

# Toxicology Research Laboratory

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**UIC** The University of Illinois  
at Chicago

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

20100915237

Contract No.: DAMD17-92-C2001  
Task Order No.: UIC-5B  
UIC/TRL Study No.: 098

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Title Page

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Volume 3 of 3

Draft Report for Task Order No. UIC-5B  
THIRTEEN WEEK ORAL TOXICITY STUDY  
OF WR238605 WITH A THIRTEEN WEEK  
RECOVERY PERIOD IN RATS

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 18, 1993

Performing Laboratory

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

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## REPORT DOCUMENTATION PAGE

Form Approved  
OMB No. 0704-0188

1a. REPORT SECURITY CLASSIFICATION			1b. RESTRICTIVE MARKINGS				
2a. SECURITY CLASSIFICATION AUTHORITY Unclassified			3. DISTRIBUTION / AVAILABILITY OF REPORT				
2b. DECLASSIFICATION / