0.1 mg base/kg/day

7527	0.102	0.124	0.096
7519	0.096	0.098	0.090
7529	0.106	0.106	0.110
7536	0.166	0.128	0.138
7503	0.110	0.102	--
7523	0.106	0.102	--
7517	0.104	0.114	--
7528	0.110	0.094	--
MEAN	0.113	0.109	0.109
SD	0.0221	0.0123	0.0214
N	8	8	4

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: PR INTERVAL

STUDY ID: 097  
STUDY NO: 097ECG  
ABBR: PR

SEX: MALE

UNITS: sec

ANIMAL ID    Pretest    Week 13    Week 26

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

7538	0.078	0.090	0.080
7516	0.120	0.102	0.110
7522	0.112	0.098	0.102
7510	0.108	0.092	0.104
7576	0.120	0.112	--
7506	0.106	0.094	--
7502	0.096	0.104	--
7514	0.098	0.100	--
MEAN	0.105	0.099	0.099
SD	0.0140	0.0072	0.0131
N	8	8	4

GROUP: 4-M:6.0 mg base/kg/day

7535	0.078	0.098	0.088
7511	0.102	0.100	0.106
7530	0.104	0.106	0.100
7507	0.130	0.102	0.118
7508	0.130	0.102	--
7509	0.098	0.084	--
7518	0.108	0.098	--
7524	0.094	0.090	--
MEAN	0.106	0.098	0.103
SD	0.0176	0.0072	0.0125
N	8	8	4

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: PR INTERVAL

STUDY ID: 097  
STUDY NO: 097ECG  
ABBR: PR

SEX: FEMALE

UNITS: sec

ANIMAL ID	Pretest	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
7557	0.084	0.106	0.102
7541	0.112	0.118	0.126
7566	0.104	0.094	0.120
7549	0.122	0.140	0.136
7555	0.088	0.090	--
7558	0.106	0.100	--
7573	0.104	0.118	--
7542	0.122	0.112	--
MEAN	0.105	0.110	0.121
SD	0.0139	0.0161	0.0143
N	8	8	4

GROUP: 2-F:0.1 mg base/kg/day			
7543	0.104	0.102	0.080
7553	0.120	0.112	0.100
7545	0.100	0.110	0.106
7552	0.114	0.112	0.130
7569	0.110	0.106	--
7560	0.100	0.114	--
7567	0.100	0.106	--
7550	0.108	0.108	--
MEAN	0.107	0.109	0.104
SD	0.0074	0.0040	0.0206
N	8	8	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: PR INTERVAL

STUDY ID: 097  
STUDY NO: 097ECG  
ABBR: PR

SEX: FEMALE

UNITS: sec

ANIMAL ID    Pretest        Week 13        Week 26

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

7562	0.112	0.114	0.112
7548	0.094	0.100	0.100
7571	0.096	0.102	0.116
7561	0.116	0.100	0.104
7564	0.106	0.102	--
7574	0.094	0.100	--
7556	0.104	0.098	--
7572	0.130	0.100	--
MEAN	0.107	0.102	0.108
SD	0.0125	0.0050	0.0073
N	8	8	4

GROUP: 4-F:6.0 mg base/kg/day

7539	0.096	0.112	0.096
7563	0.120	0.098	0.130
7540	0.104	0.100	0.100
7554	0.106	0.104	0.098
7568	0.120	0.120	--
7544	0.104	0.092	--
7546	0.094	0.090	--
7551	0.136	0.122	--
MEAN	0.110	0.105	0.106
SD	0.0142	0.0121	0.0161
N	8	8	4

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: QT INTERVAL

STUDY ID: 097  
STUDY NO: 097ECG  
ABBR: QT

SEX: MALE

UNITS: sec

ANIMAL ID	Pretest	Week 13	Week 26
GROUP: 1-M:0 mg base/kg/day			
7531	0.196	0.184	0.180
7532	0.222	0.182	0.196
7512	0.198	0.186	0.160
7515	0.180	0.190	0.184
7521	0.180	0.160	--
7533	0.220	0.200	--
7520	0.186	0.190	--
7505	0.200	0.198	--
MEAN	0.198	0.186	0.180
SD	0.0163	0.0123	0.0150
N	8	8	4

GROUP: 2-M:0.1 mg base/kg/day			
7527	0.214	0.198	0.180
7519	0.182	0.178	0.170
7529	0.184	0.190	0.196
7536	0.200	0.190	0.174
7503	0.220	0.200	--
7523	0.218	0.184	--
7517	0.182	0.220	--
7528	0.210	0.176	--
MEAN	0.201	0.192	0.180
SD	0.0165	0.0142	0.0114
N	8	8	4

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: QT INTERVAL

STUDY ID: 097  
STUDY NO: 097ECG  
ABBR: QT

SEX: MALE

UNITS: sec

ANIMAL ID    Pretest        Week 13        Week 26

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

7538	0.206	0.200	0.184
7516	0.180	0.190	0.190
7522	0.194	0.164	0.180
7510	0.200	0.182	0.180
7576	0.200	0.182	--
7506	0.190	0.200	--
7502	0.210	0.232	--
7514	0.198	0.176	--
MEAN	0.197	0.191	0.184
SD	0.0094	0.0206	0.0047
N	8	8	4

GROUP: 4-M:6.0 mg base/kg/day

7535	0.204	0.184	0.174
7511	0.130	0.174	0.190
7530	0.196	0.186	0.180
7507	0.194	0.190	0.196
7508	0.180	0.178	--
7509	0.208	0.192	--
7518	0.190	0.210	--
7524	0.198	0.180	--
MEAN	0.188	0.187	0.185
SD	0.0247	0.0112	0.0099
N	8	8	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: QT INTERVAL

STUDY ID: 097  
STUDY NO: 097ECG  
ABBR: QT

SEX: FEMALE

UNITS: sec

ANIMAL ID Pretest Week 13 Week 26

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

7557	0.216	0.176	0.186
7541	0.190	0.198	0.190
7566	0.208	0.190	0.170
7549	0.202	0.188	0.186
7555	0.174	0.180	--
7558	0.232	0.200	--
7573	0.204	0.240	--
7542	0.188	0.160	--
MEAN	0.202	0.192	0.183
SD	0.0180	0.0234	0.0089
N	8	8	4

GROUP: 2-F:0.1 mg base/kg/day

7543	0.200	0.186	0.180
7553	0.196	0.178	0.180
7545	0.190	0.166	0.166
7552	0.200	0.208	0.192
7569	0.180	0.180	--
7560	0.224	0.200	--
7567	0.228	0.174	--
7550	0.194	0.188	--
MEAN	0.202	0.185	0.180
SD	0.0164	0.0137	0.0106
N	8	8	4

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: QT INTERVAL

STUDY ID: 097  
STUDY NO: 097ECG  
ABBR: QT

SEX: FEMALE

UNITS: sec

ANIMAL ID	Pretest	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
7562	0.180	0.184	0.164
7548	0.204	0.204	0.180
7571	0.184	0.178	0.210
7561	0.218	0.204	0.230
7564	0.180	0.210	--
7574	0.178	0.190	--
7556	0.190	0.210	--
7572	0.186	0.160	--
MEAN	0.190	0.193	0.196
SD	0.0140	0.0178	0.0296
N	8	8	4

ANIMAL ID	Pretest	Week 13	Week 26
GROUP: 4-F:6.0 mg base/kg/day			
7539	0.212	0.184	0.210
7563	0.190	0.196	0.228
7540	0.220	0.190	0.200
7554	0.208	0.178	0.174
7568	0.226	0.180	--
7544	0.222	0.178	--
7546	0.210	0.176	--
7551	0.206	0.198	--
MEAN	0.212	0.185	0.203
SD	0.0113	0.0086	0.0225
N	8	8	4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Heart Rate

STUDY ID: 097  
STUDY NO: 097ECG  
ABBR: HR

SEX: MALE

UNITS: bpm

ANIMAL ID    Pretest        Week 13        Week 26

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

7531	119	102	111
7532	136	174	131
7512	120	137	161
7515	130	133	128
7521	150	165	--
7533	143	115	--
7520	122	108	--
7505	94	97	--
MEAN	127	129	133
SD	17.3	28.8	20.8
N	8	8	4

GROUP: 2-M:0.1 mg base/kg/day

7527	134	145	168
7519	146	143	137
7529	146	93	128
7536	144	97	134
7503	116	136	--
7523	138	120	--
7517	140	123	--
7528	95	160	--
MEAN	132	127	142
SD	18.0	23.5	17.9
N	8	8	4

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Heart Rate

STUDY ID: 097  
STUDY NO: 097ECG  
ABBR: HR

SEX: MALE

UNITS: bpm

ANIMAL ID    Pretest    Week 13    Week 26

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

7538	140	133	140
7516	139	120	158
7522	130	140	153
7510	128	140	130
7576	122	91	--
7506	137	138	--
7502	118	102	--
7514	116	150	--
MEAN	129	127	145
SD	9.5	20.7	12.7
N	8	8	4

GROUP: 4-M:6.0 mg base/kg/day

7535	155	150	141
7511	162	128	105
7530	98	87	134
7507	154	134	132
7508	139	162	--
7509	147	140	--
7518	141	136	--
7524	150	158	--
MEAN	143	137	128
SD	19.8	23.4	15.8
N	8	8	4

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Heart Rate

STUDY ID: 097  
STUDY NO: 097ECG  
ABBR: HR

SEX: FEMALE  
UNITS: bpm

ANIMAL ID	Pretest	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
7557	115	130	84
7541	142	136	154
7566	106	134	179
7549	125	105	120
7555	161	165	--
7558	92	109	--
7573	150	114	--
7542	111	127	--
MEAN	125	128	134
SD	23.8	19.1	41.3
N	8	8	4

GROUP: 2-F:0.1 mg base/kg/day			
7543	128	114	136
7553	119	100	143
7545	154	155	132
7552	120	115	118
7569	143	127	--
7560	130	120	--
7567	133	155	--
7550	135	125	--
MEAN	133	126	132
SD	11.6	19.5	10.5
N	8	8	4

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: Heart Rate

STUDY ID: 097  
STUDY NO: 097ECG  
ABBR: HR

SEX: FEMALE  
UNITS: bpm

ANIMAL ID    Pretest    Week 13    Week 26

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

7562	146	123	146
7548	123	122	117
7571	134	127	102
7561	120	120	107
7564	127	100	--
7574	135	87	--
7556	120	174	--
7572	132	173	--
MEAN	130	128	118
SD	8.9	31.0	19.7
N	8	8	4

GROUP: 4-F:6.0 mg base/kg/day

7539	125	108	123
7563	150	129	139
7540	92	87	126
7554	150	132	170
7568	135	130	--
7544	125	135	--
7546	120	115	--
7551	87	128	--
MEAN	123	121	140
SD	23.5	16.3	21.5
N	8	8	4

(--)-Data Unavailable

DRAFT

APPENDIX 10  
Ophthalmology Report

# ANIMAL EYE ASSOCIATES

# DRAFT

2845 SOUTH HARLEM • BERWYN, ILLINOIS 60402 • (708)749-4200  
372 SOUTH MILWAUKEE AVE. • WHEELING, ILLINOIS 60090 • (708) 215-3933

SAMUEL J. VAINISI, DVM  
Diplomate American College  
of Veterinary Ophthalmologists

GRETCHEN M. SCHMIDT, DVM  
Diplomate American College  
of Veterinary Ophthalmologists

## OPHTHALMIC REPORT

UIC/TRL Study No. 097

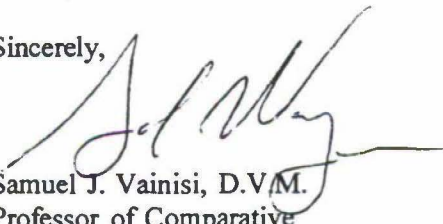
### THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

On November 11, 1992 (Week -3), seventy-four Beagle dogs were given ophthalmic examinations. A male dog (No. 7534) had focal areas of retinal dysplasia which disqualified him from the study. A female dog (No. 7570) had pseudo papilledema of the optic discs (extensive myelinization) which did not disqualify her from the study if she was needed.

On March 10, 1993 (Week 13), I re-examined the sixty-four dogs, which were used in Study No. 097. All dogs in control, low and mid dose groups appeared similar to their previous exam on November 11, 1992. One high dose female (No. 7554) had congested retinal vessels. This finding would be consistent with altered hematological values such as hemoglobin or hematocrit. There was no loss of vision in this animal.

On June 9, 1993 (Week 26), I re-examined thirty-two recovery dogs which were used in Study No. 097. All animals appeared to be comparable to the pretest state including the high dose female (No. 7554) who had congested retinal vessels at Week 13.

Sincerely,



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

Diplomate, American College of  
Veterinary Ophthalmologists

7/21/93

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

Ophthalmic Examinations

Dose	Sex	Animal Number	Week -3		Week 13		Week 26	
			R.E.	L.E.	R.E.	L.E.	R.E.	L.E.
0	M	7505	WNL	WNL	WNL	WNL	-	-
		7512	WNL	WNL	WNL	WNL	WNL	WNL
		7515	WNL	WNL	WNL	WNL	WNL	WNL
		7520	WNL	WNL	WNL	WNL	-	-
		7521	WNL	WNL	WNL	WNL	-	-
		7531	WNL	WNL	WNL	WNL	WNL	WNL
		7532	WNL	WNL	WNL	WNL	WNL	WNL
	7533	WNL	WNL	WNL	WNL	-	-	
	F	7541	WNL	WNL	WNL	WNL	WNL	WNL
		7542	WNL	WNL	WNL	WNL	-	-
		7549	WNL	WNL	WNL	WNL	WNL	WNL
		7555	WNL	WNL	WNL	WNL	-	-
		7557	WNL	WNL	WNL	WNL	-	WNL
		7558	WNL	WNL	WNL	WNL	-	-
7566		WNL	WNL	WNL	WNL	WNL	WNL	
7573	WNL	WNL	WNL	WNL	-	-		
0.1	M	7503	WNL	WNL	WNL	WNL	-	-
		7517	WNL	WNL	WNL	WNL	-	-
		7519	WNL	WNL	WNL	WNL	WNL	WNL
		7523	WNL	WNL	WNL	WNL	-	-
		7527	WNL	WNL	WNL	WNL	WNL	WNL
		7528	WNL	WNL	WNL	WNL	-	-
		7529	WNL	WNL	WNL	WNL	WNL	WNL
	7536	WNL	WNL	WNL	WNL	WNL	WNL	
	F	7543	WNL	WNL	WNL	WNL	WNL	WNL
		7545	WNL	WNL	WNL	WNL	WNL	WNL
		7550	WNL	WNL	WNL	WNL	-	-
		7552	WNL	WNL	WNL	WNL	WNL	WNL
		7553	WNL	WNL	WNL	WNL	WNL	WNL
		7560	WNL	WNL	WNL	WNL	-	-
7567		WNL	WNL	WNL	WNL	-	-	
7569	WNL	WNL	WNL	WNL	-	-		
2.0	M	7502	WNL	WNL	WNL	WNL	-	-
		7506	WNL	WNL	WNL	WNL	-	-
		7510	WNL	WNL	WNL	WNL	WNL	WNL
		7514	WNL	WNL	WNL	WNL	-	-
		7516	WNL	WNL	WNL	WNL	WNL	WNL
		7522	WNL	WNL	WNL	WNL	WNL	WNL
		7538	WNL	WNL	WNL	WNL	WNL	WNL
	7576	WNL	WNL	WNL	WNL	-	-	
	F	7548	WNL	WNL	WNL	WNL	WNL	WNL
		7556	WNL	WNL	WNL	WNL	-	-
		7561	WNL	WNL	WNL	WNL	WNL	WNL
		7562	WNL	WNL	WNL	WNL	WNL	WNL
		7564	WNL	WNL	WNL	WNL	-	-
		7571	WNL	WNL	WNL	WNL	WNL	WNL
7572		WNL	WNL	WNL	WNL	-	-	
7574	WNL	WNL	WNL	WNL	-	-		
6.0	M	7507	WNL	WNL	WNL	WNL	WNL	WNL
		7508	WNL	WNL	WNL	WNL	-	-
		7509	WNL	WNL	WNL	WNL	-	-
		7511	WNL	WNL	WNL	WNL	WNL	WNL
		7518	WNL	WNL	WNL	WNL	-	-
		7524	WNL	WNL	WNL	WNL	-	-
		7530	WNL	WNL	WNL	WNL	WNL	WNL
	7535	WNL	WNL	WNL	WNL	WNL	WNL	
	F	7539	WNL	WNL	WNL	WNL	WNL	WNL
		7540	WNL	WNL	WNL	WNL	WNL	WNL
		7544	WNL	WNL	WNL	WNL	-	-
		7546	WNL	WNL	WNL	WNL	-	-
		7551	WNL	WNL	WNL	WNL	-	-
		7554	WNL	WNL	WNL (RVC)	WNL (RVC)	WNL	WNL
7563		WNL	WNL	WNL	WNL	WNL	WNL	
7568	WNL	WNL	WNL	WNL	-	-		

Dose = mg base/kg/day  
R.E. = Right eye  
L.E. = Left eye  
- = Animal previously sacrificed  
WNL = Within normal limits  
WNL(X) = Observation noted is within normal limits  
RVC = Retinal vessels congested

DRAFT

APPENDIX 11  
Individual Organ Weights

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 097  
SEX: MALE

GROUP: 1M - 0 mg base/kg/day  
ALL FATES      DAYS: 91-92      ALL BALANCES

ANIMAL ID: BALANCE NO.:	7505	7520	7521	7533
BODY WEIGHT (KG)	10.7	11.0	10.5	11.8
Adrenals (pr) (G)	1.70	1.16	0.54	0.93
% BODY WEIGHT	0.016	0.011	0.005	0.008
% BRAIN WEIGHT	2.23	1.55	0.63	1.01
Brain (G)	76.22	74.63	85.54	91.68
% BODY WEIGHT	0.712	0.678	0.815	0.777
Heart (G)	98.79	108.20	91.01	96.63
% BODY WEIGHT	0.923	0.984	0.867	0.819
% BRAIN WEIGHT	129.61	144.98	106.39	105.40
Kidneys (pr) (G)	53.52	51.57	51.16	57.01
% BODY WEIGHT	0.500	0.469	0.487	0.483
% BRAIN WEIGHT	70.22	69.10	59.81	62.18
Liver (G)	282.01	258.30	238.49	299.84
% BODY WEIGHT	2.636	2.348	2.271	2.541
% BRAIN WEIGHT	369.99	346.11	278.81	327.05
Spleen (G)	38.13	32.88	33.33	28.03
% BODY WEIGHT	0.356	0.299	0.317	0.238
% BRAIN WEIGHT	50.03	44.06	38.96	30.57
Testes w/Epidid. (pr) (G)	17.78	8.23	15.26	15.84
% BODY WEIGHT	0.166	0.075	0.145	0.134
% BRAIN WEIGHT	23.33	11.03	17.84	17.28
Thyroids-Parathyroids (G)	1.14	0.90	--	1.21
% BODY WEIGHT	0.011	0.008	--	0.010
% BRAIN WEIGHT	1.50	1.21	--	1.32

4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 097  
SEX: MALE

GROUP: 2M - 0.1 mg base/kg/day  
ALL FATES      DAYS: 91-92      ALL BALANCES

ANIMAL ID: BALANCE NO.:	7503	7517	7523	7528
BODY WEIGHT (KG)	11.2	10.8	10.0	11.2
Adrenals (pr) (G)	1.46	1.84	1.64	0.99
% BODY WEIGHT	0.013	0.017	0.016	0.009
% BRAIN WEIGHT	1.97	2.15	2.26	1.37
Brain (G)	73.98	85.69	72.47	72.23
% BODY WEIGHT	0.661	0.793	0.725	0.645
Heart (G)	83.56	99.11	91.17	93.76
% BODY WEIGHT	0.746	0.918	0.912	0.837
% BRAIN WEIGHT	112.95	115.66	125.80	129.81
Kidneys (pr) (G)	58.63	55.77	49.87	53.42
% BODY WEIGHT	0.523	0.516	0.499	0.477
% BRAIN WEIGHT	79.25	65.08	68.81	73.96
Liver (G)	297.09	296.21	283.50	246.08
% BODY WEIGHT	2.653	2.743	2.835	2.197
% BRAIN WEIGHT	401.58	345.68	391.20	340.69
Spleen (G)	36.12	34.25	33.38	24.92
% BODY WEIGHT	0.323	0.317	0.334	0.223
% BRAIN WEIGHT	48.82	39.97	46.06	34.50
Testes w/Epidid. (pr) (G)	15.21	20.12	18.38	19.07
% BODY WEIGHT	0.136	0.186	0.184	0.170
% BRAIN WEIGHT	20.56	23.48	25.36	26.40
Thyroids-Parathyroids (G)	1.05	1.47	1.87	0.96
% BODY WEIGHT	0.009	0.014	0.019	0.009
% BRAIN WEIGHT	1.42	1.72	2.58	1.33

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

 -----  
 INDIVIDUAL ORGAN WEIGHTS  
 -----

 STUDY: 097  
 SEX: MALE

 GROUP: 3M - 2.0 mg base/kg/day  
 ALL FATES      DAYS: 91-92      ALL BALANCES

ANIMAL ID: BALANCE NO.:	7502	7506	7514	7576
BODY WEIGHT (KG)	11.0	10.8	10.0	9.9
Adrenals (pr) (G)	1.10	1.20	1.50	1.43
% BODY WEIGHT	0.010	0.011	0.015	0.014
% BRAIN WEIGHT	1.34	1.77	2.00	1.88
Brain (G)	81.93	67.72	75.18	76.03
% BODY WEIGHT	0.745	0.627	0.752	0.768
Heart (G)	92.65	84.11	89.65	97.71
% BODY WEIGHT	0.842	0.779	0.897	0.987
% BRAIN WEIGHT	113.08	124.20	119.25	128.52
Kidneys (pr) (G)	61.99	47.06	55.20	46.91
% BODY WEIGHT	0.564	0.436	0.552	0.474
% BRAIN WEIGHT	75.66	69.49	73.42	61.70
Liver (G)	301.49	294.38	362.65	313.83
% BODY WEIGHT	2.741	2.726	3.627	3.170
% BRAIN WEIGHT	367.98	434.70	482.38	412.77
Spleen (G)	57.41	33.90	36.28	43.35
% BODY WEIGHT	0.522	0.314	0.363	0.438
% BRAIN WEIGHT	70.07	50.06	48.26	57.02
Testes w/Epidid. (pr) (G)	15.10	17.89	22.15	13.40
% BODY WEIGHT	0.137	0.166	0.222	0.135
% BRAIN WEIGHT	18.43	26.42	29.46	17.62
Thyroids-Parathyroids (G)	1.39	1.02	0.94	1.32
% BODY WEIGHT	0.013	0.009	0.009	0.013
% BRAIN WEIGHT	1.70	1.51	1.25	1.74

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 097  
SEX: MALE

GROUP: 4M - 6.0 mg base/kg/day  
ALL FATES      DAYS: 91-92      ALL BALANCES

ANIMAL ID: BALANCE NO.:	7508	7509	7518	7524
BODY WEIGHT (KG)	8.9	8.3	10.5	10.5
Adrenals (pr) (G)	1.36	1.69	2.19	1.16
% BODY WEIGHT	0.015	0.020	0.021	0.011
% BRAIN WEIGHT	1.81	1.95	3.03	1.51
Brain (G)	75.09	86.71	72.17	76.66
% BODY WEIGHT	0.844	1.045	0.687	0.730
Heart (G)	87.51	86.55	88.26	99.07
% BODY WEIGHT	0.983	1.043	0.841	0.944
% BRAIN WEIGHT	116.54	99.82	122.29	129.23
Kidneys (pr) (G)	51.57	53.01	52.46	54.10
% BODY WEIGHT	0.579	0.639	0.500	0.515
% BRAIN WEIGHT	68.68	61.13	72.69	70.57
Liver (G)	363.89	381.26	356.62	355.67
% BODY WEIGHT	4.089	4.593	3.396	3.387
% BRAIN WEIGHT	484.61	439.70	494.14	463.96
Spleen (G)	35.71	71.08	57.96	53.70
% BODY WEIGHT	0.401	0.856	0.552	0.511
% BRAIN WEIGHT	47.56	81.97	80.31	70.05
Testes w/Epidid. (pr) (G)	14.92	14.88	21.52	24.12
% BODY WEIGHT	0.168	0.179	0.205	0.230
% BRAIN WEIGHT	19.87	17.16	29.82	31.46
Thyroids-Parathyroids (G)	1.29	0.69	2.27	1.60
% BODY WEIGHT	0.014	0.008	0.022	0.015
% BRAIN WEIGHT	1.72	0.80	3.15	2.09

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 097  
SEX: FEMALE

GROUP: 1F - 0 mg base/kg/day  
ALL FATES      DAYS: 91-92      ALL BALANCES

ANIMAL ID: BALANCE NO.:	7542	7555	7558	7573
BODY WEIGHT (KG)	10.7	8.5	8.2	9.7
Adrenals (pr) (G)	1.19	1.60	1.08	1.11
% BODY WEIGHT	0.011	0.019	0.013	0.011
% BRAIN WEIGHT	1.71	2.35	1.63	1.68
Brain (G)	69.40	68.19	66.09	66.04
% BODY WEIGHT	0.649	0.802	0.806	0.681
Heart (G)	87.14	68.32	77.09	82.53
% BODY WEIGHT	0.814	0.804	0.940	0.851
% BRAIN WEIGHT	125.56	100.19	116.64	124.97
Kidneys (pr) (G)	44.95	36.45	38.91	41.82
% BODY WEIGHT	0.420	0.429	0.475	0.431
% BRAIN WEIGHT	64.77	53.45	58.87	63.33
Liver (G)	291.05	232.80	214.30	254.49
% BODY WEIGHT	2.720	2.739	2.613	2.624
% BRAIN WEIGHT	419.38	341.40	324.25	385.36
Ovaries (G)	1.83	0.80	0.79	0.70
% BODY WEIGHT	0.017	0.009	0.010	0.007
% BRAIN WEIGHT	2.64	1.17	1.20	1.06
Spleen (G)	29.73	23.81	22.85	22.79
% BODY WEIGHT	0.278	0.280	0.279	0.235
% BRAIN WEIGHT	42.84	34.92	34.57	34.51
Thyroids-Parathyroids (G)	0.90	1.21	0.94	1.08
% BODY WEIGHT	0.008	0.014	0.011	0.011
% BRAIN WEIGHT	1.30	1.77	1.42	1.64
Uterus (G)	18.58	1.62	4.20	5.63
% BODY WEIGHT	0.174	0.019	0.051	0.058
% BRAIN WEIGHT	26.77	2.38	6.35	8.53

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 097  
SEX: FEMALE

GROUP: 2F - 0.1 mg base/kg/day  
ALL FATES      DAYS: 91-92      ALL BALANCES

ANIMAL ID: BALANCE NO.:	7550	7560	7567	7569
BODY WEIGHT (KG)	10.2	8.5	8.5	7.1
Adrenals (pr) (G)	1.10	1.23	1.29	1.22
% BODY WEIGHT	0.011	0.014	0.015	0.017
% BRAIN WEIGHT	1.38	1.51	1.80	1.70
Brain (G)	79.60	81.58	71.53	71.64
% BODY WEIGHT	0.780	0.960	0.842	1.009
Heart (G)	90.35	81.68	72.63	80.68
% BODY WEIGHT	0.886	0.961	0.854	1.136
% BRAIN WEIGHT	113.51	100.12	101.54	112.62
Kidneys (pr) (G)	48.42	36.46	36.68	36.01
% BODY WEIGHT	0.475	0.429	0.432	0.507
% BRAIN WEIGHT	60.83	44.69	51.28	50.27
Liver (G)	312.58	202.92	184.50	240.61
% BODY WEIGHT	3.065	2.387	2.171	3.389
% BRAIN WEIGHT	392.69	248.74	257.93	335.86
Ovaries (G)	1.94	0.71	1.11	0.85
% BODY WEIGHT	0.019	0.008	0.013	0.012
% BRAIN WEIGHT	2.44	0.87	1.55	1.19
Spleen (G)	26.79	28.07	25.26	30.33
% BODY WEIGHT	0.263	0.330	0.297	0.427
% BRAIN WEIGHT	33.66	34.41	35.31	42.34
Thyroids-Parathyroids (G)	1.74	0.66	1.08	1.27
% BODY WEIGHT	0.017	0.008	0.013	0.018
% BRAIN WEIGHT	2.19	0.81	1.51	1.77
Uterus (G)	11.32	2.90	4.03	3.68
% BODY WEIGHT	0.111	0.034	0.047	0.052
% BRAIN WEIGHT	14.22	3.55	5.63	5.14

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

 -----  
 INDIVIDUAL ORGAN WEIGHTS  
 -----

 STUDY: 097  
 SEX: FEMALE

 GROUP: 3F - 2.0 mg base/kg/day  
 ALL FATES      DAYS: 91-92      ALL BALANCES

ANIMAL ID: BALANCE NO.:	7556	7564	7572	7574
-----	-----	-----	-----	-----
BODY WEIGHT (KG)	8.1	7.6	10.7	8.0
Adrenals (pr) (G)	1.05	1.11	1.47	1.31
% BODY WEIGHT	0.013	0.015	0.014	0.016
% BRAIN WEIGHT	1.41	1.47	1.98	1.65
Brain (G)	74.30	75.44	74.35	79.42
% BODY WEIGHT	0.917	0.993	0.695	0.993
Heart (G)	91.92	77.18	79.74	78.27
% BODY WEIGHT	1.135	1.016	0.745	0.978
% BRAIN WEIGHT	123.71	102.31	107.25	98.55
Kidneys (pr) (G)	40.33	36.89	45.91	43.94
% BODY WEIGHT	0.498	0.485	0.429	0.549
% BRAIN WEIGHT	54.28	48.90	61.75	55.33
Liver (G)	259.87	298.46	338.91	277.50
% BODY WEIGHT	3.208	3.927	3.167	3.469
% BRAIN WEIGHT	349.76	395.63	455.83	349.41
Ovaries (G)	0.59	0.59	1.45	0.60
% BODY WEIGHT	0.007	0.008	0.014	0.008
% BRAIN WEIGHT	0.79	0.78	1.95	0.76
Spleen (G)	36.93	25.25	45.29	48.07
% BODY WEIGHT	0.456	0.332	0.423	0.601
% BRAIN WEIGHT	49.70	33.47	60.91	60.53
Thyroids-Parathyroids (G)	0.99	1.01	1.50	1.11
% BODY WEIGHT	0.012	0.013	0.014	0.014
% BRAIN WEIGHT	1.33	1.34	2.02	1.40
Uterus (G)	2.84	1.76	19.26	3.18
% BODY WEIGHT	0.035	0.023	0.180	0.040
% BRAIN WEIGHT	3.82	2.33	25.90	4.00

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

 -----  
 INDIVIDUAL ORGAN WEIGHTS  
 -----

 STUDY: 097  
 SEX: FEMALE

 GROUP: 4F - 6.0 mg base/kg/day  
 ALL FATES      DAYS: 91-92      ALL BALANCES

ANIMAL ID: BALANCE NO.:	7544	7546	7551	7568
BODY WEIGHT (KG)	7.6	7.7	9.7	8.0
Adrenals (pr) (G)	1.41	1.22	1.95	0.53
% BODY WEIGHT	0.019	0.016	0.020	0.007
% BRAIN WEIGHT	1.88	1.83	2.64	0.73
Brain (G)	75.17	66.80	73.75	72.33
% BODY WEIGHT	0.989	0.868	0.760	0.904
Heart (G)	68.27	69.97	85.81	69.06
% BODY WEIGHT	0.898	0.909	0.885	0.863
% BRAIN WEIGHT	90.82	104.75	116.35	95.48
Kidneys (pr) (G)	39.32	41.98	44.55	39.03
% BODY WEIGHT	0.517	0.545	0.459	0.488
% BRAIN WEIGHT	52.31	62.84	60.41	53.96
Liver (G)	243.01	280.81	353.40	271.41
% BODY WEIGHT	3.198	3.647	3.643	3.393
% BRAIN WEIGHT	323.28	420.37	479.19	375.24
Ovaries (G)	1.02	0.82	0.87	--
% BODY WEIGHT	0.013	0.011	0.009	--
% BRAIN WEIGHT	1.36	1.23	1.18	--
Spleen (G)	76.31	106.91	95.01	72.90
% BODY WEIGHT	1.004	1.388	0.979	0.911
% BRAIN WEIGHT	101.52	160.04	128.83	100.79
Thyroids-Parathyroids (G)	1.33	0.78	1.15	1.21
% BODY WEIGHT	0.018	0.010	0.012	0.015
% BRAIN WEIGHT	1.77	1.17	1.56	1.67
Uterus (G)	5.36	2.49	6.20	10.44
% BODY WEIGHT	0.071	0.032	0.064	0.131
% BRAIN WEIGHT	7.13	3.73	8.41	14.43

 -----  
 (--) - Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 097  
SEX: MALE

GROUP: 1M - 0 mg base/kg/day  
ALL FATES      DAYS: 182-183      ALL BALANCES

ANIMAL ID: BALANCE NO.:	7512	7515	7531	7532
BODY WEIGHT (KG)	11.5	12.7	11.3	10.7
Adrenals (pr) (G)	1.04	1.06	1.23	1.36
% BODY WEIGHT	0.009	0.008	0.011	0.013
% BRAIN WEIGHT	1.42	1.19	1.75	1.67
Brain (G)	73.30	89.19	70.15	81.38
% BODY WEIGHT	0.637	0.702	0.621	0.761
Heart (G)	92.49	102.63	97.88	94.52
% BODY WEIGHT	0.804	0.808	0.866	0.883
% BRAIN WEIGHT	126.18	115.07	139.53	116.15
Kidneys (pr) (G)	65.81	54.35	58.85	54.94
% BODY WEIGHT	0.572	0.428	0.521	0.513
% BRAIN WEIGHT	89.78	60.94	83.89	67.51
Liver (G)	305.84	272.88	260.10	232.09
% BODY WEIGHT	2.659	2.149	2.302	2.169
% BRAIN WEIGHT	417.24	305.95	370.78	285.19
Spleen (G)	29.52	52.33	30.66	32.23
% BODY WEIGHT	0.257	0.412	0.271	0.301
% BRAIN WEIGHT	40.27	58.67	43.71	39.60
Testes w/Epidid. (pr) (G)	24.54	24.37	17.94	19.79
% BODY WEIGHT	0.213	0.192	0.159	0.185
% BRAIN WEIGHT	33.48	27.32	25.57	24.32
Thyroids-Parathyroids (G)	1.04	1.15	0.82	1.30
% BODY WEIGHT	0.009	0.009	0.007	0.012
% BRAIN WEIGHT	1.42	1.29	1.17	1.60

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

 -----  
 INDIVIDUAL ORGAN WEIGHTS  
 -----

 STUDY: 097  
 SEX: MALE

 GROUP: 2M - 0.1 mg base/kg/day  
 ALL FATES      DAYS: 182-183      ALL BALANCES

ANIMAL ID: BALANCE NO.:	7519	7527	7529	7536
BODY WEIGHT (KG)	12.3	11.0	11.3	10.4
Adrenals (pr) (G)	1.73	1.27	1.51	1.35
% BODY WEIGHT	0.014	0.012	0.013	0.013
% BRAIN WEIGHT	2.39	1.51	2.09	1.83
Brain (G)	72.27	83.85	72.25	73.89
% BODY WEIGHT	0.588	0.762	0.639	0.710
Heart (G)	90.36	88.42	94.52	103.80
% BODY WEIGHT	0.735	0.804	0.836	0.998
% BRAIN WEIGHT	125.03	105.45	130.82	140.48
Kidneys (pr) (G)	60.17	50.56	68.79	59.83
% BODY WEIGHT	0.489	0.460	0.609	0.575
% BRAIN WEIGHT	83.26	60.30	95.21	80.97
Liver (G)	268.37	279.34	320.06	272.30
% BODY WEIGHT	2.182	2.539	2.832	2.618
% BRAIN WEIGHT	371.34	333.14	442.99	368.52
Spleen (G)	28.24	49.84	39.81	23.24
% BODY WEIGHT	0.230	0.453	0.352	0.223
% BRAIN WEIGHT	39.08	59.44	55.10	31.45
Testes w/Epidid. (pr) (G)	19.40	18.51	21.10	18.97
% BODY WEIGHT	0.158	0.168	0.187	0.182
% BRAIN WEIGHT	26.84	22.08	29.20	25.67
Thyroids-Parathyroids (G)	1.03	0.92	1.14	1.08
% BODY WEIGHT	0.008	0.008	0.010	0.010
% BRAIN WEIGHT	1.43	1.10	1.58	1.46

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 097  
SEX: MALE

GROUP: 3M - 2.0 mg base/kg/day  
ALL FATES      DAYS: 182-183      ALL BALANCES

ANIMAL ID: BALANCE NO.:	7510	7516	7522	7538
BODY WEIGHT (KG)	12.7	10.0	11.3	11.3
Adrenals (pr) (G)	2.15	1.69	1.49	1.55
% BODY WEIGHT	0.017	0.017	0.013	0.014
% BRAIN WEIGHT	2.67	2.18	2.08	1.94
Brain (G)	80.65	77.66	71.79	80.05
% BODY WEIGHT	0.635	0.777	0.635	0.708
Heart (G)	107.91	108.23	92.69	99.07
% BODY WEIGHT	0.850	1.082	0.820	0.877
% BRAIN WEIGHT	133.80	139.36	129.11	123.76
Kidneys (pr) (G)	60.21	60.35	60.36	57.87
% BODY WEIGHT	0.474	0.604	0.534	0.512
% BRAIN WEIGHT	74.66	77.71	84.08	72.29
Liver (G)	366.81	270.69	292.53	269.99
% BODY WEIGHT	2.888	2.707	2.589	2.389
% BRAIN WEIGHT	454.82	348.56	407.48	337.28
Spleen (G)	51.59	37.13	44.75	29.76
% BODY WEIGHT	0.406	0.371	0.396	0.263
% BRAIN WEIGHT	63.97	47.81	62.33	37.18
Testes w/Epidid. (pr) (G)	21.34	23.18	20.31	20.55
% BODY WEIGHT	0.168	0.232	0.180	0.182
% BRAIN WEIGHT	26.46	29.85	28.29	25.67
Thyroids-Parathyroids (G)	1.36	1.73	1.54	1.32
% BODY WEIGHT	0.011	0.017	0.014	0.012
% BRAIN WEIGHT	1.69	2.23	2.15	1.65

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 097  
SEX: MALE

GROUP: 4M - 6.0 mg base/kg/day  
ALL FATES      DAYS: 182-183      ALL BALANCES

ANIMAL ID: BALANCE NO.:	7507	7511	7530	7535
BODY WEIGHT (KG)	11.8	11.1	10.1	10.2
Adrenals (pr) (G)	1.08	1.46	1.19	1.35
% BODY WEIGHT	0.009	0.013	0.012	0.013
% BRAIN WEIGHT	1.52	1.66	1.68	2.03
Brain (G)	71.18	87.80	70.90	66.48
% BODY WEIGHT	0.603	0.791	0.702	0.652
Heart (G)	96.27	109.56	110.70	85.29
% BODY WEIGHT	0.816	0.987	1.096	0.836
% BRAIN WEIGHT	135.25	124.78	156.14	128.29
Kidneys (pr) (G)	56.18	52.62	50.22	58.83
% BODY WEIGHT	0.476	0.474	0.497	0.577
% BRAIN WEIGHT	78.93	59.93	70.83	88.49
Liver (G)	310.39	366.21	278.01	268.31
% BODY WEIGHT	2.630	3.299	2.753	2.630
% BRAIN WEIGHT	436.06	417.10	392.12	403.60
Spleen (G)	32.68	38.82	25.81	35.16
% BODY WEIGHT	0.277	0.350	0.256	0.345
% BRAIN WEIGHT	45.91	44.21	36.40	52.89
Testes w/Epidid. (pr) (G)	16.77	22.01	19.34	16.62
% BODY WEIGHT	0.142	0.198	0.191	0.163
% BRAIN WEIGHT	23.56	25.07	27.28	25.00
Thyroids-Parathyroids (G)	1.26	1.41	1.50	1.46
% BODY WEIGHT	0.011	0.013	0.015	0.014
% BRAIN WEIGHT	1.77	1.61	2.12	2.20

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 097  
SEX: FEMALE

GROUP: 1F - 0 mg base/kg/day  
ALL FATES      DAYS: 182-183      ALL BALANCES

ANIMAL ID: BALANCE NO.:	7541	7549	7557	7566
BODY WEIGHT (KG)	9.8	10.9	8.4	11.4
Adrenals (pr) (G)	1.52	1.20	1.62	1.45
% BODY WEIGHT	0.016	0.011	0.019	0.013
% BRAIN WEIGHT	2.20	1.57	2.03	2.03
Brain (G)	69.03	76.30	79.78	71.48
% BODY WEIGHT	0.704	0.700	0.950	0.627
Heart (G)	77.98	77.44	81.47	82.13
% BODY WEIGHT	0.796	0.710	0.970	0.720
% BRAIN WEIGHT	112.97	101.49	102.12	114.90
Kidneys (pr) (G)	41.31	40.01	38.80	43.81
% BODY WEIGHT	0.422	0.367	0.462	0.384
% BRAIN WEIGHT	59.84	52.44	48.63	61.29
Liver (G)	247.26	241.08	233.06	249.83
% BODY WEIGHT	2.523	2.212	2.775	2.191
% BRAIN WEIGHT	358.19	315.96	292.13	349.51
Ovaries (G)	0.75	1.56	1.74	1.33
% BODY WEIGHT	0.008	0.014	0.021	0.012
% BRAIN WEIGHT	1.09	2.04	2.18	1.86
Spleen (G)	31.50	37.54	24.97	37.79
% BODY WEIGHT	0.321	0.344	0.297	0.331
% BRAIN WEIGHT	45.63	49.20	31.30	52.87
Thyroids-Parathyroids (G)	1.14	0.96	1.02	1.26
% BODY WEIGHT	0.012	0.009	0.012	0.011
% BRAIN WEIGHT	1.65	1.26	1.28	1.76
Uterus (G)	3.84	5.45	19.11	5.77
% BODY WEIGHT	0.039	0.050	0.228	0.051
% BRAIN WEIGHT	5.56	7.14	23.95	8.07

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 097  
 SEX: FEMALE

GROUP: 2F - 0.1 mg base/kg/day  
 ALL FATES DAYS: 182-183 ALL BALANCES

ANIMAL ID: BALANCE NO.:	7543	7545	7552	7553
BODY WEIGHT (KG)	10.0	9.8	11.0	11.6
Adrenals (pr) (G)	1.39	1.57	1.40	1.17
% BODY WEIGHT	0.014	0.016	0.013	0.010
% BRAIN WEIGHT	2.02	1.98	1.80	1.58
Brain (G)	68.78	79.36	77.86	74.15
% BODY WEIGHT	0.688	0.810	0.708	0.639
Heart (G)	75.19	89.93	92.02	68.79
% BODY WEIGHT	0.752	0.918	0.837	0.593
% BRAIN WEIGHT	109.32	113.32	118.19	92.77
Kidneys (pr) (G)	40.29	42.56	47.53	37.77
% BODY WEIGHT	0.403	0.434	0.432	0.326
% BRAIN WEIGHT	58.58	53.63	61.05	50.94
Liver (G)	206.75	229.21	343.34	269.78
% BODY WEIGHT	2.068	2.339	3.121	2.326
% BRAIN WEIGHT	300.60	288.82	440.97	363.83
Ovaries (G)	1.08	0.90	2.07	1.87
% BODY WEIGHT	0.011	0.009	0.019	0.016
% BRAIN WEIGHT	1.57	1.13	2.66	2.52
Spleen (G)	30.57	36.53	34.45	23.16
% BODY WEIGHT	0.306	0.373	0.313	0.200
% BRAIN WEIGHT	44.45	46.03	44.25	31.23
Thyroids-Parathyroids (G)	0.71	1.11	1.09	0.78
% BODY WEIGHT	0.007	0.011	0.010	0.007
% BRAIN WEIGHT	1.03	1.40	1.40	1.05
Uterus (G)	3.76	6.51	19.46	504.17
% BODY WEIGHT	0.038	0.066	0.177	4.346
% BRAIN WEIGHT	5.47	8.20	24.99	679.93

DRAFT

 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

 -----  
 INDIVIDUAL ORGAN WEIGHTS  
 -----

 STUDY: 097  
 SEX: FEMALE

 GROUP: 3F - 2.0 mg base/kg/day  
 ALL FATES      DAYS: 182-183      ALL BALANCES

ANIMAL ID: BALANCE NO.:	7548	7561	7562	7571
BODY WEIGHT (KG)	9.8	8.3	10.5	9.6
Adrenals (pr) (G)	1.19	1.47	1.62	1.37
% BODY WEIGHT	0.012	0.018	0.015	0.014
% BRAIN WEIGHT	1.65	2.11	2.05	1.96
Brain (G)	72.23	69.77	78.93	69.96
% BODY WEIGHT	0.737	0.841	0.752	0.729
Heart (G)	79.46	87.77	77.29	79.65
% BODY WEIGHT	0.811	1.057	0.736	0.830
% BRAIN WEIGHT	110.01	125.80	97.92	113.85
Kidneys (pr) (G)	41.39	42.22	41.27	38.32
% BODY WEIGHT	0.422	0.509	0.393	0.399
% BRAIN WEIGHT	57.30	60.51	52.29	54.77
Liver (G)	255.80	303.64	220.96	267.30
% BODY WEIGHT	2.610	3.658	2.104	2.784
% BRAIN WEIGHT	354.15	435.20	279.94	382.08
Ovaries (G)	1.09	1.00	1.00	1.65
% BODY WEIGHT	0.011	0.012	0.010	0.017
% BRAIN WEIGHT	1.51	1.43	1.27	2.36
Spleen (G)	40.02	18.38	30.96	41.19
% BODY WEIGHT	0.408	0.221	0.295	0.429
% BRAIN WEIGHT	55.41	26.34	39.22	58.88
Thyroids-Parathyroids (G)	1.06	1.08	0.83	1.11
% BODY WEIGHT	0.011	0.013	0.008	0.012
% BRAIN WEIGHT	1.47	1.55	1.05	1.59
Uterus (G)	6.21	6.51	5.92	15.61
% BODY WEIGHT	0.063	0.078	0.056	0.163
% BRAIN WEIGHT	8.60	9.33	7.50	22.31

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 097  
SEX: FEMALE

GROUP: 4F - 6.0 mg base/kg/day  
ALL FATES DAYS: 182-183 ALL BALANCES

ANIMAL ID: BALANCE NO.:	7539	7540	7554	7563
BODY WEIGHT (KG)	8.3	10.0	11.0	9.5
Adrenals (pr) (G)	1.27	1.27	1.15	1.23
% BODY WEIGHT	0.015	0.013	0.010	0.013
% BRAIN WEIGHT	1.69	1.89	1.42	1.57
Brain (G)	74.95	67.03	80.82	78.22
% BODY WEIGHT	0.903	0.670	0.735	0.823
Heart (G)	70.20	90.11	93.41	69.39
% BODY WEIGHT	0.846	0.901	0.849	0.730
% BRAIN WEIGHT	93.66	134.43	115.58	88.71
Kidneys (pr) (G)	38.46	45.35	50.84	47.26
% BODY WEIGHT	0.463	0.454	0.462	0.497
% BRAIN WEIGHT	51.31	67.66	62.91	60.42
Liver (G)	244.78	306.11	360.96	276.54
% BODY WEIGHT	2.949	3.061	3.281	2.911
% BRAIN WEIGHT	326.59	456.68	446.62	353.54
Ovaries (G)	1.16	2.58	1.09	2.48
% BODY WEIGHT	0.014	0.026	0.010	0.026
% BRAIN WEIGHT	1.55	3.85	1.35	3.17
Spleen (G)	32.03	30.71	43.82	28.76
% BODY WEIGHT	0.386	0.307	0.398	0.303
% BRAIN WEIGHT	42.74	45.82	54.22	36.77
Thyroids-Parathyroids (G)	0.68	1.21	0.95	0.93
% BODY WEIGHT	0.008	0.012	0.009	0.010
% BRAIN WEIGHT	0.91	1.81	1.18	1.19
Uterus (G)	4.76	16.33	15.56	22.40
% BODY WEIGHT	0.057	0.163	0.141	0.236
% BRAIN WEIGHT	6.35	24.36	19.25	28.64

DRAFT

APPENDIX 12  
Pathology Report

DRAFT

THIRD DRAFT PATHOLOGY REPORT FOR  
TRL STUDY NUMBER 097  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

PREPARED  
BY  
PATHOLOGY ASSOCIATES, INC.  
10 WEST 35TH STREET  
CHICAGO, IL 60616

FOR  
TOXICOLOGY RESEARCH LABORATORY  
UNIVERSITY OF ILLINOIS AT CHICAGO (UIC)  
DEPARTMENT OF PHARMACOLOGY  
P.O. BOX 6998  
CHICAGO, IL 60680

MARCH 18, 1994

TABLE OF CONTENTS

D R A F T

SECTION	TITLE	PAGE
I	Pathology Narrative .....	3
	Summary of Experimental Design (Table I) .....	12
	Protocol Required Tissues (Table II) .....	12
	Report Codes Table .....	13
	Abbreviation List .....	14
II	Project Summary Table .....	15
	Males .....	16
	Females .....	22
III	Severity Summary Table .....	27
	Males .....	28
	Females .....	33
IV	Tabulated Animal Data .....	38
	Males .....	39
	Females .....	65
V	Correlation of Gross and Microscopic (Micro) Findings .....	89
	Males .....	90
	Females .....	99
VI	Quality Assurance Statement .....	107
VII	Appendix I: Bone Marrow Report .....	109

DRAFT

SECTION I  
PATHOLOGY NARRATIVE

THIRD DRAFT PATHOLOGY REPORT

D R A F T

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INTRODUCTION

This pathology report, submitted by Pathology Associates, Inc. (PAI) to Toxicology Research Laboratory (TRL), represents the gross and histopathology findings for the study designated as "Thirteen Week Oral Toxicity Study of WR 238605 with a Thirteen Week Recovery Period in Dogs", TRL Study Number 097.

EXPERIMENTAL DESIGN AND METHODS

Four groups, each composed of male and female Beagle dogs, were given the test article (WR 238605) or test article vehicle (aqueous 1% methylcellulose/0.4% Tween 80) by gastric intubation for 13 weeks, starting with Day 0. Dose levels administered are shown in the Summary of Experimental Design (Table I). The animals designated to be sacrificed after the 13-week dosing period were dosed up to and including the day prior to scheduled necropsy on Days 91 and 92 (week 14). Recovery animals were dosed for 91 days and then held for a 13-week recovery period. At the beginning of week 27, the recovery animals were sacrificed and necropsied. No animals were sacrificed moribund or found dead during the study. Necropsies were performed according to TRL Standard Operating Procedures under the supervision of Ralph M. Bunte, DVM or Michael J. Tomlinson, DVM, Ph.D. Tissues required by protocol for animals sacrificed at the end of dosing (Table II), except as noted below, were processed and slides prepared in accordance with PAI Standard Operating Procedures.

Except as noted below, these tissues from all animals sacrificed at the end of dosing were examined microscopically. Mammary gland was not present in sections from six animals (#7524, #7533, #7555, #7564, #7572, and #7573) even after repeated attempts to obtain this tissue. Thyroid/parathyroid gland (#7521), urinary bladder and prostate (#7502), skin/mammary gland (#7509), aorta (#7542), and pituitary gland (#7546) were missing from one animal each at trimming. Wet tissues from these animals were reviewed after trimming to verify that these tissues were missing. As no test article-related changes were detected in corresponding tissues in other animals, the absence of these tissues is not believed to have affected the outcome of the study.

After identification of test article-related changes, target tissues were examined in all recovery animals. Target tissues in animals sacrificed after dosing were re-examined at the time the sections of target tissues from recovery animals were examined. When necessary to clarify interpretation or grading of changes, the target tissue slides were mixed up and examined without knowledge of treatment group or time of sacrifice.

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). The mean group severity scores were determined by dividing the sum of all severity scores for a finding by the number of tissues examined. 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. Abbreviations used in these tables are explained in the Abbreviation List.

## RESULTS AND DISCUSSION

The Results and Discussion section is divided into two parts: Diagnostic Terms and Histopathology Findings. The Diagnostic Terms portion lists and clarifies diagnostic terminology that may be unclear. Terms listed in the Diagnostic Terms portion of this section were not necessarily considered to be test article-related. The Histopathology Findings portion of this section reports the results and provides discussion of the histopathologic evaluation of the tissues.

### 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.

#### Lungs

The principal change in the lungs of these animals had three distinct components. First, there was pale eosinophilic amorphous to fibrillar material within alveoli. This was accompanied by large round to oval discrete cells which had abundant vacuolated cytoplasm. These cells were free in the lumina of alveoli and terminal bronchioles and did not appear to line alveolar septa. The third component of this change was the presence of neutrophils in variable numbers in affected alveoli. In order to be consistent with morphologically similar changes that occurred in the lungs of rats given this test article under similar conditions (TRL Study Number 098), this change was diagnosed as alveolar proteinosis.

Subacute inflammation consisted of macrophages and a few lymphocytes forming cuffs around venules and small arterioles. This change occurred within areas of alveolar proteinosis and acute inflammation, but occurred independent of these areas as well. This morphologic pattern suggests that subacute inflammation may have been related to or exacerbated by alveolar proteinosis and acute inflammation.

Chronic inflammation was seen in animals sacrificed after the recovery period. It was usually focal and subcapsular. It consisted of interstitial fibrosis, mononuclear cell infiltration, and sometimes hyperplasia of alveolar or bronchiolar epithelium. Cholesterol clefts were also present in many of these foci.

#### Spleen

Extramedullary hematopoiesis consisted of increased hematopoietic tissue in sinusoids of the spleen.

Hemosiderin pigment was represented by golden-brown granular pigment filling the cytoplasm of macrophages in sinusoids.

#### Liver

Hepatocyte necrosis consisted of individual or small clusters of hepatocytes which were pyknotic. These foci were often infiltrated by a few macrophages and lymphocytes.

Hemosiderin pigment was a granular golden-brown pigment found in Kupffer cells.

Kupffer cell hypertrophy was characterized by enlargement of sinusoidal Kupffer cells. The enlargement was due to pale brown material, not identifiable as hemosiderin, in the cytoplasm. Hyperplasia was diagnosed when Kupffer cell numbers appeared to be increased.

Subacute inflammation in the liver occurred focally around small veins. There were usually hemosiderin-laden macrophages present, but small mononuclear cells and neutrophils were

also present. These foci tended not to extend into the surrounding parenchyma and were not related to hepatocyte necrosis.

#### Thymus

Lymphocyte depletion was characterized by a decrease in cortical lymphocytes. This varied from a pale-staining cortex with increased pyknotic lymphocytes to distinct thinning of the cortex. The diagnosis of lymphocyte depletion is analogous to thymic atrophy.

#### Bone Marrow

Hypercellularity was diagnosed when hematopoietic cells in the marrow were increased, replacing fat cells.

#### Kidney

Nephrocalcinosis refers to focal deposits of laminated purple mineral found within renal tubules in the cortico-medullary zone or renal papilla.

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

### Histopathology Findings

#### Lungs

Among animals sacrificed at the end of dosing, alveolar proteinosis was diagnosed in 0 out of 4, 2 out of 4, and 4 out of 4 males, and in 0 out of 4, 4 out of 4, and 4 out of 4 females in the low, middle, and high dose groups, respectively. Mean group severity scores for this change were 0.00, 0.50, and 2.50 in males, and 0.00, 1.00, and 2.00 in females in the low, middle, and high dose groups, respectively. Alveolar proteinosis was not diagnosed in males or females in the control group sacrificed at the end of dosing. Alveolar proteinosis did not occur in males sacrificed after the recovery period. This change did occur in 2 out of 4 females in the high dose group but not in any other females sacrificed after the recovery period. The mean group severity score for this change in high dose recovery females was 0.50, as the change was of minimal severity in each affected animal. The incidence and mean group severity scores for alveolar proteinosis in animals sacrificed at the end of dosing were interpreted as consistent with a dose-related response. This observation, in conjunction with resolution (males) or near resolution (females) of this change in animals sacrificed after the recovery period, indicates alveolar proteinosis to be a test article-related change.

Subacute inflammation in the lungs occurred in control and in all treated groups in both males and females. Among animals sacrificed at the end of dosing, this change occurred in 1 out of 4, 2 out of 4, 4 out of 4, and 4 out of 4 males, and in 2 out of 4, 4 out of 4, 4 out of 4, and 4 out of 4 females in the control, low, middle, and high dose groups, respectively. Mean group severity scores for this change in these animals were 0.25, 0.50, 2.50, and 3.25 in males and 1.00, 1.25, 2.75, and 2.25 in females in the control, low, middle, and high dose groups, respectively. Among animals sacrificed after the recovery period, this change occurred in 2 out of 4, 2 out of 4, 3 out of 4, and 4 out of 4 males, and in 3 out of 4, 1 out of 4, 4 out of 4, and 4 out of 4 females in the control, low, middle, and high dose groups, respectively. Mean group severity scores for these animals were 0.50, 0.50, 0.75, and 1.25 in males, and 0.75, 0.25, 1.00, and 1.50 in females in the control, low, middle, and high dose groups, respectively. Subacute inflammation can occur as a spontaneous lesion in the lungs of control or untreated animals. The cause of the inflammation in such animals is usually unknown, but in dogs it can occur in response to parasite larval migration in neonatal or juvenile puppies. It can also result from inhaled particulates or biological agents. There is a clear increase in incidence and severity of this change in middle and high dose males and females sacrificed at

the end of dosing compared to controls. Though less clearly so than in the middle and high dose females, the incidence and mildly increased mean group severity score for this change in low dose females as compared to controls may also represent a test article-related response. The small increases in incidence and mean group severity in control animals sacrificed after the recovery period as compared to those sacrificed at the end of dosing are probably due to the increased age of the recovery dogs. The differences in incidence and mean group severity of this change between control and treated recovery animals are less than the differences in animals sacrificed at the end of dosing. This change is clearly still more severe in high dose than in control animals sacrificed at the end of the recovery period, indicating that resolution of subacute inflammation in the lung was not complete after the 13 week recovery period. Resolution of this change has been substantial during the recovery period, though, as incidence and mean group severity scores for this change in low and middle dose recovery animals are not clearly different from those of control recovery animals. For all of these reasons, subacute inflammation in the lungs of males and females was interpreted as a spontaneous process that was exacerbated by treatment with the test article. It was interpreted as a test article-related change that had not completely resolved by the end of dosing.

Chronic inflammation in the lungs was observed only in animals sacrificed after the recovery period. In males sacrificed after the recovery period, chronic inflammation in the lungs occurred in 2 out of 4 and 3 out of 4 animals in the middle and high dose groups, with mean group severity scores of 0.75 and 1.00, respectively. In females sacrificed at this time, this change occurred in 1 out of 4, 1 out of 4, 2 out of 4, and 0 out of 4 animals in the control, low, middle, and high dose groups, with mean group severity scores of 0.50, 0.25, 0.50, and 0.00, respectively. Chronic inflammation was focal or multifocal, and was usually subcapsular in the lungs. It was not necessarily related to areas of subacute inflammation in animals sacrificed after the recovery period. A possible relationship of chronic inflammation to alveolar proteinosis and subacute inflammation can only be speculated on, as chronic inflammation did not occur in animals sacrificed at the end of dosing. Such a relationship seems likely, however, as alveolar proteinosis had largely resolved after the recovery period and no other change that could have resulted in chronic inflammation was noted in animals sacrificed at the end of dosing. For these reasons, chronic inflammation in recovery animals was interpreted as part of the resolution process of alveolar proteinosis and was, thus, secondary to a direct test article-related change.

Spontaneous alveolar proteinosis has been described in the Fischer 344 rat, but its causes are unknown. Altered vascular permeability and abnormal surfactant production and degradation have been suggested as possible causes of this change.<sup>1</sup> The clinical and anatomic pathology observations in this study do not allow identification of the specific mechanism of injury that lead to the features described as alveolar proteinosis. They do, however, suggest that increased vascular permeability in the pulmonary microvasculature may have been involved in the development of this change. The amorphous to fibrillar eosinophilic material in the alveoli is consistent with fibrin that would leak into the alveoli as fibrinogen if vascular permeability were increased. The large foamy cells, also in the alveoli, are macrophages attempting to remove this fibrin by phagocytosis. Neutrophils present in this change may have migrated from capillaries in response to chemoattractants released during the primary injury. These features are consistent with pulmonary edema due to toxic alteration of the pulmonary microvascular or epithelial membrane resulting in alveolar fluid that is rich in fibrinogen and other plasma proteins.<sup>2</sup> Mechanisms by which such toxic changes may occur have been described for cytotoxic and non-cytotoxic drugs. These include injury to the oxidant/antioxidant, immunological, matrix repair, and protease/antiprotease systems in the lungs, and injury to the central nervous system.<sup>3,4</sup> Oxidative injury in the lung is a likely mechanism by which alveolar proteinosis developed in these animals, as there is other evidence that the test article causes oxidative injury. This evidence is primarily the occurrence of

statistically significant methemoglobin formation in the middle and high dose males and females at weeks 2, 4, 8, and 13. Both methemoglobin formation and oxidant/antioxidant system injury in the lung have been associated with superoxide anion and hydrogen peroxide formation.<sup>3,4,5</sup> Subacute inflammation in the lung may occur as a spontaneous lesion but was increased in incidence and severity in a dose-related manner in this study. This increase was considered to be most likely related to the diffuse lung injury that resulted in alveolar proteinosis. For these reasons, and due to incidence and mean group severity scores at the end of dosing and after the recovery period, alveolar proteinosis and subacute inflammation in the lungs were interpreted as test article-related changes. Chronic inflammation in the lungs occurred only in recovery animals. The morphologic features of the chronic inflammation were consistent with it representing the resolution of alveolar proteinosis, and as such, this change was interpreted as a secondary test article-related change. Though the chronic inflammation in the lung did contain fibrosis, this was a focal change, usually subcapsular in location and was minimal to mild in severity. For these reasons, it seems most likely that chronic inflammation would have little negative long-term effect on pulmonary function. Studies of longer duration would be necessary to verify or refute this interpretation, though. The chronic inflammation that occurred in the lung of one female in the control recovery group was considered incidental. This was a focal interstitial area of chronic inflammation lacking the cholesterol clefts seen in treated dogs. The cause of chronic lung inflammation in this dog was not evident. The acute inflammation that occurred in one low dose recovery female was a focal change of minimal severity. It was considered incidental and most likely a response to an inhaled microbe or irritant.

#### Spleen

Among animals sacrificed at the end of dosing, deposition of hemosiderin in the spleen was diagnosed in 0 out of 4, 1 out of 4, 1 out of 4, and 3 out of 4 males, and in 0 out of 4, 0 out of 4, 3 out of 4, and 4 out of 4 females in the control, low, middle, and high dose groups, respectively. Mean group severity scores for this finding in these animals were 0.00, 0.25, 0.50, and 1.00 in males, and 0.00, 0.00, 1.00, and 1.25 in females in the control, low, middle, and high dose groups, respectively. Among animals sacrificed at the end of the recovery period, this change occurred in 2 out of 4, 1 out of 4, 1 out of 4, and 2 out of 4 males, and in 1 out of 4, 0 out of 4, 3 out of 4, and 3 out of 4 females in the control, low, middle, and high dose groups, respectively. Mean group severity scores for this change in these animals were 0.75, 0.25, 0.25, and 0.50 in males, and 0.25, 0.00, 0.75, and 1.00 in females in the control, low, middle, and high dose groups, respectively.

Extramedullary hematopoiesis (EMH) was observed in the spleen in males and females in the middle and high dose groups that were sacrificed at the end of dosing. In these animals, EMH occurred in 1 out of 4 and 2 out of 4 males, and in 1 out of 4 and 3 out of 4 females in the middle and high dose groups, respectively. Mean group severity scores for this change in these animals were 0.25 and 0.50 in males, and 0.25 and 1.25 in females in the middle and high dose groups, respectively. This change did not occur in males or females in the control and low dose groups sacrificed at the end of dosing, or in any animals sacrificed after the recovery period.

Excess iron in the body is normally stored in the liver, spleen, and bone marrow. These stores are visible by light microscopy as hemosiderin deposits which can be seen in these tissues in normal dogs. Iron is highly conserved in dogs; normal losses are small and are through the intestine. Consequently, absorption of iron by the small intestine is also in small amounts. Regulation of iron absorption is primarily by need. Iron released from erythrocytes by hemolysis or hemorrhage into body tissues is stored as increased hemosiderin. Iron stored in hemosiderin is readily available for use in erythropoiesis. Hemosiderin deposits which are increased due to an episode of hemolysis or hemorrhage will be gradually depleted over time.

The rate will be dependent on the amount of hemosiderin deposited and the rate at which erythropoiesis proceeds.<sup>6</sup> In this study, incidence and severity of hemosiderin deposition in the spleen are consistent with a test article-related effect in high dose group males sacrificed at the end of dosing but only equivocally suggest a test article-related effect in low and middle dose group males at this time. In females sacrificed at the end of dosing, incidence and mean group severity scores indicate this to be a test article-related effect. Among females sacrificed after the recovery period, incidence and mean group severity scores indicate that resolution of the hemosiderin deposits was in progress but was not yet complete. Incidence and mean group severity scores for this change in males sacrificed after the recovery period are difficult to interpret, but are consistent with hemosiderin deposition in the spleen being a test article-related effect in males only in the high dose group sacrificed at the end of dosing. The difficulty in interpreting this change in male recovery dogs lies in the spontaneous occurrence of this change in dogs. The deposition of hemosiderin in the spleen indicates increased destruction of erythrocytes. This is also indicated by the incidence and mean group severity scores for EMH in males and females sacrificed at the end of dosing. The low mean group severity scores for these changes, however, indicate that the increase in erythrocyte destruction was mild and suggest that clinical anemia, if present, was mild. Both hemosiderin deposition and EMH in the spleen were interpreted as secondary to increased erythrocyte destruction.

#### Liver

Among animals sacrificed at the end of dosing, deposition of hemosiderin pigment was diagnosed in the liver in 0 out of 4, 0 out of 4, 2 out of 4, and 1 out of 4 males, and in 0 out of 4, 1 out of 4, 2 out of 4, and 4 out of 4 females in the control, low, middle, and high dose groups, respectively. Mean group severity scores for this change in these animals were 0.00, 0.00, 0.75, and 0.75 in males, and 0.00, 0.25, 0.50, and 2.25 in females in the control, low, middle, and high dose groups, respectively. Among animals sacrificed after the recovery period, this change was diagnosed only in the middle and high dose groups. This change occurred in 1 out of 4 and 2 out of 4 males, and in 4 out of 4 and 3 out of 4 females, with mean group severity scores of 0.25 and 0.75 in males, and 1.00 and 1.25 in females in the middle and high dose groups, respectively.

Kupffer cell hypertrophy was diagnosed in males and females sacrificed after the dosing period but not in those sacrificed after the recovery period. Among animals sacrificed at the end of dosing, this change occurred in 1 out of 4 and 2 out of 4 males, and in 1 out of 4 and 4 out of 4 females, with mean group severity scores of 0.25 and 1.00 in males, and 0.50 and 2.00 in females in the middle and high dose groups, respectively. There were no changes in Kupffer cells recorded for recovery animals.

Subacute inflammation in the liver was diagnosed in animals sacrificed at the end of dosing in 0 out of 4, 1 out of 4, 1 out of 4, and 1 out of 4 males, and in 0 out of 4, 0 out of 4, 1 out of 4, and 4 out of 4 females in the control, low, middle, and high dose groups, respectively. Mean group severity scores for this change were 0.00, 0.25, 0.25, and 0.75 in males, and 0.00, 0.00, 0.50, and 1.75 in females in the control, low, middle, and high dose groups, respectively. Subacute inflammation in the liver had resolved by the end of the recovery period, as it was not diagnosed in recovery animals.

Deposition of hemosiderin pigment, hypertrophy of Kupffer cells, and subacute inflammation were interpreted to be pathophysiologically-related changes. Like hemosiderin deposition and EMH in the spleen, they are consistent with responses to increased destruction of erythrocytes which may have been associated with mild clinical anemia. For these reasons, deposition of hemosiderin pigment, Kupffer cell hypertrophy, and subacute inflammation in the liver were interpreted as secondary to increased erythrocyte destruction, rather than as direct test article-related effects. Subacute inflammation and Kupffer cell hypertrophy had resolved by the end

of the recovery period. Hemosiderin pigment had not resolved at the end of the recovery period.

Hepatocyte necrosis occurred in 2 out of 4 high dose males sacrificed at the end of dosing but did not occur in any other animals in this study. It is not clear whether this change is incidental or whether it is related to other changes in the liver and, thus, a test article-related change. This is because the necrosis was of minimal severity and occurred in very small, widely and randomly distributed foci.

#### Thymus

Depletion of thymic lymphocytes occurred only in animals sacrificed at the end of dosing. Among these animals, this change occurred in 0 out of 4 and 3 out of 4 males, and in 1 out of 4 and 1 out of 4 females, with mean group severity scores of 0.00 and 1.75 in males, and 0.50 and 0.25 in females in the middle and high dose groups, respectively. Depletion of thymic lymphocytes is well known as a manifestation of generalized toxicity and stress. The lungs, spleen, and liver in the dogs in this study all had changes interpreted as direct or secondary to test article-related changes. For these reasons, thymic lymphocyte depletion was interpreted as secondary to generalized toxicity or stress.

#### Bone Marrow

Bone marrow hypercellularity was diagnosed only in animals sacrificed at the end of dosing. Among these animals, this change occurred in 1 out of 4, 1 out of 4, and 4 out of 4 males, and in 0 out of 4, 4 out of 4, and 4 out of 4 females in the low, middle, and high dose groups, respectively. Mean group severity scores for this change in these animals were 0.25, 0.25, and 1.00 in males, and 0.00, 1.00, and 1.00 in females in the low, middle, and high dose groups, respectively. This change did not occur in control males or females sacrificed at the end of dosing. Evaluation of rib bone marrow smears revealed a significant decrease in M:E ratios in middle and high dose males and females (see Appendix I). A decrease in M:E ratios can result from an absolute decrease in myeloid cells or from an absolute increase in erythroid cells in the bone marrow. Results of evaluation of rib bone marrow sections were considered consistent with the results of bone marrow smear evaluations, and indicated that the decreased M:E ratios were due to increased erythroid cells rather than to decreased myeloid cells. These observations are also consistent with observations in the liver and spleen that suggested hemolytic anemia. For these reasons, bone marrow hypercellularity and decreased M:E ratios were interpreted as secondary to increased erythrocyte destruction that may or may not have been associated with clinical anemia. Bone marrow, in histologic section and in smears, had returned to normal in males and in females after the recovery period.

#### Kidney

Nephrocalcinosis is a common spontaneous change which occurs in the kidneys of a variety of species, including dogs. In this study, nephrocalcinosis occurred in one or both kidneys of animals in the control and all treated groups. Because the incidence of this change was similar in control and treated animals, nephrocalcinosis was considered not related to the test article.

#### Other Lesions

All other lesions seen were considered to be incidental changes not related to the test article.

In summary, the principal histopathology findings in this study were those in the lungs and those in spleen, liver, and bone marrow suggesting increased erythrocyte destruction. The findings in the lungs were distinct morphologically, but the mechanism (mechanisms) of their development was (were) less clear. The two most likely causes would be either alteration of vascular permeability, causing persistent alveolar edema, or the process of surfactant production and degradation. Changes present in the spleen, liver, and bone marrow were considered to be related to increased erythrocyte destruction that may or may not have been severe enough to cause

clinical anemia. Changes in these tissues were thus considered secondary, rather than direct, test article-related findings. The degree of lymphocyte depletion which occurred in the thymus was probably secondary to generalized toxicity or to stress.

### CONCLUSIONS

Under the conditions of this study, oral administration of WR 238605 was associated with changes in the lungs, spleen, liver, bone marrow, and thymus. Alveolar proteinosis and subacute inflammation were direct test article-related changes which occurred in the lungs of animals sacrificed at the end of dosing. Alveolar proteinosis had resolved in males and almost resolved in females by the end of the recovery period. Chronic inflammation, which occurred in recovery animal lungs, was interpreted as representing part of the resolution of alveolar proteinosis.

Hemosiderin deposition in the spleen and liver, EMH in the spleen, Kupffer cell hypertrophy and subacute inflammation in the liver, and increased erythroid cells in the bone marrow were interpreted as secondary to increased erythrocyte destruction, which may or may not have resulted in clinical anemia. These changes were, thus, considered to be secondary test article-related effects.

Depletion of thymic lymphocytes was a test article-related change in males and females and was considered to be most likely secondary to generalized toxicity or stress.

Direct test article-related effects, alveolar proteinosis and subacute inflammation in the lungs, were clearly present at the end of dosing. Subacute inflammation in the lungs was an equivocal effect in low dose females sacrificed at the end of dosing. These effects had largely, but not completely, resolved by the end of the recovery period. Effects considered secondarily related to the test article in middle and high dose groups included chronic inflammation in the lungs of recovery animals, and changes in the liver, spleen, bone marrow, and thymus present in animals sacrificed at the end of dosing. Except for hemosiderin deposition, secondary effects in the liver, spleen, bone marrow, and thymus had resolved by the end of the recovery period. For these reasons, the no-effect level in this study was equivocal, but was interpreted to probably be the low dose (0.1 mg base/kg/day).

\_\_\_\_\_  
Michael J. Tomlinson, DVM, Ph.D.  
Diplomate, ACVP

\_\_\_\_\_  
Date

<sup>1</sup> G.A. Boorman and S.L. Eustis, "Lung," Pathology of the Fischer Rat. Reference Atlas, eds. G.A. Boorman, S.L. Eustis, M.R. Elwell, C.A. Montgomery, Jr., and W.F. MacKenzie, (San Diego: Academic Press, Inc., 1990), pp. 345-346.

<sup>2</sup> C.E. Cross, G.H. Parsons, A.B. Gorin, and J.A. Last, "Pulmonary Edema: Emphasis on Physiologic and Toxicologic Considerations," Mechanisms in Respiratory Toxicology, eds. H. Witschi and P. Neshesheim, (Boca Raton: CRC Press, 1982), Volume I, pp. 219-246.

<sup>3</sup> J.A.D. Cooper, Jr., D.A. White, and R.A. Matthay, "Drug Induced Pulmonary Disease, Part 1: Cytotoxic Drugs," Am Rev Respir Disease, 133:321-340, 1986.

<sup>4</sup> J.A.D. Cooper, Jr., D.A. White, and R.A. Matthay, "Drug Induced Pulmonary Disease, Part 2: Non-cytotoxic Drugs," Am Rev Respir Disease, 133:488-505, 1986.

<sup>5</sup> N.C. Jain, Schalm's Veterinary Hematology, Fourth Edition, (Philadelphia: Lea & Febiger, 1986), pp. 643-645.

<sup>6</sup> N.C. Jain, Schalm's Veterinary Hematology, Fourth Edition, (Philadelphia: Lea & Febiger, 1986), pp. 382-383.

TABLE I

## SUMMARY OF EXPERIMENTAL DESIGN

Group	Dose Level (mg base/kg/day)	Number of Dogs	
		Male	Female
1	0	4 + 4*	4 + 4*
2	0.1	4 + 4*	4 + 4*
3	2.0	4 + 4*	4 + 4*
4	6.0	4 + 4*	4 + 4*

\* Recovery animals.

TABLE II

## PROTOCOL-REQUIRED TISSUES

Adrenal glands	Ovaries
Aorta (thoracic)	Pancreas
Brain (fore-, mid-, and hind-)	Pituitary gland
Cecum	Prostate
Colon	Rib with costochondral junction
Diaphragm	Rib with marrow
Duodenum	Salivary gland (mandibular)
Esophagus	Sciatic nerve
Eyes and optic nerve	Skin
Heart	Spinal cord (thoracic)
Gallbladder	Spleen
Gross lesions	Stomach
Ileum	Testes with epididymides
Jejunum	Thymus
Kidneys	Thyroid gland with parathyroids
Liver	Tongue
Lungs/bronchi	Tonsil
Lymph nodes (submandibular and mesenteric)	Trachea
Mammary gland	Ureter
Muscle, skeletal	Urinary bladder
	Uterus

# DRAFT

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

---

Report Codes Table

---

A. Codes applying to organs

N	Tissues within normal histological limits
A	Autolysis precluding adequate evaluation
P	Paired organ missing
U	Tissues unsuitable for complete evaluation
S	Tissues not applicable to animal
*	Tissues not required by protocol

---

B. Codes applying to microscopic diagnoses

1	minimal
2	mild
3	moderate
4	marked
)	focal
]	locally extensive
>	multifocal
P	Present
B	Neoplasm, benign
M	Neoplasm, malignant without metastasis
C	Neoplasm, malignant with metastasis
X	Metastasis site (+)
-	No data entered

DRAFT

Third Draft Pathology Report  
Toxicology Research Laboratory  
Study Number 097

HISTOPATHOLOGY TABLES

ABBREVIATION LIST

Cytopl - Cytoplasm

Epith - Epithelium

LN - Lymph node

MBK - Mg base/kg/day

R - Recovery

Vacu - Vacuolation

DRAFT

Third Draft Pathology Report  
Toxicology Research Laboratory  
Study Number 097

SECTION II  
PROJECT SUMMARY TABLE

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

**Project Summary Table**

SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

D R A F T

PAGE 16

PROJECT ID. NO: TRL097  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: MALE

GROUP:	0.0mbk		0.1mbk		2.0mbk		6.0mbk		0.0mbk-R		0.1mbk-R		2.0mbk-R		6.0mbk-R		
NUMBER OF ANIMALS:	4		4		4		4		4		4		4		4		
	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%	
BRAIN (FORE)	# Ex	4		4		4		4		0		0		0		0	
THORACIC CORD	# Ex	4		4		4		4		0		0		0		0	
BRAIN (MID)	# Ex	4		4		4		4		0		0		0		0	
BRAIN (CEREBELLUM)	# Ex	4		4		4		4		0		0		0		0	
PONS	# Ex	4		4		4		4		0		0		0		0	
HEART	# Ex	4		4		4		4		0		0		0		0	
AORTA	# Ex	4		4		4		4		0		0		0		0	
TRACHEA	# Ex	4		4		4		4		0		0		0		0	
ESOPHAGUS	# Ex	4		4		4		4		0		0		0		0	
LUNG	# Ex	4		4		4		4		4		4		4		4	
Alveolar proteinosis		0	(0)	0	(0)	2	(50)	4	(100)	0	(0)	0	(0)	0	(0)	0	(0)
Infiltrate, macrophage		0	(0)	0	(0)	0	(0)	0	(0)	1	(25)	0	(0)	2	(50)	2	(50)
Inflammation, chronic		0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	2	(50)	3	(75)
Inflammation, subacute		1	(25)	2	(50)	4	(100)	4	(100)	2	(50)	2	(50)	3	(75)	4	(100)
Pigment, hemosiderin		0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	1	(25)	0	(0)
KIDNEY, RIGHT	# Ex	4		4		4		4		0		0		0		0	
Nephrocalcinosis		4	(100)	3	(75)	4	(100)	2	(50)	0		0		0		0	
Renal tubule, casts, proteinic		0	(0)	0	(0)	1	(25)	0	(0)	0		0		0		0	

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

**Project Summary Table**

SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

DRAFT

PAGE 17

PROJECT ID. NO: TRL097  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: MALE

GROUP:	0.0mbk	0.1mbk	2.0mbk	6.0mbk	0.0mbk-R	0.1mbk-R	2.0mbk-R	6.0mbk-R
NUMBER OF ANIMALS:	4	4	4	4	4	4	4	4
<b>KIDNEY, LEFT</b>	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 0	# Ex 0	# Ex 0	# Ex 0
Nephrocalcinosis	3 (75)	2 (50)	4 (100)	2 (50)	0	0	0	0
Nephropathy	0 (0)	1 (25)	0 (0)	0 (0)	0	0	0	0
Renal tubule, casts, proteinic	0 (0)	0 (0)	1 (25)	1 (25)	0	0	0	0
<b>SPLEEN</b>	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 4
Extramedullary hematopoiesis	0 (0)	0 (0)	1 (25)	2 (50)	0 (0)	0 (0)	0 (0)	0 (0)
Pigment, hemosiderin	0 (0)	1 (25)	1 (25)	3 (75)	2 (50)	1 (25)	1 (25)	2 (50)
Siderofibrotic plaque	0 (0)	1 (25)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
<b>PANCREAS</b>	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 0	# Ex 0	# Ex 0	# Ex 0
<b>DUODENUM</b>	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 0	# Ex 0	# Ex 0	# Ex 0
<b>LIVER</b>	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 4
Hepatocyte, necrosis	0 (0)	0 (0)	0 (0)	2 (50)	0 (0)	0 (0)	0 (0)	0 (0)
Inflammation, subacute	0 (0)	1 (25)	1 (25)	1 (25)	0 (0)	0 (0)	0 (0)	0 (0)
Kupffer cell, hyperplasia	0 (0)	0 (0)	1 (25)	2 (50)	0 (0)	0 (0)	0 (0)	0 (0)
Kupffer cell, hypertrophy	0 (0)	0 (0)	1 (25)	2 (50)	0 (0)	0 (0)	0 (0)	0 (0)
Nodular hyperplasia	0 (0)	1 (25)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Pigment, hemosiderin	0 (0)	0 (0)	2 (50)	1 (25)	0 (0)	0 (0)	1 (25)	2 (50)
<b>GALLBLADDER</b>	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 0	# Ex 0	# Ex 0	# Ex 0
Infiltrate, cellular	0 (0)	1 (25)	0 (0)	0 (0)	0	0	0	0
<b>ADRENAL GLAND</b>	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 0	# Ex 0	# Ex 0	# Ex 0
<b>SALIVARY GLAND</b>	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 0	# Ex 0	# Ex 0	# Ex 0
<b>LYMPH NODE, SUBMANDIBULAR</b>	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 0	# Ex 0	# Ex 0	# Ex 0

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

**Project Summary Table**

SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: TRL097  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: MALE

D R A F T

PAGE 18

GROUP:	NUMBER OF ANIMALS:	0.0mbk		0.1mbk		2.0mbk		6.0mbk		0.0mbk-R		0.1mbk-R		2.0mbk-R		6.0mbk-R	
		#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%
JEJUNUM	# Ex	4		4		4		4		0		0		0		0	
COLON	# Ex	4		4		4		4		0		0		0		0	
TONSIL	# Ex	4		4		4		4		0		0		0		0	
URETER	# Ex	4		4		4		4		0		0		0		0	
ILEUM	# Ex	4		4		4		4		0		0		0		0	
LYMPH NODE, MESENTERIC	# Ex	4		4		4		4		0		0		0		0	
TONGUE	# Ex	4		4		4		4		0		0		0		0	
Granuloma, foreign body		0	(0)	1	(25)	0	(0)	0	(0)	0		0		0		0	
DIAPHRAGM	# Ex	4		4		4		4		0		0		0		0	
THYMUS	# Ex	4		4		4		4		4		4		4		4	
Depletion, lymphocyte		0	(0)	0	(0)	0	(0)	3	(75)	0	(0)	0	(0)	0	(0)	0	(0)
SKELETAL MUSCLE	# Ex	4		4		4		4		0		0		0		0	
Inflammation, subacute		1	(25)	0	(0)	0	(0)	0	(0)	0		0		0		0	
THYROID GLAND	# Ex	3		4		4		4		0		0		0		0	
Infiltrate, cellular		0	(0)	1	(25)	0	(0)	0	(0)	0		0		0		0	
PARATHYROID GLAND	# Ex	3		4		4		4		0		0		0		0	

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

**Project Summary Table**

SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: TRL097  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: MALE

DRAFT

PAGE 19

GROUP:		0.0mbk	0.1mbk	2.0mbk	6.0mbk	0.0mbk-R	0.1mbk-R	2.0mbk-R	6.0mbk-R
NUMBER OF ANIMALS:		4	4	4	4	4	4	4	4
		#	%	#	%	#	%	#	%
PITUITARY GLAND	# Ex	4		4		4		4	
Craniopharyngeal duct, cyst		1 (25)		0 (0)		0 (0)		1 (25)	
CECUM	# Ex	4		4		4		4	
STOMACH	# Ex	4		4		4		4	
URINARY BLADDER	# Ex	4		4		3		4	
TESTIS	# Ex	4		4		4		4	
Germinal epith, degeneration		0 (0)		0 (0)		1 (25)		1 (25)	
EPIDIDYMIS	# Ex	4		4		4		4	
Hypospermia		0 (0)		0 (0)		1 (25)		0 (0)	
PROSTATE	# Ex	4		4		3		4	
Atrophy		0 (0)		0 (0)		0 (0)		1 (25)	
MAMMARY GLAND	# Ex	3		4		4		2	
SKIN	# Ex	4		4		4		3	
Follicle, inflammation		1 (25)		0 (0)		0 (0)		0 (0)	
SCIATIC NERVE	# Ex	4		4		4		4	
EYE	# Ex	4		4		4		4	
OPTIC NERVE	# Ex	4		4		4		4	

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

**Project Summary Table**

SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

D R A F T

PAGE 20

PROJECT ID. NO: TRL097  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: MALE

GROUP:	0.0mbk		0.1mbk		2.0mbk		6.0mbk		0.0mbk-R		0.1mbk-R		2.0mbk-R		6.0mbk-R		
NUMBER OF ANIMALS:	4		4		4		4		4		4		4		4		
	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%	
RIB	# Ex	4		4		4		4		0		0		0		0	
BONE MARROW	# Ex	4		4		4		4		4		4		4		4	
Hypercellular		0	(0)	1	(25)	1	(25)	4	(100)	0	(0)	0	(0)	0	(0)	0	(0)
COSTOCHONDRAL JUNCTION	# Ex	4		4		4		4		0		0		0		0	

03-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

**Project Summary Table**

SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: TRL097  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: MALE

D R A F T

PAGE 21

GROUP:	0.0mbk	0.1mbk	2.0mbk	6.0mbk	0.0mbk-R	0.1mbk-R	2.0mbk-R	6.0mbk-R
NUMBER OF ANIMALS:	4	4	4	4	4	4	4	4

OTHER TISSUES AND LESIONS:	#	%	#	%	#	%	#	%	#	%	#	%	#	%
LN, MEDIASTINAL - Hyperplasia	1	(25)	0	(0)	1	(25)	0	(0)	0	(0)	0	(0)	0	(0)

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

**Project Summary Table**

SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: TRL097  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: FEMALE

DRAFT

PAGE 22

GROUP:	0.0mbk	0.1mbk	2.0mbk	6.0mbk	0.0mbk-R	0.1mbk-R	2.0mbk-R	6.0mbk-R
NUMBER OF ANIMALS:	4	4	4	4	4	4	4	4

	# Ex	0.0mbk		0.1mbk		2.0mbk		6.0mbk		0.0mbk-R		0.1mbk-R		2.0mbk-R		6.0mbk-R	
		#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%
BRAIN (FORE)	# Ex	4		4		4		4		0		0		0		0	
THORACIC CORD	# Ex	4		4		4		4		0		0		0		0	
BRAIN (MID)	# Ex	4		4		4		4		0		0		0		0	
BRAIN (CEREBELLUM)	# Ex	4		4		4		4		0		0		0		0	
PONS	# Ex	4		4		4		4		0		0		0		0	
HEART	# Ex	4		4		4		4		0		0		0		0	
AORTA	# Ex	3		4		4		4		0		0		0		0	
TRACHEA	# Ex	4		4		4		4		0		0		0		0	
Infiltrate, cellular		0	(0)	1	(25)	1	(25)	0	(0)	0		0		0		0	
ESOPHAGUS	# Ex	4		4		4		4		0		0		0		0	
LUNG	# Ex	4		4		4		4		4		4		4		4	
Alveolar proteinosis		0	(0)	0	(0)	4	(100)	4	(100)	0	(0)	0	(0)	0	(0)	2	(50)
Heteropic bone		0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	1	(25)
Infiltrate, macrophage		0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	1	(25)	2	(50)
Inflammation, acute		0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	1	(25)	0	(0)	0	(0)
Inflammation, chronic		0	(0)	0	(0)	0	(0)	0	(0)	1	(25)	1	(25)	2	(50)	0	(0)
Inflammation, subacute		2	(50)	4	(100)	4	(100)	4	(100)	3	(75)	1	(25)	4	(100)	4	(100)
Pigment, hemosiderin		0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	1	(25)
KIDNEY, RIGHT	# Ex	4		4		4		4		0		0		0		0	
Cortex, infiltrate, cellular		0	(0)	1	(25)	0	(0)	0	(0)	0		0		0		0	
Nephrocalcinosis		3	(75)	3	(75)	4	(100)	4	(100)	0		0		0		0	

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

**Project Summary Table**

SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

D R A F T

PAGE 23

PROJECT ID. NO: TRL097  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: FEMALE

GROUP:	0.0mbk		0.1mbk		2.0mbk		6.0mbk		0.0mbk-R		0.1mbk-R		2.0mbk-R		6.0mbk-R	
NUMBER OF ANIMALS:	4		4		4		4		4		4		4		4	
	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%
KIDNEY, RIGHT	# Ex	4	4	4	4	4	0	0	0	0	0	0	0	0	0	0
Renal tubule, casts, proteinic		1 (25)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Tubular epith, vacuo, cytopl		1 (25)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
KIDNEY, LEFT	# Ex	4	4	4	4	0	0	0	0	0	0	0	0	0	0	0
Cortex, hemorrhage		0 (0)	0 (0)	1 (25)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Nephrocalcinosis		2 (50)	4 (100)	4 (100)	4 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Renal tubule, casts, proteinic		1 (25)	0 (0)	1 (25)	2 (50)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Tubular epith, vacuo, cytopl		1 (25)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
SPLEEN	# Ex	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
Capsule, scar		0 (0)	0 (0)	0 (0)	0 (0)	1 (25)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Extramedullary hematopoiesis		0 (0)	0 (0)	1 (25)	3 (75)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Pigment, hemosiderin		0 (0)	0 (0)	3 (75)	4 (100)	1 (25)	0 (0)	3 (75)	3 (75)	3 (75)	3 (75)	3 (75)	3 (75)	3 (75)	3 (75)	3 (75)
PANCREAS	# Ex	4	4	4	4	0	0	0	0	0	0	0	0	0	0	0
DUODENUM	# Ex	4	4	4	4	0	0	0	0	0	0	0	0	0	0	0
LIVER	# Ex	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
Hepatocyte, vacuo, cytoplasm		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (25)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (25)	1 (25)
Inflammation, subacute		0 (0)	0 (0)	1 (25)	4 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Kupffer cell, hyperplasia		0 (0)	1 (25)	1 (25)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Kupffer cell, hypertrophy		0 (0)	0 (0)	1 (25)	4 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Pigment, hemosiderin		0 (0)	1 (25)	2 (50)	4 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (100)	3 (75)	3 (75)	3 (75)	3 (75)	3 (75)
GALLBLADDER	# Ex	4	4	4	4	0	0	0	0	0	0	0	0	0	0	0
ADRENAL GLAND	# Ex	4	4	4	4	0	0	0	0	0	0	0	0	0	0	0
Cortex, cyst		0 (0)	0 (0)	1 (25)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Cortex, vacuolation, cytoplasm		0 (0)	0 (0)	0 (0)	1 (25)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

**Project Summary Table**

SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: TRL097  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: FEMALE

DRAFT

PAGE 24

GROUP:	0.0mbk	0.1mbk	2.0mbk	6.0mbk	0.0mbk-R	0.1mbk-R	2.0mbk-R	6.0mbk-R
NUMBER OF ANIMALS:	4	4	4	4	4	4	4	4
SALIVARY GLAND	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 0	# Ex 0	# Ex 0	# Ex 0
Infiltrate, cellular	2 (50)	1 (25)	1 (25)	1 (25)	0	0	0	0
LYMPH NODE, SUBMANDIBULAR	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 0	# Ex 0	# Ex 0	# Ex 0
Hyperplasia	0 (0)	0 (0)	0 (0)	1 (25)	0	0	0	0
JEJUNUM	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 0	# Ex 0	# Ex 0	# Ex 0
COLON	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 0	# Ex 0	# Ex 0	# Ex 0
TONSIL	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 0	# Ex 0	# Ex 0	# Ex 0
URETER	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 0	# Ex 0	# Ex 0	# Ex 0
ILEUM	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 0	# Ex 0	# Ex 0	# Ex 0
Inflammation, acute	0 (0)	1 (25)	0 (0)	0 (0)	0	0	0	0
LYMPH NODE, MESENTERIC	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 0	# Ex 0	# Ex 0	# Ex 0
TONGUE	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 0	# Ex 0	# Ex 0	# Ex 0
DIAPHRAGM	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 0	# Ex 0	# Ex 0	# Ex 0
THYMUS	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 4
Depletion, lymphocyte	0 (0)	0 (0)	1 (25)	1 (25)	0 (0)	0 (0)	0 (0)	0 (0)
SKELETAL MUSCLE	# Ex 4	# Ex 4	# Ex 4	# Ex 4	# Ex 0	# Ex 0	# Ex 0	# Ex 0

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

**Project Summary Table**

SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: TRL097  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: FEMALE

D R A F T

PAGE 25

GROUP:	0.0mbk	0.1mbk	2.0mbk	6.0mbk	0.0mbk-R	0.1mbk-R	2.0mbk-R	6.0mbk-R
NUMBER OF ANIMALS:	4	4	4	4	4	4	4	4
THYROID GLAND	# Ex	# %	# %	# %	# %	# %	# %	# %
C-Cell, hyperplasia	4	0 (0)	4 (25)	4 (0)	4 (0)	4 (0)	4 (0)	4 (0)
Follicular cell, vacuo, cytopl	4	0 (0)	0 (0)	0 (0)	1 (25)	0	0	0
Infiltrate, cellular	4	0 (0)	0 (0)	1 (25)	0 (0)	0	0	0
PARATHYROID GLAND	# Ex	4	4	4	4	0	0	0
PITUITARY GLAND	# Ex	4	4	4	3	0	0	0
Chromophobe, vacuo, cytoplasm	4	0 (0)	0 (0)	0 (0)	1 (33)	0	0	0
Craniopharyngeal duct, cyst	4	2 (50)	2 (50)	0 (0)	2 (67)	0	0	0
CECUM	# Ex	4	4	4	4	0	0	0
STOMACH	# Ex	4	4	4	4	0	0	0
URINARY BLADDER	# Ex	4	4	4	4	0	0	0
Infiltrate, cellular	4	0 (0)	1 (25)	0 (0)	0 (0)	0	0	0
OVARIES	# Ex	4	4	4	4	0	0	0
UTERUS	# Ex	4	4	4	4	0	0	0
Hemorrhage	4	0 (0)	0 (0)	1 (25)	0 (0)	0	0	0
MAMMARY GLAND	# Ex	2	4	2	4	0	0	0
SKIN	# Ex	4	4	4	4	0	0	0
SCIATIC NERVE	# Ex	4	4	4	4	0	0	0

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

**Project Summary Table**

SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: TRL097  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: FEMALE

D R A F T

PAGE 26

GROUP:	0.0mbk	0.1mbk	2.0mbk	6.0mbk	0.0mbk-R	0.1mbk-R	2.0mbk-R	6.0mbk-R
NUMBER OF ANIMALS:	4	4	4	4	4	4	4	4

	#	%	#	%	#	%	#	%	#	%	#	%	#	%			
EYE	# Ex	4		4		4		4		0		0		0		0	
OPTIC NERVE	# Ex	4		4		4		4		0		0		0		0	
RIB	# Ex	4		4		4		4		0		0		0		0	
BONE MARROW	# Ex	4		4		4		4		4		4		4		4	
Hypercellular		0	(0)	0	(0)	4	(100)	4	(100)	0	(0)	0	(0)	0	(0)	0	(0)
COSTOCHONDRAL JUNCTION	# Ex	4		4		4		4		0		0		0		0	

31-Aug-1993

D R A F T

SECTION III  
SEVERITY SUMMARY TABLE

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Severity Summary Table

DRAFT

PAGE 28

PROJECT ID. NO: TRL097  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: MALE

GROUP:		0.0mbk	0.1mbk	2.0mbk	6.0mbk	0.0mbk-R	0.1mbk-R	2.0mbk-R	6.0mbk-R
NUMBER OF ANIMALS:		4	4	4	4	4	4	4	4
BRAIN (FORE)	# Ex	4	4	4	4	0	0	0	0
THORACIC CORD	# Ex	4	4	4	4	0	0	0	0
BRAIN (MID)	# Ex	4	4	4	4	0	0	0	0
BRAIN (CEREBELLUM)	# Ex	4	4	4	4	0	0	0	0
PONS	# Ex	4	4	4	4	0	0	0	0
HEART	# Ex	4	4	4	4	0	0	0	0
AORTA	# Ex	4	4	4	4	0	0	0	0
TRACHEA	# Ex	4	4	4	4	0	0	0	0
ESOPHAGUS	# Ex	4	4	4	4	0	0	0	0
LUNG	# Ex	4	4	4	4	4	4	4	4
Alveolar proteinosis		0	0	2 0.50	4 2.50	0	0	0	0
Infiltrate, macrophage		0	0	0	0	1 0.25	0	2 0.50	2 0.50
Inflammation, chronic		0	0	0	0	0	0	2 0.75	3 1.00
Inflammation, subacute		1 0.25	2 0.50	4 2.50	4 3.25	2 0.50	2 0.50	3 0.75	4 1.25
Pigment, hemosiderin		0	0	0	0	0	0	1 0.25	0
KIDNEY, RIGHT	# Ex	4	4	4	4	0	0	0	0
Nephrocalcinosis		4 1.00	3 0.75	4 1.00	2 0.50	0	0	0	0
Renal tubule, casts, proteinic		0	0	1 0.25	0	0	0	0	0

\* Severity calculated by the number of tissues examined.

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Severity Summary Table

D R A F T

PAGE 29

PROJECT ID. NO: TRL097  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: MALE

GROUP:		0.0mbk	0.1mbk	2.0mbk	6.0mbk	0.0mbk-R	0.1mbk-R	2.0mbk-R	6.0mbk-R
NUMBER OF ANIMALS:		4	4	4	4	4	4	4	4
KIDNEY, LEFT	# Ex	4	4	4	4	0	0	0	0
Nephrocalcinosis		3 0.75	2 0.50	4 1.00	2 0.50	0	0	0	0
Nephropathy		0	1 0.25	0	0	0	0	0	0
Renal tubule, casts, proteinic		0	0	1 0.25	1 0.50	0	0	0	0
SPLEEN	# Ex	4	4	4	4	4	4	4	4
Extramedullary hematopoiesis		0	0	1 0.25	2 0.50	0	0	0	0
Pigment, hemosiderin		0	1 0.25	1 0.50	3 1.00	2 0.75	1 0.25	1 0.25	2 :.50
Siderofibrotic plaque		0	1 0.25	0	0	0	0	0	0
PANCREAS	# Ex	4	4	4	4	0	0	0	0
DUODENUM	# Ex	4	4	4	4	0	0	0	0
LIVER	# Ex	4	4	4	4	4	4	4	4
Hepatocyte, necrosis		0	0	0	2 0.50	0	0	0	0
Inflammation, subacute		0	1 0.25	1 0.25	1 0.75	0	0	0	0
Kupffer cell, hyperplasia		0	0	1 0.25	2 0.50	0	0	0	0
Kupffer cell, hypertrophy		0	0	1 0.25	2 1.00	0	0	0	0
Modular hyperplasia		0	1 0.25	0	0	0	0	0	0
Pigment, hemosiderin		0	0	2 0.75	1 0.75	0	0	1 0.25	2 :.75
GALLBLADDER	# Ex	4	4	4	4	0	0	0	0
Infiltrate, cellular		0	1 0.50	0	0	0	0	0	0
ADRENAL GLAND	# Ex	4	4	4	4	0	0	0	0
SALIVARY GLAND	# Ex	4	4	4	4	0	0	0	0
LYMPH NODE, SUBMANDIBULAR	# Ex	4	4	4	4	0	0	0	0

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Severity Summary Table

PROJECT ID. NO: TRL097 WEEKS: 14-27	FATES: Terminal Sacrifice		DRAFT								PAGE 30
	SEX: MALE		0.0mbk	0.1mbk	2.0mbk	6.0mbk	0.0mbk-R	0.1mbk-R	2.0mbk-R	6.0mbk-R	
GROUP: NUMBER OF ANIMALS:			4	4	4	4	4	4	4	4	
	# Ex	# SEV	# SEV	# SEV	# SEV	# SEV	# SEV	# SEV	# SEV	# SEV	
JEJUNUM	4	4	4	4	4	0	0	0	0	0	
COLON	4	4	4	4	4	0	0	0	0	0	
TONSIL	4	4	4	4	4	0	0	0	0	0	
URETER	4	4	4	4	4	0	0	0	0	0	
ILEUM	4	4	4	4	4	0	0	0	0	0	
LYMPH NODE, MESENTERIC	4	4	4	4	4	0	0	0	0	0	
TONGUE	4	4	4	4	4	0	0	0	0	0	
Granuloma, foreign body	0	1 0.50	0	0	0	0	0	0	0	0	
DIAPHRAGM	4	4	4	4	4	0	0	0	0	0	
THYMUS	4	4	4	4	4	4	4	4	4	4	
Depletion, lymphocyte	0	0	0	3 1.75	0	0	0	0	0	0	
SKELETAL MUSCLE	4	4	4	4	4	0	0	0	0	0	
Inflammation, subacute	1 0.25	0	0	0	0	0	0	0	0	0	
THYROID GLAND	3	4	4	4	4	0	0	0	0	0	
Infiltrate, cellular	0	1 0.75	0	0	0	0	0	0	0	0	
PARATHYROID GLAND	3	4	4	4	4	0	0	0	0	0	

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Severity Summary Table

PROJECT ID. NO: TRL097  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: MALE

DRAFT

PAGE 31

GROUP:		0.0mbk	0.1mbk	2.0mbk	6.0mbk	0.0mbk-R	0.1mbk-R	2.0mbk-R	6.0mbk-R
NUMBER OF ANIMALS:		4	4	4	4	4	4	4	4
PITUITARY GLAND	# Ex	4	4	4	4	0	0	0	0
CECUM	# Ex	4	4	4	4	0	0	0	0
STOMACH	# Ex	4	4	4	4	0	0	0	0
URINARY BLADDER	# Ex	4	4	3	4	0	0	0	0
TESTIS	# Ex	4	4	4	4	0	0	0	0
Germinal epith, degeneration		0	0	1 0.50	1 0.50	0	0	0	0
EPIDIDYMIS	# Ex	4	4	4	4	0	0	0	0
Hypospermia		0	0	1 0.75	0	0	0	0	0
PROSTATE	# Ex	4	4	3	4	0	0	0	0
Atrophy		0	0	0	1 0.50	0	0	0	0
MAMMARY GLAND	# Ex	3	4	4	2	0	0	0	0
SKIN	# Ex	4	4	4	3	0	0	0	0
Follicle, inflammation		1 0.25	0	0	0	0	0	0	0
SCIATIC NERVE	# Ex	4	4	4	4	0	0	0	0
EYE	# Ex	4	4	4	4	0	0	0	0
OPTIC NERVE	# Ex	4	4	4	4	0	0	0	0

\* Severity calculated by the number of tissues examined.

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Severity Summary Table

DRAFT

PAGE 32

PROJECT ID. NO: TRL097  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: MALE

GROUP:		0.0mbk	0.1mbk	2.0mbk	6.0mbk	0.0mbk-R	0.1mbk-R	2.0mbk-R	6.0mbk-R
NUMBER OF ANIMALS:		4	4	4	4	4	4	4	4
		# SEV	# SEV	# SEV	# SEV	# SEV	# SEV	# SEV	# SEV
RIB	# Ex	4	4	4	4	0	0	0	0
BONE MARROW	# Ex	4	4	4	4	4	4	4	4
Hypercellular		0	1 0.25	1 0.25	4 1.00	0	0	0	0
COSTOCHONDRAL JUNCTION	# Ex	4	4	4	4	0	0	0	0

\* Severity calculated by the number of tissues examined.

03-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Severity Summary Table

D R A F T

PAGE 33

PROJECT ID. NO: TRL097  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: FEMALE

GROUP:		0.0mbk	0.1mbk	2.0mbk	6.0mbk	0.0mbk-R	0.1mbk-R	2.0mbk-R	6.0mbk-R
NUMBER OF ANIMALS:		4	4	4	4	4	4	4	4
BRAIN (FORE)	# Ex	4	4	4	4	0	0	0	0
THORACIC CORD	# Ex	4	4	4	4	0	0	0	0
BRAIN (MID)	# Ex	4	4	4	4	0	0	0	0
BRAIN (CEREBELLUM)	# Ex	4	4	4	4	0	0	0	0
PONS	# Ex	4	4	4	4	0	0	0	0
HEART	# Ex	4	4	4	4	0	0	0	0
AORTA	# Ex	3	4	4	4	0	0	0	0
TRACHEA	# Ex	4	4	4	4	0	0	0	0
Infiltrate, cellular		0	1 0.25	1 0.25	0	0	0	0	0
ESOPHAGUS	# Ex	4	4	4	4	0	0	0	0
LUNG	# Ex	4	4	4	4	4	4	4	4
Alveolar proteinosis		0	0	4 1.00	4 2.00	0	0	0	2 0.50
Infiltrate, macrophage		0	0	0	0	0	0	1 0.25	2 0.75
Inflammation, acute		0	0	0	0	0	1 0.25	0	0
Inflammation, chronic		0	0	0	0	1 0.50	1 0.25	2 0.50	0
Inflammation, subacute		2 1.00	4 1.25	4 2.75	4 2.25	3 0.75	1 0.25	4 1.00	4 1.50
Pigment, hemosiderin		0	0	0	0	0	0	0	1 0.50
KIDNEY, RIGHT	# Ex	4	4	4	4	0	0	0	0
Cortex, infiltrate, cellular		0	1 0.25	0	0	0	0	0	0
Nephrocalcinosis		3 0.75	3 0.75	4 1.00	4 1.00	0	0	0	0

03-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Severity Summary Table

D R A F T

PAGE 34

PROJECT ID. NO: TRL097  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: FEMALE

GROUP:	0.0mbk	0.1mbk	2.0mbk	6.0mbk	0.0mbk-R	0.1mbk-R	2.0mbk-R	6.0mbk-R
NUMBER OF ANIMALS:	4	4	4	4	4	4	4	4
	# SEV	# SEV	# SEV	# SEV	# SEV	# SEV	# SEV	# SEV
Renal tubule, casts, proteinic	1 0.25	0	0	0	0	0	0	0
Tubular epith, vacuo, cytopl	1 0.25	0	0	0	0	0	0	0
<b>KIDNEY, LEFT</b>	# Ex 4	4	4	4	0	0	0	0
Cortex, hemorrhage	0	0	1 0.50	0	0	0	0	0
Nephrocalcinosis	2 0.50	4 1.00	4 1.00	4 1.00	0	0	0	0
Renal tubule, casts, proteinic	1 0.25	0	1 0.25	2 0.50	0	0	0	0
Tubular epith, vacuo, cytopl	1 0.25	0	0	0	0	0	0	0
<b>SPLEEN</b>	# Ex 4	4	4	4	4	4	4	4
Capsule, scar	0	0	0	0	1 0.50	0	0	0
Extramedullary hematopoiesis	0	0	1 0.25	3 1.25	0	0	0	0
Pigment, hemosiderin	0	0	3 1.00	4 1.25	1 0.25	0	3 0.75	3 1.00
<b>PANCREAS</b>	# Ex 4	4	4	4	0	0	0	0
<b>DUODENUM</b>	# Ex 4	4	4	4	0	0	0	0
<b>LIVER</b>	# Ex 4	4	4	4	4	4	4	4
Hepatocyte, vacuo, cytoplasm	0	0	0	0	0	1 0.50	0	1 0.50
Inflammation, subacute	0	0	1 0.50	4 1.75	0	0	0	0
Kupffer cell, hyperplasia	0	1 0.25	1 0.25	0	0	0	0	0
Kupffer cell, hypertrophy	0	0	1 0.50	4 2.00	0	0	0	0
Pigment, hemosiderin	0	1 0.25	2 0.50	4 2.25	0	0	4 1.00	3 1.25
<b>GALLBLADDER</b>	# Ex 4	4	4	4	0	0	0	0
<b>ADRENAL GLAND</b>	# Ex 4	4	4	4	0	0	0	0
Cortex, vacuolation, cytoplasm	0	0	0	1 0.25	0	0	0	0
<b>SALIVARY GLAND</b>	# Ex 4	4	4	4	0	0	0	0
Infiltrate, cellular	2 0.50	1 0.25	1 0.25	1 0.25	0	0	0	0

\* Severity calculated by the number of tissues examined.

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Severity Summary Table

DRAFT

PAGE 35

PROJECT ID. NO: TRL097  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: FEMALE

GROUP:		0.0mbk	0.1mbk	2.0mbk	6.0mbk	0.0mbk-R	0.1mbk-R	2.0mbk-R	6.0mbk-R
NUMBER OF ANIMALS:		4	4	4	4	4	4	4	4
LYMPH NODE, SUBMANDIBULAR	# Ex	4	4	4	4	0	0	0	0
Hyperplasia		0	0	0	1 0.50	0	0	0	0
JEJUNUM	# Ex	4	4	4	4	0	0	0	0
COLON	# Ex	4	4	4	4	0	0	0	0
TONSIL	# Ex	4	4	4	4	0	0	0	0
URETER	# Ex	4	4	4	4	0	0	0	0
ILEUM	# Ex	4	4	4	4	0	0	0	0
Inflammation, acute		0	1 0.50	0	0	0	0	0	0
LYMPH NODE, MESENTERIC	# Ex	4	4	4	4	0	0	0	0
TONGUE	# Ex	4	4	4	4	0	0	0	0
DIAPHRAGM	# Ex	4	4	4	4	0	0	0	0
THYMUS	# Ex	4	4	4	4	4	4	4	4
Depletion, lymphocyte		0	0	1 0.50	1 0.25	0	0	0	0
SKELETAL MUSCLE	# Ex	4	4	4	4	0	0	0	0
THYROID GLAND	# Ex	4	4	4	4	0	0	0	0
C-Cell, hyperplasia		0	1 0.25	0	0	0	0	0	0
Follicular cell, vacuo, cytopl		0	0	0	1 0.50	0	0	0	0
Infiltrate, cellular		0	0	1 0.25	0	0	0	0	0

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Severity Summary Table

DRAFT

PAGE 36

PROJECT ID. NO: TRL097  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: FEMALE

GROUP:		0.0mbk	0.1mbk	2.0mbk	6.0mbk	0.0mbk-R	0.1mbk-R	2.0mbk-R	6.0mbk-R
NUMBER OF ANIMALS:		4	4	4	4	4	4	4	4
PARATHYROID GLAND	# Ex	4	4	4	4	0	0	0	0
PITUITARY GLAND	# Ex	4	4	4	3	0	0	0	0
Chromophobe, vacuo, cytoplasm		0	0	0	1 0.33	0	0	0	0
CECUM	# Ex	4	4	4	4	0	0	0	0
STOMACH	# Ex	4	4	4	4	0	0	0	0
URINARY BLADDER	# Ex	4	4	4	4	0	0	0	0
Infiltrate, cellular		0	1 0.25	0	0	0	0	0	0
OVARIES	# Ex	4	4	4	4	0	0	0	0
UTERUS	# Ex	4	4	4	4	0	0	0	0
Hemorrhage		0	0	1 0.25	0	0	0	0	0
MAMMARY GLAND	# Ex	2	4	2	4	0	0	0	0
SKIN	# Ex	4	4	4	4	0	0	0	0
SCIATIC NERVE	# Ex	4	4	4	4	0	0	0	0
EYE	# Ex	4	4	4	4	0	0	0	0
OPTIC NERVE	# Ex	4	4	4	4	0	0	0	0
RIB	# Ex	4	4	4	4	0	0	0	0

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Severity Summary Table

DRAFT

PAGE 37

PROJECT ID. NO: TRL097  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: FEMALE

GROUP:		0.0mbk	0.1mbk	2.0mbk	6.0mbk	0.0mbk-R	0.1mbk-R	2.0mbk-R	6.0mbk-R
NUMBER OF ANIMALS:		4	4	4	4	4	4	4	4
BONE MARROW	# Ex	4	4	4	4	4	4	4	4
Hypercellular		0	0	4 1.00	4 1.00	0	0	0	0
COSTOCHONDRAL JUNCTION	# Ex	4	4	4	4	0	0	0	0

\* Severity calculated by the number of tissues examined.

20-Aug-1993

D R A F T

SECTION IV  
TABULATED ANIMAL DATA

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097  
WEEKS: 14-27

GROUP: 0.0mbk      SEX: MALE  
FATES: Terminal Sacrifice

DRAFT

PAGE 39

ANIMAL ID:	7505	7520	7521	7533
BRAIN (FORE)	N	N	N	N
THORACIC CORD	N	N	N	N
BRAIN (MID)	N	N	N	N
BRAIN (CEREBELLUM)	N	N	N	N
PONS	N	N	N	N
HEART	N	N	N	N
AORTA	N	N	N	N
TRACHEA	N	N	N	N
ESOPHAGUS	N	N	N	N
LUNG	N	N		N
Inflammation, subacute	-	-	1	-
KIDNEY, RIGHT				
Nephrocalcinosis	1	1	1	1

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 0.0mbk      SEX: MALE  
WEEKS: 14-27      FATES: Terminal Sacrifice

DRAFT

PAGE 40

ANIMAL ID:	7505	7520	7521	7533
KIDNEY, LEFT				N
Nephrocalcinosis	1	1	1	-
SPLEEN	N	N	N	N
PANCREAS	N	N	N	N
DUODENUM	N	N	N	N
LIVER	N	N	N	N
GALLBLADDER	N	N	N	N
ADRENAL GLAND	N	N	N	N
SALIVARY GLAND	N	N	N	N
LYMPH NODE, SUBMANDIBULAR	N	N	N	N
JEJUNUM	N	N	N	N
COLON	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

**Tabulated Animal Data**

PROJECT ID: TRL097      GROUP: 0.0mbk      SEX: MALE  
 WEEKS: 14-27          FATES: Terminal Sacrifice

D R A F T

PAGE 41

ANIMAL ID:	7505	7520	7521	7533
TONSIL	N	N	N	N
URETER	N	N	N	N
ILEUM	N	N	N	N
LYMPH NODE, MESENTERIC	N	N	N	N
TONGUE	N	N	N	N
DIAPHRAGM	N	N	N	N
THYMUS	N	N	N	N
SKELETAL MUSCLE Inflammation, subacute	-	-	1	-
THYROID GLAND	N	N	U	N
PARATHYROID GLAND	N	N	U	N
PITUITARY GLAND Craniopharyngeal duct, cyst	-	P	-	-

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097  
WEEKS: 14-27

GROUP: 0.Dmbk      SEX: MALE  
FATES: Terminal Sacrifice

DRAFT

PAGE 42

ANIMAL ID:	7505	7520	7521	7533
CECUM	N	N	N	N
STOMACH	N	N	N	N
URINARY BLADDER	N	N	N	N
TESTIS	N	N	N	N
EPIDIDYMIS	N	N	N	N
PROSTATE	N	N	N	N
MAMMARY GLAND	N	N	N	U
SKIN	N		N	N
Follicle, inflammation	-	1	-	-
SCIATIC NERVE	N	N	N	N
EYE	N	N	N	N
OPTIC NERVE	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 0.0mbk      SEX: MALE  
WEEKS: 14-27      FATES: Terminal Sacrifice

DRAFT

PAGE 43

ANIMAL ID:	7505	7520	7521	7533
RIB	N	N	N	N
BONE MARROW	N	N	N	N
COSTOCHONDRAL JUNCTION	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

---

**Tabulated Animal Data**

---

PROJECT ID: TRL097  
WEEKS: 14-27

GROUP: 0.0mbk      SEX: MALE  
FATES: Terminal Sacrifice

DRAFT

PAGE 44

---

ANIMAL ID:	7505	7520	7521	7533
OTHER TISSUES AND LESIONS:				
LN, MEDIASTINAL - Hyperplasia	-	2	-	-

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

**Tabulated Animal Data**

PROJECT ID: TRL097      GROUP: 0.1mbk      SEX: MALE  
 WEEKS: 14-27          FATES: Terminal Sacrifice

D R A F T

PAGE 45

ANIMAL ID:	7503	7517	7523	7528
BRAIN (FORE)	N	N	N	N
THORACIC CORD	N	N	N	N
BRAIN (MID)	N	N	N	N
BRAIN (CEREBELLUM)	N	N	N	N
PONS	N	N	N	N
HEART	N	N	N	N
AORTA	N	N	N	N
TRACHEA	N	N	N	N
ESOPHAGUS	N	N	N	N
LUNG	N		N	
Inflammation, subacute	-	1	-	1
KIDNEY, RIGHT		N		
Nephrocalcinosis	1	-	1	1

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

**Tabulated Animal Data**

PROJECT ID: TRL097      GROUP: 0.1mbk      SEX: MALE  
 WEEKS: 14-27          FATES: Terminal Sacrifice

D R A F T

PAGE 46

ANIMAL ID:	7503	7517	7523	752B
KIDNEY, LEFT		N		N
Nephrocalcinosis	1	-	1	-
Nephropathy	1	-	-	-
SPLEEN			N	N
Pigment, hemosiderin	1	-	-	-
Siderofibrotic plaque	-	1	-	-
PANCREAS	N	N	N	N
DUODENUM	N	N	N	N
LIVER			N	N
Inflammation, subacute	-	1	-	-
Nodular hyperplasia	1	-	-	-
GALLBLADDER		N	N	N
Infiltrate, cellular	2	-	-	-
ADRENAL GLAND	N	N	N	N
SALIVARY GLAND	N	N	N	N
LYMPH NODE, SUBMANDIBULAR	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

**Tabulated Animal Data**

PROJECT ID: TRL097      GROUP: 0.1mbk      SEX: MALE  
 WEEKS: 14-27          FATES: Terminal Sacrifice

D R A F T

PAGE 47

ANIMAL ID:	7503	7517	7523	7528
JEJUNUM	N	N	N	N
COLON	N	N	N	N
TONSIL	N	N	N	N
URETER	N	N	N	N
ILEUM	N	N	N	N
LYMPH NODE, MESENTERIC	N	N	N	N
TONGUE	N	N	N	
Granuloma, foreign body	-	-	-	2
DIAPHRAGM	N	N	N	N
THYMUS	N	N	N	N
SKELETAL MUSCLE	N	N	N	N
THYROID GLAND	N	N	N	
Infiltrate, cellular	-	-	-	3

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097  
WEEKS: 14-27

GROUP: 0.1mbk  
FATES: Terminal Sacrifice

SEX: MALE

DRAFT

PAGE 48

ANIMAL ID:	7503	7517	7523	7528
PARATHYROID GLAND	N	N	N	N
PITUITARY GLAND	N	N	N	N
CECUM	N	N	N	N
STOMACH	N	N	N	N
URINARY BLADDER	N	N	N	N
TESTIS	N	N	N	N
EPIDIDYMIS	N	N	N	N
PROSTATE	N	N	N	N
MAMMARY GLAND	N	N	N	N
SKIN	N	N	N	N
SCIATIC NERVE	N	N	N	N
EYE	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097  
WEEKS: 14-27

GROUP: 0.1mbk  
FATES: Terminal Sacrifice

SEX: MALE

DRAFT

PAGE 49

ANIMAL ID:	7503	7517	7523	7528
OPTIC NERVE	N	N	N	N
RIB	N	N	N	N
BONE MARROW	N	N		N
Hypercellular	-	-	1	-
COSTOCHONDRAL JUNCTION	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 2.0mbk      SEX: MALE  
WEEKS: 14-27      FATES: Terminal Sacrifice

DRAFT

PAGE 50

ANIMAL ID:	7502	7506	7514	7576
BRAIN (FORE)	N	N	N	N
THORACIC CORD	N	N	N	N
BRAIN (MID)	N	N	N	N
BRAIN (CEREBELLUM)	N	N	N	N
PONS	N	N	N	N
HEART	N	N	N	N
AORTA	N	N	N	N
TRACHEA	N	N	N	N
ESOPHAGUS	N	N	N	N
LUNG				
Alveolar proteinosis	1	-	1	-
Inflammation, subacute	3	3	3	1
KIDNEY, RIGHT				
Nephrocalcinosis	1	1	1	1
Renal tubule, casts, proteinic	-	1	-	-

03-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

**Tabulated Animal Data**

PROJECT ID: TRL097      GROUP: 2.Ombk      SEX: MALE  
 WEEKS: 14-27          FATES: Terminal Sacrifice

D R A F T

PAGE 51

ANIMAL ID:	7502	7506	7514	7576
KIDNEY, LEFT				
Nephrocalcinosis	1	1	1	1
Renal tubule, casts, proteinic	-	1	-	-
SPLEEN			N	N
Extramedullary hematopoiesis	1	-	-	-
Pigment, hemosiderin	-	2	-	-
PANCREAS	N	N	N	N
DUODENUM	N	N	N	N
LIVER				N
Inflammation, subacute	-	-	1	-
Kupffer cell, hyperplasia	1	-	-	-
Kupffer cell, hypertrophy	-	1	-	-
Pigment, hemosiderin	1	2	-	-
GALLBLADDER	N	N	N	N
ADRENAL GLAND	N	N	N	N
SALIVARY GLAND	N	N	N	N
LYMPH NODE, SUBMANDIBULAR	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 2.0mbk      SEX: MALE  
WEEKS: 14-27      FATES: Terminal Sacrifice

DRAFT

PAGE 52

ANIMAL ID:	7502	7506	7514	7576
JEJUNUM	N	N	N	N
COLON	N	N	N	N
TONSIL	N	N	N	N
URETER	N	N	N	N
ILEUM	N	N	N	N
LYMPH NODE, MESENTERIC	N	N	N	N
TONGUE	N	N	N	N
DIAPHRAGM	N	N	N	N
THYMUS	N	N	N	N
SKELETAL MUSCLE	N	N	N	N
THYROID GLAND	N	N	N	N
PARATHYROID GLAND	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 2.0mbk      SEX: MALE  
WEEKS: 14-27      FATES: Terminal Sacrifice

DRAFT

PAGE 53

ANIMAL ID:	7502	7506	7514	7576
PITUITARY GLAND	N	N	N	N
CECUM	N	N	N	N
STOMACH	N	N	N	N
URINARY BLADDER	U	N	N	N
TESTIS	N	N	N	
Germinal epith, degeneration	-	-	-	2
EPIDIDYMIS	N	N	N	
Hyospermia	-	-	-	3
PROSTATE	U	N	N	N
MAMMARY GLAND	N	N	N	N
SKIN	N	N	N	N
SCIATIC NERVE	N	N	N	N
EYE	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 2.0mbk      SEX: MALE  
WEEKS: 14-27      FATES: Terminal Sacrifice

DRAFT

PAGE 54

ANIMAL ID:	7502	7506	7514	7576
OPTIC NERVE -	N	N	N	N
RIB	N	N	N	N
BONE MARROW	N	N		N
Hypercellular	-	-	1	-
COSTOCHONDRAL JUNCTION	N	N	N	N

03-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

---

**Tabulated Animal Data**

---

PROJECT ID: TRL097  
WEEKS: 14-27

GROUP: 2.0mbk      SEX: MALE  
FATES: Terminal Sacrifice

**D R A F T**

PAGE 55

---

ANIMAL ID:	7502	7506	7514	7576
OTHER TISSUES AND LESIONS:				
LN, MEDIASTINAL - Hyperplasia	-	-	2	-

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

**Tabulated Animal Data**

PROJECT ID: TRL097      GROUP: 6.0mbk      SEX: MALE  
 WEEKS: 14-27          FATES: Terminal Sacrifice

D R A F T

PAGE 56

ANIMAL ID:	7508	7509	7518	7524
BRAIN (FORE)	N	N	N	N
THORACIC CORD	N	N	N	N
BRAIN (MID)	N	N	N	N
BRAIN (CEREBELLUM)	N	N	N	N
PONS	N	N	N	N
HEART	N	N	N	N
AORTA	N	N	N	N
TRACHEA	N	N	N	N
ESOPHAGUS	N	N	N	N
LUNG				
Alveolar proteinosis	2	3	2	3
Inflammation, subacute	3	3	3	4
KIDNEY, RIGHT	N	N		
Nephrocalcinosis	-	-	1	1

03-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

**Tabulated Animal Data**

PROJECT ID: TRL097      GROUP: 6.0mbk      SEX: MALE  
 WEEKS: 14-27          FATES: Terminal Sacrifice

D R A F T

PAGE 57

ANIMAL ID:	7508	7509	7518	7524
KIDNEY, LEFT	N		N	
Nephrocalcinosis	-	1	-	1
Renal tubule, casts, proteinic	-	2	-	-
SPLEEN		N		
Extramedullary hematopoiesis	-	-	1	1
Pigment, hemosiderin	1	-	2	1
PANCREAS	N	N	N	N
DUODENUM	N	N	N	N
LIVER				
Hepatocyte, necrosis	1	-	1	-
Inflammation, subacute	-	3	-	-
Kupffer cell, hyperplasia	1	-	-	1
Kupffer cell, hypertrophy	-	3	1	-
Pigment, hemosiderin	-	3	-	-
GALLBLADDER	N	N	N	N
ADRENAL GLAND	N	N	N	N
SALIVARY GLAND	N	N	N	N
LYMPH NODE, SUBMANDIBULAR	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 6.0mbk      SEX: MALE  
WEEKS: 14-27      FATES: Terminal Sacrifice

DRAFT

PAGE 58

ANIMAL ID:	7508	7509	7518	7524
JEJUNUM	N	N	N	N
COLON	N	N	N	N
TONSIL	N	N	N	N
URETER	N	N	N	N
ILEUM	N	N	N	N
LYMPH NODE, MESENTERIC	N	N	N	N
TONGUE	N	N	N	N
DIAPHRAGM	N	N	N	N
THYMUS			N	
Depletion, lymphocyte	2	3	-	2
SKELETAL MUSCLE	N	N	N	N
THYROID GLAND	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

**Tabulated Animal Data**

PROJECT ID: TRL097      GROUP: 6.Ombk      SEX: MALE  
 WEEKS: 14-27          FATES: Terminal Sacrifice

D R A F T

PAGE 59

ANIMAL ID:	7508	7509	7518	7524
PARATHYROID GLAND	N	N	N	N
PITUITARY GLAND	N	N		N
Cranio-pharyngeal duct, cyst	-	-	P	-
CECUM	N	N	N	N
STOMACH	N	N	N	N
URINARY BLADDER	N	N	N	N
TESTIS	N		N	N
Germinal epith, degeneration	-	2	-	-
EPIDIDYMIS	N	N	N	N
PROSTATE	N		N	N
Atrophy	-	2	-	-
MAMMARY GLAND	N	U	N	U
SKIN	N	U	N	N
SCIATIC NERVE	N	N	N	N

03-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 6.0mbk      SEX: MALE  
WEEKS: 14-27      FATES: Terminal Sacrifice

D R A F T

PAGE 60

ANIMAL ID:	7508	7509	7518	7524
EYE	N	N	N	N
OPTIC NERVE	N	N	N	N
RIB	N	N	N	N
BONE MARROW Hypercellular	1	1	1	1
COSTOCHONDRAL JUNCTION	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 0.0mbk-R      SEX: MALE  
WEEKS: 14-27            FATES: Terminal Sacrifice

DRAFT PAGE 61

ANIMAL ID:	7512	7515	7531	7532
LUNG	N	N		
Infiltrate, macrophage	-	-	1	-
Inflammation, subacute	-	-	1	1
SPLEEN			N	N
Pigment, hemosiderin	2	1	-	-
LIVER	N	N	N	N
THYMUS	N	N	N	N
BONE MARROW	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 0.1mbk-R      SEX: MALE  
WEEKS: 14-27          FATES: Terminal Sacrifice

DRAFT

PAGE 62

ANIMAL ID:	7519	7527	7529	7536
LUNG	N	N		
Inflammation, subacute	-	-	1	1
SPLEEN	N	N		N
Pigment, hemosiderin	-	-	1	-
LIVER	N	N	N	N
THYMUS	N	N	N	N
BONE MARROW	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 2.Ombk-R      SEX: MALE  
WEEKS: 14-27          FATES: Terminal Sacrifice

DRAFT

PAGE 63

ANIMAL ID:	7510	7516	7522	7538
LUNG		N		
Infiltrate, macrophage	-	-	1	1
Inflammation, chronic	1	-	2	-
Inflammation, subacute	1	-	1	1
Pigment, hemosiderin	-	-	-	1
SPLEEN	N		N	N
Pigment, hemosiderin	-	1	-	-
LIVER	N	N	N	
Pigment, hemosiderin	-	-	-	1
THYMUS	N	N	N	N
BONE MARROW	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 6.Ombk-R      SEX: MALE  
WEEKS: 14-27          FATES: Terminal Sacrifice

D R A F T

PAGE 64

ANIMAL ID:	7507	7511	7530	7535
LUNG				
Infiltrate, macrophage	-	-	1	1
Inflammation, chronic	1	1	2	-
Inflammation, subacute	1	2	1	1
SPLEEN			N	N
Pigment, hemosiderin	1	1	-	-
LIVER		N		N
Pigment, hemosiderin	1	-	2	-
THYMUS	N	N	N	N
BONE MARROW	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

**Tabulated Animal Data**

PROJECT ID: TRL097      GROUP: 0.0mbk      SEX: FEMALE  
 WEEKS: 14-27          FATES: Terminal Sacrifice

D R A F T

PAGE 65

ANIMAL ID:	7542	7555	7558	7573
BRAIN (FORE)	N	N	N	N
THORACIC CORD	N	N	N	N
BRAIN (MID)	N	N	N	N
BRAIN (CEREBELLUM)	N	N	N	N
PONS	N	N	N	N
HEART	N	N	N	N
AORTA	U	N	N	N
TRACHEA	N	N	N	N
ESOPHAGUS	N	N	N	N
LUNG		N	N	
Inflammation, subacute	1	-	-	3
KIDNEY, RIGHT				
Nephrocalcinosis	-	1	1	1
Renal tubule, casts, proteinic	1	-	-	-
Tubular epith, vacuo, cytopl	-	-	1	-

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 0.0mbk      SEX: FEMALE  
 WEEKS: 14-27      FATES: Terminal Sacrifice

DRAFT PAGE 66

ANIMAL ID:	7542	7555	7558	7573
KIDNEY, LEFT	N			
Nephrocalcinosis	-	1	1	-
Renal tubule, casts, proteinic	-	-	-	1
Tubular epith, vacuo, cytopl	-	-	1	-
SPLEEN	N	N	N	N
PANCREAS	N	N	N	N
DUODENUM	N	N	N	N
LIVER	N	N	N	N
GALLBLADDER	N	N	N	N
ADRENAL GLAND	N	N	N	N
SALIVARY GLAND		N		N
Infiltrate, cellular	1	-	1	-
LYMPH NODE, SUBMANDIBULAR	N	N	N	N
JEJUNUM	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097  
WEEKS: 14-27

GROUP: 0.0mbk  
FATES: Terminal Sacrifice

SEX: FEMALE

DRAFT

PAGE 67

ANIMAL ID:	7542	7555	7558	7573
COLON	N	N	N	N
TONSIL	N	N	N	N
URETER	N	N	N	N
ILEUM	N	N	N	N
LYMPH NODE, MESENTERIC	N	N	N	N
TONGUE	N	N	N	N
DIAPHRAGM	N	N	N	N
THYMUS	N	N	N	N
SKELETAL MUSCLE	N	N	N	N
THYROID GLAND	N	N	N	N
PARATHYROID GLAND	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 0.0mbk      SEX: FEMALE  
WEEKS: 14-27      FATES: Terminal Sacrifice

DRAFT      PAGE 68

ANIMAL ID:	7542	7555	7558	7573
PITUITARY GLAND	N	N		
Craniopharyngeal duct, cyst	-	-	P	P
CECUM	N	N	N	N
STOMACH	N	N	N	N
URINARY BLADDER	N	N	N	N
OVARIES	N	N	N	N
UTERUS	N	N	N	N
MAMMARY GLAND	N	U	N	U
SKIN	N	N	N	N
SCIATIC NERVE	N	N	N	N
EYE	N	N	N	N
OPTIC NERVE	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097  
WEEKS: 14-27

GROUP: 0.0mbk  
FATES: Terminal Sacrifice

SEX: FEMALE

DRAFT

PAGE 69

ANIMAL ID:	7542	7555	7558	7573
RIB	N	N	N	N
BONE MARROW	N	N	N	N
COSTOCHONDRAL JUNCTION	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 0.1mbk      SEX: FEMALE  
WEEKS: 14-27          FATES: Terminal Sacrifice

DRAFT

PAGE 70

ANIMAL ID:	7550	7560	7567	7569
BRAIN (FORE)	N	N	N	N
THORACIC CORD	N	N	N	N
BRAIN (MID)	N	N	N	N
BRAIN (CEREBELLUM)	N	N	N	N
PONS	N	N	N	N
HEART	N	N	N	N
AORTA	N	N	N	N
TRACHEA	N	N		N
Infiltrate, cellular	-	-	1	-
ESOPHAGUS	N	N	N	N
LUNG				
Inflammation, subacute	1	2	1	1

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

**Tabulated Animal Data**

PROJECT ID: TRL097      GROUP: 0.1mbk      SEX: FEMALE  
 WEEKS: 14-27          FATES: Terminal Sacrifice

D R A F T

PAGE 71

ANIMAL ID:	7550	7560	7567	7569
KIDNEY, RIGHT	N			
Cortex, infiltrate, cellular	-	1	-	-
Nephrocalcinosis	-	1	1	1
KIDNEY, LEFT				
Nephrocalcinosis	1	1	1	1
SPLEEN	N	N	N	N
PANCREAS	N	N	N	N
DUODENUM	N	N	N	N
LIVER		N	N	N
Kupffer cell, hyperplasia	1	-	-	-
Pigment, hemosiderin	1	-	-	-
GALLBLADDER	N	N	N	N
ADRENAL GLAND	N	N	N	N
SALIVARY GLAND	N	N		N
Infiltrate, cellular	-	-	1	-
LYMPH NODE, SUBMANDIBULAR	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 0.1mbk      SEX: FEMALE  
WEEKS: 14-27          FATES: Terminal Sacrifice

DRAFT

PAGE 72

ANIMAL ID:	7550	7560	7567	7569
JEJUNUM	N	N	N	N
COLON	N	N	N	N
TONSIL	N	N	N	N
URETER	N	N	N	N
ILEUM Inflammation, acute	2	-	-	-
LYMPH NODE, MESENTERIC	N	N	N	N
TONGUE	N	N	N	N
DIAPHRAGM	N	N	N	N
THYMUS	N	N	N	N
SKELETAL MUSCLE	N	N	N	N
THYROID GLAND C-Cell, hyperplasia	1	-	-	-

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097  
WEEKS: 14-27

GROUP: 0.1mbk  
FATES: Terminal Sacrifice

SEX: FEMALE

DRAFT

PAGE 73

ANIMAL ID:	7550	7560	7567	7569
PARATHYROID GLAND	N	N	N	N
PITUITARY GLAND	N		N	
Craniopharyngeal duct, cyst	-	P	-	P
CECUM	N	N	N	N
STOMACH	N	N	N	N
URINARY BLADDER	N		N	N
Infiltrate, cellular	-	1	-	-
OVARIES	N	N	N	N
UTERUS	N	N	N	N
MAMMARY GLAND	N	N	N	N
SKIN	N	N	N	N
SCIATIC NERVE	N	N	N	N
EYE	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 0.1mbk      SEX: FEMALE  
WEEKS: 14-27      FATES: Terminal Sacrifice

DRAFT

PAGE 74

ANIMAL ID:	7550	7560	7567	7569
OPTIC NERVE	N	N	N	N
RIB	N	N	N	N
BONE MARROW	N	N	N	N
COSTOCHONDRAL JUNCTION	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 2.Ombk      SEX: FEMALE  
WEEKS: 14-27          FATES: Terminal Sacrifice

D R A F T

PAGE 75

ANIMAL ID:	7556	7564	7572	7574
BRAIN (FORE)	N	N	N	N
THORACIC CORD	N	N	N	N
BRAIN (MID)	N	N	N	N
BRAIN (CEREBELLUM)	N	N	N	N
PONS	N	N	N	N
HEART	N	N	N	N
AORTA	N	N	N	N
TRACHEA	N	N	N	
Infiltrate, cellular	-	-	-	1
ESOPHAGUS	N	N	N	N
LUNG				
Alveolar proteinosis	1	1	1	1
Inflammation, subacute	3	2	3	3
KIDNEY, RIGHT				
Nephrocalcinosis	1	1	1	1

03-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

**Tabulated Animal Data**

PROJECT ID: TRL097      GROUP: 2.Ombk      SEX: FEMALE  
 WEEKS: 14-27      FATES: Terminal Sacrifice

D R A F T

PAGE 76

ANIMAL ID:	7556	7564	7572	7574
KIDNEY, LEFT				
Cortex, hemorrhage	-	-	2	-
Nephrocalcinosis	1	1	1	1
Renal tubule, casts, proteinic	1	-	-	-
SPLEEN				
Extramedullary hematopoiesis	-	-	-	1
Pigment, hemosiderin	2	1	-	1
PANCREAS				
	N	N	N	N
DUODENUM				
	N	N	N	N
LIVER				
Inflammation, subacute	2	-	-	-
Kupffer cell, hyperplasia	-	-	-	1
Kupffer cell, hypertrophy	2	-	-	-
Pigment, hemosiderin	1	-	-	1
GALLBLADDER				
	N	N	N	N
ADRENAL GLAND				
Cortex, cyst	-	P	-	-
SALIVARY GLAND				
Infiltrate, cellular	-	-	-	1

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 2.0mbk      SEX: FEMALE  
WEEKS: 14-27      FATES: Terminal Sacrifice

DRAFT      PAGE 77

ANIMAL ID:	7556	7564	7572	7574
LYMPH NODE, SUBMANDIBULAR	N	N	N	N
JEJUNUM	N	N	N	N
COLON	N	N	N	N
TONSIL	N	N	N	N
URETER	N	N	N	N
ILEUM	N	N	N	N
LYMPH NODE, MESENTERIC	N	N	N	N
TONGUE	N	N	N	N
DIAPHRAGM	N	N	N	N
THYMUS		N	N	N
Depletion, lymphocyte	2	-	-	-
SKELETAL MUSCLE	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 2.0mbk      SEX: FEMALE  
WEEKS: 14-27      FATES: Terminal Sacrifice

D R A F T

PAGE 78

ANIMAL ID:	7556	7564	7572	7574
THYROID GLAND	N	N	N	
Infiltrate, cellular	-	-	-	1
PARATHYROID GLAND	N	N	N	N
PITUITARY GLAND	N	N	N	N
CECUM	N	N	N	N
STOMACH	N	N	N	N
URINARY BLADDER	N	N	N	N
OVARIES	N	N	N	N
UTERUS	N	N		N
Hemorrhage	-	-	1	-
MAMMARY GLAND	N	U	U	N
SKIN	N	N	N	N
SCIATIC NERVE	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 2.0mbk      SEX: FEMALE  
WEEKS: 14-27      FATES: Terminal Sacrifice

D R A F T

PAGE 79

ANIMAL ID:	7556	7564	7572	7574
EYE	N	N	N	N
OPTIC NERVE	N	N	N	N
RIB	N	N	N	N
BONE MARROW Hypercellular	1	1	1	1
COSTOCHONDRAL JUNCTION	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 6.Ombk      SEX: FEMALE  
WEEKS: 14-27      FATES: Terminal Sacrifice

DRAFT

PAGE 80

ANIMAL ID:	7544	7546	7551	7568
BRAIN (FORE)	N	N	N	N
THORACIC CORD	N	N	N	N
BRAIN (MID)	N	N	N	N
BRAIN (CEREBELLUM)	N	N	N	N
PONS	N	N	N	N
HEART	N	N	N	N
AORTA	N	N	N	N
TRACHEA	N	N	N	N
ESOPHAGUS	N	N	N	N
LUNG				
Alveolar proteinosis	2	3	1	2
Inflammation, subacute	2	3	2	2
KIDNEY, RIGHT				
Nephrocalcinosis	1	1	1	1

03-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 6.0mbk      SEX: FEMALE  
 WEEKS: 14-27      FATES: Terminal Sacrifice

**DRAFT**      PAGE 81

ANIMAL ID:	7544	7546	7551	7568
<b>KIDNEY, LEFT</b>				
Nephrocalcinosis	1	1	1	1
Renal tubule, casts, proteinic	1	-	-	1
<b>SPLEEN</b>				
Extramedullary hematopoiesis	-	1	2	2
Pigment, hemosiderin	1	2	1	1
<b>PANCREAS</b>				
	N	N	N	N
<b>DUODENUM</b>				
	N	N	N	N
<b>LIVER</b>				
Inflammation, subacute	2	2	2	1
Kupffer cell, hypertrophy	3	2	1	2
Pigment, hemosiderin	2	2	3	2
<b>GALLBLADDER</b>				
	N	N	N	N
<b>ADRENAL GLAND</b>				
Cortex, vacuolation, cytoplasm	-	-	1	-
<b>SALIVARY GLAND</b>				
Infiltrate, cellular	-	-	-	1

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 6.0mbk      SEX: FEMALE  
WEEKS: 14-27      FATES: Terminal Sacrifice

DRAFT      PAGE 82

ANIMAL ID:	7544	7546	7551	7568
LYMPH NODE, SUBMANDIBULAR Hyperplasia	2	-	-	-
JEJUNUM	N	N	N	N
COLON	N	N	N	N
TONSIL	N	N	N	N
URETER	N	N	N	N
ILEUM	N	N	N	N
LYMPH NODE, MESENTERIC	N	N	N	N
TONGUE	N	N	N	N
DIAPHRAGM	N	N	N	N
THYMUS Depletion, lymphocyte	-	1	-	-
SKELETAL MUSCLE	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

**Tabulated Animal Data**

PROJECT ID: TRL097      GROUP: 6.0mbk      SEX: FEMALE  
 WEEKS: 14-27          FATES: Terminal Sacrifice

D R A F T

PAGE 83

ANIMAL ID:	7544	7546	7551	7568
THYROID GLAND	N	N		N
Follicular cell, vacuo, cytopl	-	-	2	-
PARATHYROID GLAND	N	N	N	N
PITUITARY GLAND		U		
Chromophobe, vacuo, cytoplasm	-	-	1	-
Craniopharyngeal duct, cyst	P	-	-	P
CECUM	N	N	N	N
STOMACH	N	N	N	N
URINARY BLADDER	N	N	N	N
OVARIES	N	N	N	N
UTERUS	N	N	N	N
MAMMARY GLAND	N	N	N	N
SKIN	N	N	N	N
SCIATIC NERVE	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 6.Dmbk      SEX: FEMALE  
WEEKS: 14-27      FATES: Terminal Sacrifice

DRAFT PAGE 84

ANIMAL ID:	7544	7546	7551	7568
EYE	N	N	N	N
OPTIC NERVE	N	N	N	N
RIB	N	N	N	N
BONE MARROW Hypercellular	1	1	1	1
COSTOCHONDRAL JUNCTION	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 0.0mbk-R      SEX: FEMALE  
WEEKS: 14-27          FATES: Terminal Sacrifice

DRAFT      PAGE 85

ANIMAL ID:	7541	7549	7557	7566
LUNG				
Inflammation, chronic	2	-	-	-
Inflammation, subacute	-	1	1	1
SPLEEN	N		N	N
Capsule, scar	-	2	-	-
Pigment, hemosiderin	-	1	-	-
LIVER	N	N	N	N
THYMUS	N	N	N	N
BONE MARROW	N	N	N	N

03-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 0.1mbk-R      SEX: FEMALE  
WEEKS: 14-27      FATES: Terminal Sacrifice

D R A F T

PAGE 86

ANIMAL ID:	7543	7545	7552	7553
LUNG		N		
Inflammation, acute	1	-	-	-
Inflammation, chronic	-	-	1	-
Inflammation, subacute	-	-	-	1
SPLEEN	N	N	N	N
LIVER	N	N		N
Hepatocyte, vacuo, cytoplasm	-	-	2	-
THYMUS	N	N	N	N
BONE MARROW	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 2.Dmbk-R      SEX: FEMALE  
WEEKS: 14-27            FATES: Terminal Sacrifice

DRAFT

PAGE 87

ANIMAL ID:	7548	7561	7562	7571
LUNG				
Infiltrate, macrophage	-	-	1	-
Inflammation, chronic	1	-	1	-
Inflammation, subacute	1	1	1	1
SPLEEN		N		
Pigment, hemosiderin	1	-	1	1
LIVER				
Pigment, hemosiderin	1	1	1	1
THYMUS	N	N	N	N
BONE MARROW	N	N	N	N

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Tabulated Animal Data

PROJECT ID: TRL097      GROUP: 6.0mbk-R      SEX: FEMALE  
 WEEKS: 14-27          FATES: Terminal Sacrifice

**DRAFT** PAGE 88

ANIMAL ID:	7539	7540	7554	7563
<b>LUNG</b>				
Alveolar proteinosis	1	-	1	-
Heteropic bone	-	P	-	-
Infiltrate, macrophage	1	-	2	-
Inflammation, subacute	2	1	2	1
Pigment, hemosiderin	-	-	2	-
<b>SPLEEN</b>				
Pigment, hemosiderin	N	-	1	1
<b>LIVER</b>				
Hepatocyte, vacuo, cytoplasm	N	-	2	-
Pigment, hemosiderin	-	2	1	2
<b>THYMUS</b>				
	N	N	N	N
<b>BONE MARROW</b>				
	N	N	N	N

03-Sep-1993

DRAFT

SECTION V  
CORRELATION OF GROSS AND MICROSCOPIC (MICRO) FINDINGS

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL097  
WEEKS: 14-27

GROUP: 0.0mbk      SEX: MALE  
FATES: Terminal Sacrifice

PAGE 90

ANIMAL ID: 7505      PATHOLOGY ID. NO: TI097-7505      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 7520      PATHOLOGY ID. NO: TI097-7520      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LYMPH NODE, MEDIASTINAL - ENLARGED

LN, MEDIASTINAL - Hyperplasia

ANIMAL ID: 7521      PATHOLOGY ID. NO: TI097-7521      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 7533      PATHOLOGY ID. NO: TI097-7533      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL097  
WEEKS: 14-27

GROUP: 0.1mbk      SEX: MALE  
FATES: Terminal Sacrifice

PAGE 91

ANIMAL ID: 7503      PATHOLOGY ID. NO: TI097-7503      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LIVER, MEDIAN LOBE - NODULE, 1,  
25X27X5 MM

LIVER- Nodular hyperplasia

ANIMAL ID: 7517      PATHOLOGY ID. NO: TI097-7517      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 7523      PATHOLOGY ID. NO: TI097-7523      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 7528      PATHOLOGY ID. NO: TI097-7528      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>SPLEEN - NODULE, 1, ROUND, RED,  
2X2.5 MM

No corresponding lesion

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

---

Correlation of Gross & Micro Findings

DRAFT

---

PROJECT ID: TRL097  
WEEKS: 14-27

GROUP: 2.0mbk      SEX: MALE  
FATES: Terminal Sacrifice

PAGE 92

---

ANIMAL ID: 7502      PATHOLOGY ID. NO: TI097-7502      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7506      PATHOLOGY ID. NO: TI097-7506      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7514      PATHOLOGY ID. NO: TI097-7514      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LYMPH NODE, MEDIASTINAL - ENLARGED

LN, MEDIASTINAL - Hyperplasia

>TESTIS, UNILATERAL - SMALL

No corresponding lesion

---

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

---

Correlation of Gross & Micro Findings

DRAFT

---

PROJECT ID: TRL097  
WEEKS: 14-27

GROUP: 2.0mbk      SEX: MALE  
FATES: Terminal Sacrifice

PAGE 93

---

ANIMAL ID: 7576  
ANIMAL FATE: Terminal Sacrifice

PATHOLOGY ID. NO: TI097-7576      PATHOLOGIST: MJT

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>EPIDIDYMIS - SMALL, 3.5X2 MM

EPIDIDYMIS- Hypospermia

---

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

---

Correlation of Gross & Micro Findings

DRAFT

---

PROJECT ID: TRL097  
WEEKS: 14-27

GROUP: 6.0mbk  
FATES: Terminal Sacrifice

SEX: MALE

PAGE 94

---

ANIMAL ID: 7508                      PATHOLOGY ID. NO: TI097-7508      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7509                      PATHOLOGY ID. NO: TI097-7509      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7518                      PATHOLOGY ID. NO: TI097-7518      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7524                      PATHOLOGY ID. NO: TI097-7524      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

---

Correlation of Gross & Micro Findings

DRAFT

---

PROJECT ID: TRL097  
WEEKS: 14-27

GROUP: 0.0mbk-R      SEX: MALE  
FATES: Terminal Sacrifice

PAGE 95

---

ANIMAL ID: 7512      PATHOLOGY ID. NO: TI097-7512      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7515      PATHOLOGY ID. NO: TI097-7515      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7531      PATHOLOGY ID. NO: TI097-7531      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7532      PATHOLOGY ID. NO: TI097-7532      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL097  
WEEKS: 14-27

GROUP: 0.1mbk-R      SEX: MALE  
FATES: Terminal Sacrifice

PAGE 96

ANIMAL ID: 7519      PATHOLOGY ID. NO: TI097-7519      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 7527      PATHOLOGY ID. NO: TI097-7527      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 7529      PATHOLOGY ID. NO: TI097-7529      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 7536      PATHOLOGY ID. NO: TI097-7536      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

---

Correlation of Gross & Micro Findings

DRAFT

---

PROJECT ID: TRL097  
WEEKS: 14-27

GROUP: 2.0mbk-R      SEX: MALE  
FATES: Terminal Sacrifice

PAGE 97

---

ANIMAL ID: 7510                      PATHOLOGY ID. NO: TI097-7510      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7516                      PATHOLOGY ID. NO: TI097-7516      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7522                      PATHOLOGY ID. NO: TI097-7522      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7538                      PATHOLOGY ID. NO: TI097-7538      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

---

Correlation of Gross & Micro Findings

DRAFT

---

PROJECT ID: TRL097  
WEEKS: 14-27

GROUP: 6.0mbk-R      SEX: MALE  
FATES: Terminal Sacrifice

PAGE 98

---

ANIMAL ID: 7507      PATHOLOGY ID. NO: TI097-7507      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7511      PATHOLOGY ID. NO: TI097-7511      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7530      PATHOLOGY ID. NO: TI097-7530      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7535      PATHOLOGY ID. NO: TI097-7535      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

---

Correlation of Gross & Micro Findings

DRAFT

---

PROJECT ID: TRL097  
WEEKS: 14-27

GROUP: 0.0mbk  
FATES: Terminal Sacrifice

SEX: FEMALE

PAGE 99

---

ANIMAL ID: 7542                      PATHOLOGY ID. NO: TI097-7542    PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7555                      PATHOLOGY ID. NO: TI097-7555    PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7558                      PATHOLOGY ID. NO: TI097-7558    PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7573                      PATHOLOGY ID. NO: TI097-7573    PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

---

Correlation of Gross & Micro Findings

DRAFT

---

PROJECT ID: TRL097  
WEEKS: 14-27

GROUP: 0.1mbk      SEX: FEMALE  
FATES: Terminal Sacrifice

PAGE 100

---

ANIMAL ID: 7550      PATHOLOGY ID. NO: TI097-7550      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7560      PATHOLOGY ID. NO: TI097-7560      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7567      PATHOLOGY ID. NO: TI097-7567      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7569      PATHOLOGY ID. NO: TI097-7569      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

---

Correlation of Gross & Micro Findings

DRAFT

---

PROJECT ID: TRL097  
WEEKS: 14-27

GROUP: 2.0mbk  
FATES: Terminal Sacrifice

SEX: FEMALE

PAGE 101

---

ANIMAL ID: 7556                      PATHOLOGY ID. NO: TI097-7556      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7564                      PATHOLOGY ID. NO: TI097-7564      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7572                      PATHOLOGY ID. NO: TI097-7572      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7574                      PATHOLOGY ID. NO: TI097-7574      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

---

Correlation of Gross & Micro Findings

DRAFT

---

PROJECT ID: TRL097  
WEEKS: 14-27

GROUP: 6.0mbk      SEX: FEMALE  
FATES: Terminal Sacrifice

PAGE 102

---

ANIMAL ID: 7544      PATHOLOGY ID. NO: TI097-7544      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7546      PATHOLOGY ID. NO: TI097-7546      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7551      PATHOLOGY ID. NO: TI097-7551      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7568      PATHOLOGY ID. NO: TI097-7568      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

---

Correlation of Gross & Micro Findings

DRAFT

---

PROJECT ID: TRL097  
WEEKS: 14-27

GROUP: 0.0mbk-R      SEX: FEMALE  
FATES: Terminal Sacrifice

PAGE 103

---

ANIMAL ID: 7541      PATHOLOGY ID. NO: TI097-7541      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7549      PATHOLOGY ID. NO: TI097-7549      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>SPLEEN, CAPSULE - SCAR, 2, WHITE

SPLEEN- Capsule, scar

---

ANIMAL ID: 7557      PATHOLOGY ID. NO: TI097-7557      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7566      PATHOLOGY ID. NO: TI097-7566      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

03-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

---

Correlation of Gross & Micro Findings

DRAFT

---

PROJECT ID: TRL097  
WEEKS: 14-27

GROUP: 0.1mbk-R      SEX: FEMALE  
FATES: Terminal Sacrifice

PAGE 104

---

ANIMAL ID: 7543      PATHOLOGY ID. NO: TI097-7543      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7545      PATHOLOGY ID. NO: TI097-7545      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7552      PATHOLOGY ID. NO: TI097-7552      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7553      PATHOLOGY ID. NO: TI097-7553      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

---

Correlation of Gross & Micro Findings

DRAFT

---

PROJECT ID: TRL097  
WEEKS: 14-27

GROUP: 2.0mbk-R      SEX: FEMALE  
FATES: Terminal Sacrifice

PAGE 105

---

ANIMAL ID: 7548      PATHOLOGY ID. NO: TI097-7548      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7561      PATHOLOGY ID. NO: TI097-7561      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7562      PATHOLOGY ID. NO: TI097-7562      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7571      PATHOLOGY ID. NO: TI097-7571      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

20-Aug-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 097

---

Correlation of Gross & Micro Findings

DRAFT

---

PROJECT ID: TRL097  
WEEKS: 14-27

GROUP: 6.0mbk-R      SEX: FEMALE  
FATES: Terminal Sacrifice

PAGE 106

---

ANIMAL ID: 7539      PATHOLOGY ID. NO: TI097-7539      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7540      PATHOLOGY ID. NO: TI097-7540      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 7554      PATHOLOGY ID. NO: TI097-7554      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG - FOCUS, MULTIPLE, GREEN, 7X10      No corresponding lesion  
MM

---

ANIMAL ID: 7563      PATHOLOGY ID. NO: TI097-7563      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

20-Aug-1993

D R A F T

SECTION VI  
QUALITY ASSURANCE STATEMENT

QUALITY ASSURANCE STATEMENT

DRAFT

This histopathology project was 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. Results of these activities indicate that the portions of the study performed by PAI conformed with GLP regulations and applicable Standard Operating Procedures. 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
* 04/22/93	Tissue Trimming	04/22/93
* 06/08/93	Processing/Embedding	06/08/93
* 04/12/93	Microtomy	04/12/93
* 07/14/93	Staining	07/19/93
* 07/14/93	Coverslipping	07/19/93
** 04/15/93	Labeling	04/15/93
* 06/09/93	Quality Control/Checkout	06/09/93
** 09/03/93	Individual Animal Data	09/03/93
** 09/03/93	Data Entry	09/03/93
** 09/03/93	Computer-Generated Tables	09/03/93
** 09/03/93	Draft Pathology Report	09/03/93
** 09/28/93	Second Draft Pathology Report	09/28/93
** 03/18/94	Third Draft Pathology Report	03/18/94

\*General quarterly phase inspection  
 \*\*Inspection specific for Study Number

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.

  
 \_\_\_\_\_  
 Quality Assurance Unit  
 PAI Illinois Division

03/18/94  
 \_\_\_\_\_  
 Date

Thirteen Week Oral Toxicity Study of WR 238605 with a Thirteen Week Recovery Period in Dogs, TRL Study Number 097.

DRAFT

SECTION VII  
APPENDIX I: BONE MARROW REPORT



# Pathology Associates, Inc.

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

---

BONE MARROW EVALUATION REPORT  
FOR

D R A F T

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

STUDY NUMBER 097

PREPARED FOR  
TOXICOLOGY RESEARCH LABORATORY  
CHICAGO, ILLINOIS

TABLE OF CONTENTS

DRAFT

Bone Marrow Evaluation Narrative	I
M:E Ratio Group Summary Tables	II
Individual Animal M:E Ratio Data	III
Individual Animal Data Sheets	IV
Quality Assurance Statement	V

I. Bone Marrow Evaluation Narrative

DRAFT

## BONE MARROW EVALUATION REPORT

### THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605 WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

DRAFT

#### INTRODUCTION

This report prepared by Pathology Associates, Inc. (PAI) for Toxicology Research Laboratory (TRL), University of Illinois at Chicago, Department of Pharmacology, P. O. Box 6998, Chicago, IL, 60680, presents the results of bone marrow evaluation from dogs given WR 238605 orally for at least thirteen weeks.

#### EXPERIMENTAL DESIGN AND METHODS

Thirty-two male and thirty-two female dogs were randomized into one of four groups as described below.

Treatment Group	Dose Level (mg base/kg/day)	Number of Males	Number of Females
1	0	4 + 4*	4 + 4*
2	0.1	4 + 4*	4 + 4*
3	2.0	4 + 4*	4 + 4*
4	6.0	4 + 4*	4 + 4*

\*Recovery Animals.

Four animals per sex in each dose group were necropsied during Week 14. The remainder of the animals were held for a thirteen week recovery period at which time they were necropsied.

Bone marrow smears were prepared from the rib of each animal at both necropsies. 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 TRL and provided to PAI for inclusion in this report.

D R A F T

## RESULTS

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

The M:E Ratios from bone marrow smears collected during week 14 in this study were within normal limits for animals in Groups 1 and 2. The M:E Ratios from male and female animals in Groups 3 and 4 were significantly decreased in a dose-related manner as compared to controls.

The M:E Ratios from bone marrow smears collected after the thirteen week recovery period in this study were within normal limits for animals in all dose groups as compared to controls.

## CONCLUSION

Under the conditions of this study, WR 238605 resulted in a treatment-related effect in the M:E Ratio of the rib bone marrow of male and female treated dogs at Week 14. The M:E Ratios from male and female animals in Groups 3 and 4 were significantly decreased in a dose-related manner as compared to controls. The M:E Ratios from bone marrow smears collected after the thirteen week recovery period in this study were within normal limits for animals in all dose groups as compared to controls.

---

Lynda L. Pippin, DVM  
August 6, 1993

DRAFT

II. M:E Ratio Group Summary Tables

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

SUMMARY REPORT  
TEST: M:E RATIO

STUDY: 097  
STUDY NO: 097BM

SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

PERIOD(s):      Week 14      Week 27

Group: 1M : 0 mg base/kg/day  
MEAN            1.76            1.76  
SD              0.054          0.062  
N                4                4

Group: 2M : 0.1 mg base/kg/day  
MEAN            1.84            1.76  
SD              0.048          0.083  
N                4                4

Group: 3M : 2.0 mg base/kg/day  
MEAN            1.64\*           1.75  
SD              0.043          0.048  
N                4                4

Group: 4M : 6.0 mg base/kg/day  
MEAN            1.57\*\*          1.76  
SD              0.059          0.070  
N                4                4

DRAFT

\*-Significant Difference from Control P < .05

\*\*-Significant Difference from Control P < .01

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

SUMMARY REPORT  
TEST: M:E RATIO

STUDY: 097  
STUDY NO: 097BM

SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

PERIOD(s):    Week 14    Week 27

Group: 1F : 0 mg base/kg/day  
MEAN            1.84            1.80  
SD              0.077           0.047  
N                4                4

Group: 2F : 0.1 mg base/kg/day  
MEAN            1.80            1.82  
SD              0.104           0.056  
N                4                4

Group: 3F : 2.0 mg base/kg/day  
MEAN            1.65\*           1.79  
SD              0.072           0.088  
N                4                4

Group: 4F : 6.0 mg base/kg/day  
MEAN            1.57\*\*          1.82  
SD              0.074           0.078  
N                4                4

D R A F T

\*-Significant Difference from Control P < .05

\*\*-Significant Difference from Control P < .01

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

SUMMARY REPORT  
TEST: M:E RATIO

DRAFT

STUDY: 097  
STUDY NO: 0978M

SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 14

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES				Source	Degree Fdm	Sum of Squares	Mean Square
						LO	-95%-	HI	LO				
1M	4	7.05	1.76	0.054						TREATMENTS	3	0.169	0.056
2M	4	7.35	1.84	0.048	2.06	1.67	1.86	1.63	1.89	ERROR	12	0.032	0.003
3M	4	6.57	1.64	0.043	3.30	1.67	1.86*	1.63	1.89				
4M	4	6.29	1.57	0.059	5.23	1.67	1.86*	1.63	1.89**	TOTAL	15	0.201	

F Ratio = 21.36 'F' table values F.01 = 5.95 F.05 = 3.49  
Coeff. Var. % = 3.017 Dunnett's 'T' table values P.01 = 3.58 P.05 = 2.68

Week 27

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES				Source	Degree Fdm	Sum of Squares	Mean Square
						LO	-95%-	HI	LO				
1M	4	7.02	1.76	0.062						TREATMENTS	3	0.0008	0.0003
2M	4	7.05	1.76	0.083						ERROR	12	0.0542	0.0045
3M	4	6.98	1.75	0.048									
4M	4	7.05	1.76	0.070						TOTAL	15	0.0550	

F Ratio = 0.06 'F' table values F.01 = 5.95 F.05 = 3.49  
Coeff. Var. % = 3.825 Dunnett's 'T' table values P.01 = 3.58 P.05 = 2.68

\*-Significant Difference from Control P < .05

\*\*-Significant Difference from Control P < .01

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

SUMMARY REPORT  
TEST: M:E RATIO

DRAFT

STUDY: 097  
STUDY NO: 097BH

SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 14

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES				Source	Degree Fdm	Sum of Squares	Mean Square
						LO	-95%-	HI	LO				
1F	4	7.35	1.84	0.077						TREATMENTS	3	0.194	0.065
2F	4	7.18	1.80	0.104	0.73	1.68	1.99	1.63	2.05	ERROR	12	0.082	0.007
3F	4	6.59	1.65	0.072	3.25	1.68	1.99*	1.63	2.05				
4F	4	6.26	1.57	0.074	4.66	1.68	1.99*	1.63	2.05**	TOTAL	15	0.276	

F Ratio = 9.43 'F' table values F.01 = 5.95 F.05 = 3.49  
Coeff. Var. % = 4.835 Dunnett's 'T' table values P.01 = 3.58 P.05 = 2.68

Week 27

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES				Source	Degree Fdm	Sum of Squares	Mean Square
						LO	-95%-	HI	LO				
1F	4	7.20	1.80	0.047						TREATMENTS	3	0.0020	0.0007
2F	4	7.26	1.82	0.056						ERROR	12	0.0574	0.0048
3F	4	7.17	1.79	0.088									
4F	4	7.28	1.82	0.078						TOTAL	15	0.0593	

F Ratio = 0.14 'F' table values F.01 = 5.95 F.05 = 3.49  
Coeff. Var. % = 3.827 Dunnett's 'T' table values P.01 = 3.58 P.05 = 2.68

\*-Significant Difference from Control P < .05

\*\*-Significant Difference from Control P < .01

III. Individual Animal M:E Ratio Data

D R A F T

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: M:E RATIO

STUDY ID: 097  
STUDY NO: 097BM  
ASBR: M:E RATIO

DRAFT

SEX: MALE  
UNITS: -

ANIMAL ID    Week 14    Week 27

GROUP: 1M:0 mg base/kg/day  
7531            --            1.84  
7532            --            1.70  
7512            --            1.72  
7515            --            1.76  
7521            1.69            --  
7533            1.82            --  
7520            1.78            --  
7505            1.76            --  
  
MEAN            1.76            1.76  
SD              0.054           0.062  
N                4                4

GROUP: 2M:0.1 mg base/kg/day  
7527            --            1.82  
7519            --            1.66  
7529            --            1.73  
7536            --            1.84  
7503            1.78            --  
7523            1.89            --  
7517            1.86            --  
7528            1.82            --  
  
MEAN            1.84            1.76  
SD              0.048           0.083  
N                4                4

GROUP: 3M:2.0 mg base/kg/day  
7538            --            1.72  
7516            --            1.81  
7522            --            1.75  
7510            --            1.70  
7576            1.69            --  
7506            1.63            --  
7502            1.59            --  
7514            1.66            --  
  
MEAN            1.64            1.75  
SD              0.043           0.048  
N                4                4

GROUP: 4M:6.0 mg base/kg/day  
7535            --            1.76  
7511            --            1.78  
7530            --            1.84  
7507            --            1.67  
7508            1.55            --  
7509            1.58            --  
7518            1.51            --  
7524            1.65            --  
  
MEAN            1.57            1.76  
SD              0.059           0.070  
N                4                4

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: M:E RATIO

STUDY ID: 097  
STUDY NO: 097BM  
ABBR: M:E RATIO

DRAFT

SEX: FEMALE  
UNITS: -

ANIMAL ID    Week 14    Week 27

GROUP: 1F:0 mg base/kg/day  
7557            --            1.75  
7541            --            1.78  
7566            --            1.86  
7549            --            1.81  
7555            1.87            --  
7558            1.84            --  
7573            1.73            --  
7542            1.91            --  
  
MEAN            1.84            1.80  
SD              0.077           0.047  
N                4                4

GROUP: 2F:0.1 mg base/kg/day  
7543            --            1.89  
7553            --            1.82  
7545            --            1.76  
7552            --            1.79  
7569            1.70            --  
7560            1.92            --  
7567            1.84            --  
7550            1.72            --  
  
MEAN            1.80            1.82  
SD              0.104           0.056  
N                4                4

GROUP: 3F:2.0 mg base/kg/day  
7562            --            1.72  
7548            --            1.73  
7571            --            1.81  
7561            --            1.91  
7564            1.72            --  
7574            1.56            --  
7556            1.62            --  
7572            1.69            --  
  
MEAN            1.65            1.79  
SD              0.072           0.088  
N                4                4

GROUP: 4F:6.0 mg base/kg/day  
7539            --            1.76  
7563            --            1.75  
7540            --            1.91  
7554            --            1.86  
7568            1.50            --  
7544            1.67            --  
7546            1.53            --  
7551            1.56            --  
  
MEAN            1.57            1.82  
SD              0.074           0.078  
N                4                4

(--)-Data Unavailable

IV. Individual Animal Data Sheets

DRAFT

**BONE MARROW M:E RATIO DATA**

Group 1

Vehicle Control: 0 mg base/kg/day

ANIMAL NO.	7505	7520	7521	7533
ABSOLUTE	319:181	320:180	314:186	323:177
RATIO	1.76:1.00	1.78:1.00	1.69:1.00	1.82:1.00

DRAFT

Group 2

Low-Dose: 0.1 mg base/kg/day

ANIMAL NO.	7503	7517	7523	7528
ABSOLUTE	320:180	325:175	327:173	323:177
RATIO	1.78:1.00	1.86:1.00	1.89:1.00	1.82:1.00

Group 3

Mid-Dose: 2.0 mg base/kg/day

ANIMAL NO.	7502	7506	7514	7576
ABSOLUTE	307:193	310:190	312:188	314:186
RATIO	1.59:1.00	1.63:1.00	1.66:1.00	1.69:1.00

Group 4

High-Dose: 6.0 mg base/kg/day

ANIMAL NO.	7508	7509	7518	7524
ABSOLUTE	304:196	306:194	301:199	311:189
RATIO	1.55:1.00	1.58:1.00	1.51:1.00	1.65:1.00

**BONE MARROW M:E RATIO DATA**

Group 1

Vehicle Control: 0 mg base/kg/day

ANIMAL NO.	7542	7555	7558	7573
ABSOLUTE	328:172	326:174	324:176	317:183
RATIO	1.91:1.00	1.87:1.00	1.84:1.00	1.73:1.00

DRAFT

Group 2

Low-Dose: 0.1 mg base/kg/day

ANIMAL NO.	7550	7560	7567	7569
ABSOLUTE	316:184	329:171	324:176	315:185
RATIO	1.72:1.00	1.92:1.00	1.84:1.00	1.70:1.00

Group 3

Mid-Dose: 2.0 mg base/kg/day

ANIMAL NO.	7556	7564	7572	7574
ABSOLUTE	309:191	316:184	314:186	305:195
RATIO	1.62:1.00	1.72:1.00	1.69:1.00	1.56:1.00

Group 4

High-Dose: 6.0 mg base/kg/day

ANIMAL NO.	7544	7546	7551	7568
ABSOLUTE	313:187	302:198	305:195	300:200
RATIO	1.67:1.00	1.53:1.00	1.56:1.00	1.50:1.00

**BONE MARROW M:E RATIO DATA**

Group 1

Vehicle Control: 0 mg base/kg/day

ANIMAL NO.	7512	7515	7531	7532
ABSOLUTE	316:184	319:181	324:176	315:185
RATIO	1.72:1.00	1.76:1.00	1.84:1.00	1.70:1.00

DRAFT

Group 2

Low-Dose: 0.1 mg base/kg/day

ANIMAL NO.	7519	7527	7529	7536
ABSOLUTE	312:188	323:177	317:183	324:176
RATIO	1.66:1.00	1.82:1.00	1.73:1.00	1.84:1.00

Group 3

Mid-Dose: 2.0 mg base/kg/day

ANIMAL NO.	7510	7516	7522	7538
ABSOLUTE	315:185	322:178	318:182	316:184
RATIO	1.70:1.00	1.81:1.00	1.75:1.00	1.72:1.00

Group 4

High-Dose: 6.0 mg base/kg/day

ANIMAL NO.	7507	7511	7530	7535
ABSOLUTE	313:187	320:180	324:176	319:181
RATIO	1.67:1.00	1.78:1.00	1.84:1.00	1.76:1.00

**BONE MARROW M:E RATIO DATA**

Group 1

Vehicle Control: 0 mg base/kg/day

ANIMAL NO.	7541	7549	7557	7566
ABSOLUTE	320:180	322:178	318:182	325:175
RATIO	1.78:1.00	1.81:1.00	1.75:1.00	1.86:1.00

DRAFT

Group 2

Low-Dose: 0.1 mg base/kg/day

ANIMAL NO.	7543	7545	7552	7553
ABSOLUTE	327:173	319:181	321:179	323:177
RATIO	1.89:1.00	1.76:1.00	1.79:1.00	1.82:1.00

Group 3

Mid-Dose: 2.0 mg base/kg/day

ANIMAL NO.	7548	7561	7562	7571
ABSOLUTE	317:183	328:172	316:184	322:178
RATIO	1.73:1.00	1.91:1.00	1.72:1.00	1.81:1.00

Group 4

High-Dose: 6.0 mg base/kg/day

ANIMAL NO.	7539	7540	7554	7563
ABSOLUTE	319:181	328:172	325:175	318:182
RATIO	1.76:1.00	1.91:1.00	1.86:1.00	1.75:1.00

V. Quality Assurance Statement

DRAFT



# Pathology Associates, Inc.

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

# DRAFT

## QUALITY ASSURANCE STATEMENT

This bone marrow 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. Results of these activities indicate that the portions of the study performed by PAI conformed with GLP regulations and applicable Standard Operating Procedures. The bone marrow evaluation 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.

<u>Date of Inspection</u>	<u>Phase Inspected</u>	<u>Date Findings Reported to Management/ Study Pathologist</u>
08/03/93	Individual Animal Data	08/03/93
08/03/93	Summary Data	08/03/93
08/03/93	Draft Bone Marrow Evaluation Report	08/03/93

J. Hawk  
Quality Assurance Specialist

August 12, 1993  
Date

Bone Marrow Evaluation Report  
Study No. 097  
Thirteen Week Oral Toxicity Study Of WR 238605 With A Thirteen Week Recovery Period in Dogs

DRAFT

APPENDIX 13  
Protocol and Protocol Amendments

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN DOGS

D R A F T

1.0 PURPOSE OF THE STUDY:

The purpose of this study is to determine specific target organ toxicity, dose-response relationships, and a no adverse effect level of WR 238605 in Beagle dogs following thirteen weeks of daily oral administration. In addition, the reversibility of these toxic effects over a 90-day recovery period will be assessed. This study will be conducted in accordance with the specifications of the Sponsor as described in Task Order UIC-5. The protocol for this study was approved by the UIC Animal Care Committee.

2.0 SPONSOR:

- 2.1 Name: U.S. Army Medical Research  
and Development Command
- 2.2 Address: Fort Detrick  
Frederick, MD 21702-5009
- 2.3 Representative: George 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  
P. O. Box 6998  
Chicago, IL 60680
- 3.3 Study Director: Barry S. Levine, D.Sc., D.A.B.T.

4.0 DATES:

- 4.1 Study Initiation Date  
(see 11.0; Protocol Approval): 9/1/92
- 4.2 Proposed Initiation of Dosing: 12/10/92
- 4.3 Proposed Necropsy Dates: 3/11/12/93; 6/10,11/93
- 4.4 Proposed Study Completion Date  
(Draft Study Report): 10/15/93

5.0 TEST ARTICLE

- 5.1 Name or Code No: WR 238605 Succinate

DRAFT

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:

Study Director	Barry S. Levine, D.Sc., D.A.B.T.
Toxicologist	E. Marianna Furedi-Machacek, D.V.M.
Pathologist	Michael J. Tomlinson, D.V.M., Ph.D., D.A.C.V.P.
Clinical Veterinarian	Terry Hewett, D.V.M.
Veterinarian Support	Documented in raw data
Clinical Laboratory	Maria Lang, A.H.T., C.V.T.
Ophthalmologist	Samuel J. Vainisi D.V.M., D.A.V.C.O.
Cardiologist	Robert Hamlin, D.V.M., Ph.D., D.A.C.V.I.M.
Tox. Lab Supervisor	Soudabeh Soura, B.S.
Technician	Nancy Dinger, B.S.
Quality Assurance	Ronald C. Schoenbeck

7.0 TEST SYSTEM:

7.1 Species: Dog

7.2 Strain: Beagle

7.3 Sex(s)/Number: 32 Males & 32 Females

7.4 Age of Animals: Approximately 7 - 8 months old upon initiation of treatment.

7.5 Weight of Animals: Approximately 10 - 12 kg (males) and ≈ 8 - 10 kg (females) upon initiation of treatment.

REVISED PAGE	INITIAL: <i>BL</i>
STUDY NO: 097	DATE: 5/16/97

DRAFT

- 7.6 Source of Animals: Marshall Farms, North Rose, NY.
- 7.7 Justification for Selection of Test System: The dog is a standard and accepted non-rodent species for regulatory toxicology studies, and is specified by the Sponsor.
- 7.8 Procedure for Unique Identification of Test System: Upon arrival each animal will be given a facility unique number. This number will appear as an ear tattoo and a neck collar tag and will also appear on a cage card visible on the front of each run. The cage card will additionally contain the study number, test article identification, treatment group number 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 runs in a temperature ( $72 \pm 6^\circ\text{F}$ ) and humidity (approx.  $50 \pm 20\%$ ) controlled room with a 12 hour light/12 hour dark cycle. A few dogs may be housed two/run (within sex) during the quarantine/pretest period. The run size, 15 square feet, is adequate to house dogs at the upper weight range as described in the Guide for the Care and Use of Laboratory Animals, DHEW (NIH) No. 86.23. All runs will be cleaned and fresh bedding replaced daily. The runs will be sanitized once every two weeks.
- 7.10 Quarantine Procedure: Animals will be quarantined for approximately three 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, Toxicologist or Clinical Veterinarian. Body weights and physical examinations will be done upon the dogs' arrival at the animal facility. Additionally, each dog will be lightly sprayed upon arrival with PARA PYRETHRIN MIST for fleas, lice, and ticks. Within a few days of arrival, hematology (to include methemoglobin level determination) and clinical chemistry tests, and fecal examination for internal parasites will be performed. If parasites are found, the affected animal will be treated with a vermifuge approved by the Sponsor, and at least 10 days and a negative fecal examination will elapse before the animal is used on a study. All dogs will have been vaccinated against canine distemper, infectious canine hepatitis, leptospirosis, parainfluenza, parvo, oral papilloma, and rabies by the animal supplier. Animals will be examined during quarantine and approved for use by the Clinical Veterinarian prior to being placed on test. Any sickly animal will be eliminated from 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 treatment under the direction of the Study Director or Toxicologist. Quarantine release will be documented on the Clinical Veterinarian Log by the veterinarian prior to study initiation.
- 7.11 Food: Purina Certified Canine Diet No. 5007 (Ralston Purina Company, St. Louis, MO), approximately 400 g, will be provided daily from arrival until termination. Exactly 400 g will be provided when food consumption is measured. The food will be removed for an

overnight fast ( $\approx$  16 - 20 hours) prior to blood collection or scheduled sacrifice.

- 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 untreated 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 bi-monthly comprehensive chemical analyses of Chicago water are documented in files maintained by Quality Assurance.

## 8.0 EXPERIMENTAL DESIGN:

### 8.1 Treatment Groups:

Treatment Group	Dose Level (mg base/kg/day)	Number of Males	Number of Females
1	0	4 + 4*	4 + 4*
2	0.1	4 + 4*	4 + 4*
3	2.0	4 + 4*	4 + 4*
4	6.0	4 + 4*	4 + 4*

\*Recovery Animals

Dose levels were selected by the Sponsor based upon the results of an earlier 28-day gavage study in the dog (UIC/TRL Study No. 047).

Four animals/sex/group will be necropsied in Week 14. The remaining animals will be held for a thirteen week recovery period, at which time they will be necropsied.

- 8.2 Frequency and Route of Administration of the Test Article: The test article will be administered once daily by gastric intubation starting with Day 0 for at least 13 weeks. Control animals will receive the vehicle (aqueous 1% methylcellulose/0.4% Tween 80). The animals will be acclimated to the gavage procedure for at least three days prior to Day 0. Following dosing, the test article or vehicle alone will be flushed from the catheter with approximately 20 ml distilled water. The quantity of the test article (mg/kg) will be adjusted weekly, based on each animal's most recent body weight. The animals to be sacrificed after the 13 week treatment period will be dosed up to and including the day prior to scheduled necropsy on Days 91 and 92. The recovery animals will be dosed for 91 days. Dosing volume will be 1 ml/kg, and the actual volume (ml) administered will be documented in the raw data.

- 8.3 Justification of Route(s): Oral treatment is the intended clinical route and is specified by the Sponsor.

- 8.4 Procedure to Control Bias during the Assignment of Animals to Treatment Groups: The animals will be randomized using a restricted randomization procedure, stratified by body weight. Baseline data

DRAFT

Contract No.: DAMD17-92-C-2001  
Task Order No.: UIC-5A  
Study No.: 097

including clinical pathology, ophthalmology, and ECG data will be used to select appropriate animals for randomization.

- 8.5 Test Article Vehicle: Aqueous 1% methylcellulose/0.4% Tween 80. Both chemicals will be obtained from Sigma. If another source is used, it will be identified in the raw data.
- 8.6 Test Article Dosage Form Preparation and Analyses: The test article dosing suspensions will be prepared every two weeks based on stability data from a previously conducted dog toxicity study by gastric intubation (UIC/TRL Study No. 047). WR 238605 dosage formulations were previously shown to be homogeneous in that study. The test article will be suspended in the vehicle to result in concentrations necessary to administer the dosage formulations at a volume of 1 ml/kg. The specific volume (ml) administered will be calculated on the basis of each animal's most recent body weight. Samples of all dosage formulations used in Weeks 1 & 2, 7 & 8 and 13 will be analyzed for test article concentration prior to their use. Only samples within 10% of their target concentration will be used.
- 8.7 Type and Frequency of Observations, Tests, Analyses and Measurements:
- 8.7.1 Clinical Signs: All animals will be observed once daily for clinical signs of toxicity approximately 1 - 2 hours after dosing. Additionally, all animals will be observed for moribundity/mortality in the afternoon and immediately prior to dosing in the morning. During the recovery period, clinical signs will be recorded once daily in the morning.
- 8.7.2 Clinical Observations: All animals will be subjected to a physical examination including examination of eyes and all orifices in Week -2/-1, on Day 0, and weekly thereafter.
- 8.7.3 Body Weight: Body weights of all animals will be recorded at test animal selection in the quarantine/pretest period, weekly during the treatment and recovery periods, and at scheduled necropsy.
- 8.7.4 Food Consumption: Food consumption for all animals will be measured over an approximate 24 hour period twice during the quarantine/pretest period, and weekly during the treatment and recovery periods.
- 8.7.5 Ophthalmologic Examinations: All dogs will be examined by indirect ophthalmoscopy prior to study initiation and during Week 13, and in Week 26 for the recovery animals.
- 8.7.6 Clinical Pathology: Hematology and clinical chemistry parameters will be measured within one week of arrival (Week -3), and in Weeks -1, 2, 4, 8, and 13. Hematology and clinical chemistry tests will also be performed for the

# DRAFT

Contract No.: DAMD17-92-C-2001  
Task Order No.: UIC-5A  
Study No.: 097

recovery animals in Weeks 18 and Week 26. The overnight fasted animals will be unanesthetized and sufficient blood will be collected from the cephalic vein to measure the following parameters in random order. Water will be available *ad libitum* during all fasting periods.

## Hematology

<sup>a</sup> Erythrocyte count and morphology	Mean cell volume (MCV)
Hematocrit	Mean cell hemoglobin (MCH)
Hemoglobin	Mean cell hemoglobin concentration (MCHC)
Leukocyte count, total and differential	Activated partial thromboplastin time
Platelet count	Prothrombin time
Reticulocyte count	<sup>b</sup> Methemoglobin
Heinz bodies	

<sup>a</sup> Includes nucleated RBCs.

<sup>b</sup> To be measured with a Co-oximeter (Instrumentation Laboratory, Model No. 282). 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/SGPT)	Gamma glutamyl transferase
Albumin	Globulin (calculated)
Albumin/globulin ratio (calculated)	Glucose
Alkaline phosphatase	Haptoglobin
Aspartate aminotransferase (AST/SGOT)	Lactate dehydrogenase (LDH)
Calcium	Inorganic phosphorus
Chloride	Potassium
Cholesterol	Sodium
Creatinine	Total bilirubin
Creatine kinase (CK)	Total protein
	Triglycerides
	Urea nitrogen (BUN)

Urine specimens will be collected in Week -1, and in Weeks 2, 4, 8 and 13, and during the recovery period in Weeks 18, and 26. The following parameters will be measured.

## Urinalysis

Qualitative Bilirubin	Nitrite
Glucose	pH
Ketones	Protein
Occult Blood	Urobilinogen
Leukocytes	

DRAFT

Contract No.: DAMD17-92-C-2001  
Task Order No.: UIC-5A  
Study No.: 097

Color  
Specific Gravity  
Microscopic examination of spun sediment

- 8.7.7 Plasma Drug Levels: Sufficient blood will be collected to provide approximately 1 ml of plasma for drug level measurements at the following times: Weeks -1, 4, 8, 13, 18 and 26. The plasma samples will be sent to Dr. Emil Lin as specified by the Sponsor, and the results will not be included in the study report.
- 8.7.8 Electrocardiography: ECG tracings will be collected from all dogs in the quarantine/pretest period and in Week 13, and in Week 26 for the recovery animals. The following leads will be measured: I, aV<sub>F</sub> and V<sub>3</sub>. Heart rate, and PQ and QRST intervals will be measured from Lead I.
- 8.7.9 Pathology: All animals which die on test or sacrificed if moribund will be necropsied. Four animals/sex/group will be sacrificed and necropsied in random order over a two consecutive day period (Days 91 and 92). The remaining recovery animals will be sacrificed and necropsied in random order at the onset of Week 27, after a thirteen week recovery period. This will be accomplished by sodium pentobarbital anesthesia and exsanguination. 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 to include the external surface, all orifices, the cranial cavity, external surface of the brain, cross section of the spinal cord, the nasal cavity and nasal turbinates, thoracic, abdominal and pelvic cavities and their viscera, and cervical tissues and organs. The following tissues and organs will be collected and fixed in 10% neutral buffered formalin (NBF).

REVISED PAGE
STUDY NO: 097 INITIAL: BLZ
DATE: 11/30/92

# DRAFT

Contract No.: DAMD17-92-C-2001  
Task Order No.: UIC-5A  
Study No.: 097

*Adrenal glands	Muscle, skeletal
Aorta (thoracic)	*Ovaries
*Brain	Pancreas
(fore-, mid-, and hind-)	Pituitary
Cecum	Prostate
Colon	Rib with costochondral junction
Diaphragm	Rib with Marrow
Duodenum	Salivary gland (mandibular)
Esophagus	Sciatic Nerve
Eyes and optic nerve	Skin
*Heart	Spinal cord (thoracic)
Gallbladder	*Spleen
Gross lesions	Stomach
Ileum	*Testes with epididymides
Jejunum	Thymus
*Kidneys	*Thyroid gland with parathyroids
*Liver (with gallbladder drained)	Tongue
Lungs/Bronchi	Tonsil
Lymph node (submandibular and mesenteric)	Trachea
Mammary gland	Ureter
	Urinary bladder
	*Uterus

\*Weighed at scheduled necropsy. Paired organs will be weighed as a unit.

## Histopathology requirements:

The above tissues from all dogs found dead, sacrificed either *in extremis* or at scheduled necropsy in Week 14 will be embedded in paraffin, sectioned, stained with hematoxylin and eosin, and examined microscopically. Those tissues/organs for which treatment-related lesions were observed will be examined microscopically for all recovery animals.

Bone marrow (rib) smears will be prepared for all animals at their scheduled necropsy. Myeloid:erythroid (M:E) ratios will be determined for all animals necropsied in Week 14. If treatment-related changes are seen, M:E ratios will be determined for all recovery animals.

8.7.10 Statistical Analyses: For each sex, Analysis of Variance tests will be conducted on body weight, ECG measurements, hematology, clinical chemistry and organ weight data. Organ weight analyses will include absolute weights, weights relative to body weight, and weights relative to brain weight. If a significant F ratio is obtained ( $p \leq 0.05$ ), Dunnett's t test will be used for pairwise comparisons to the control group. Food consumption data will be analyzed by the Kruskal-Wallis test ( $p \leq 0.05$ ). If a significant effect is seen, the Mann-Whitney U test will be used for pairwise comparisons to the control group.

DRAFT

Contract No.: DAMD17-92-C-2001  
Task Order No.: UIC-5A  
Study No.: 097

Frequency data such as incidence of mortality, gross necropsy observations and tissue morphology observations will be compared by Fishers Exact Test or Chi-square analyses as necessary. Quantitative data will be tabulated and presented in the report. In addition to the written report, summary data tables of parameters and variability will be transmitted to the Sponsor on magnetic media (computer diskette) in "ASCII" form. The transcribed data on disk will no longer be considered GLP compliant.

9.0 RECORDS TO BE MAINTAINED:

All data generated during the conduct of the 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 data 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 a 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.

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)? Food and Drug Administration

Does the Sponsor request that test article samples be returned? Yes

Does the Sponsor request that samples of the test article/carrier mixture(s) be returned? No

DRAFT

Contract No.: DAMD17-92-C-2001  
Task Order No.: UIC-5A  
Study No.: 097

11.0 PROTOCOL APPROVAL:

<u>STUDY DIRECTOR:</u>	<u>Barry S. Levine</u> Barry S. Levine, D.Sc. D.A.B.T.	<u>9/1/92</u> Date
<u>QUALITY ASSURANCE:</u>	<u>Ronald Schoenbeck</u> Ronald Schoenbeck	<u>9/1/92</u> Date
<u>SPONSOR APPROVAL:</u>	<u>George Schieferstein</u> George Schieferstein, Ph.D. Contracting Officer's Representative (COR)	<u>9/2/92</u> Date

COMMENTS FROM THE COR:

DRAFT

Protocol Amendment

Study No.: 097

Title: Thirteen Week Oral Toxicity Study of WR238605 with a Thirteen Week Recovery Period in Dogs

1. Page 4 Section 8.2

Change dosing volume in the last sentence of the paragraph from 0.5 ml/kg to 1 ml/kg.

Reason: Mistake in protocol.


2. Page 5 Section 8.6

Change dosing volume in the eighth line from 5 ml/kg to 1 ml/kg.

Reason: Mistake in protocol.

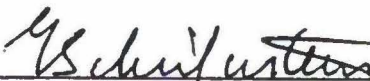
Approvals:

STUDY DIRECTOR:

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

9/23/92  
Date

SPONSOR APPROVAL:

  
\_\_\_\_\_  
George Schieferstein, Ph.D.  
Contracting Officer's  
Representative (COR)

9/24/92  
Date

Protocol Amendment

Study No.: 097

Title: Thirteen Week Oral Toxicity Study of WR238605 with a Thirteen Week Recovery Period in Dogs

3. Page 4 Section 8.2

Add the following sentences after the second sentence:

"The animals will be acclimated to the gavage procedure for at least three days prior to Day 0. Following dosing, the test article or vehicle alone will be flushed from the catheter with approximately 20 ml distilled water."

Reason: Clarification of procedures.

4. Page 5 Section 8.7.2

Change "Week -1" to "Week -2/-1".

Reason: Clarification of procedures.

5. Pages 5 & 6 Section 8.7.6

Remove the following blood sampling periods for clinical pathology measurements:

during the latter half of Week 1  
Week 6  
Week 10  
Week 22

Also remove the following urine sampling period:

Week 22

Reason: Sponsor request.

6. Page 7 Section 8.7.7

Remove the following blood sampling period for plasma drug levels:

Week 22

Reason: Sponsor request.

DRAFT

Protocol Amendment

Study No.: 097

Title: Thirteen Week Oral Toxicity Study of WR238605 with a Thirteen Week Recovery Period in Dogs

7. Page 8 Section 8.7.9

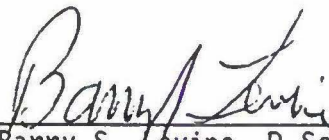
Add the following to the tissue list:

"Rib with marrow"

Reason: Inadvertently left off protocol.

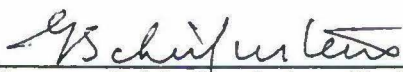
Approvals:

STUDY DIRECTOR:

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

11/30/92  
Date

SPONSOR APPROVAL:

  
George Schieferstein, Ph.D.  
Contracting Officer's  
Representative (COR)

12-8-92  
Date

DRAFT

Protocol Amendment

Study No.: 097

Title: Thirteen Week Oral Toxicity Study of WR238605 with a Thirteen Week Recovery Period in Dogs

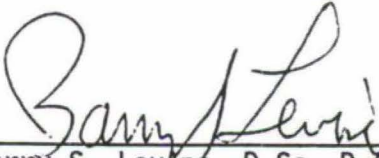
8. Page 2 Section 5.3

Change "White powder" to "Pale yellow powder"

Reason: Mistake in the protocol

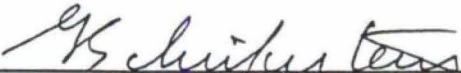
Approvals:

STUDY DIRECTOR:

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

5/5/93  
Date

SPONSOR APPROVAL:

  
\_\_\_\_\_  
George Schieferstein, Ph.D.  
Contracting Officer's  
Representative (COR)

5/25/93  
Date

(ENCL)

DRAFT

APPENDIX 14  
Study Deviations

THIRTEEN WEEK ORAL TOXICITY STUDY OF  
WR238605 WITH A THIRTEEN WEEK  
RECOVERY PERIOD IN DOGS

DRAFT

Study Deviations\*

<u>Deviation Type</u>	<u>Specific Deviation</u>	<u>Effect on Study</u>
Protocol	On several occasions the temperature and/or relative humidity deviated outside the specified range in the animal room(s.) The temperature and humidity deviations ranged from -0 to +2°F and -5 to +2%, respectively, outside the specified ranges.	None. These sporadic occurrences were not considered to have had an impact on the outcome of the study.
Protocol	Sponsor has requested that the PQ interval be reported as the PR interval and that the QRST interval be reported as the QT interval.	None. These are acceptable interval designations.
Protocol	The following tissues sections were not examined microscopically. Mammary gland was not present in sections from six animals (#7524, #7533, #7555, #7564, #7572 and #7573). The following tissues were missing from one animal each at trimming: thyroid-parathyroid gland (#7521); urinary bladder and prostate (#7502); skin/mammary gland (#7509); aorta (#7542); and pituitary gland (#7546).	None. No test article-related changes were detected in corresponding tissues in other animals.

\*The detailed "Deviation Reports" are contained in the raw data which are archive at the University of Illinois at Chicago, Department of Pharmacology, Chicago, Illinois.

The above deviations did not affect the integrity of the study.

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

\_\_\_\_\_  
Date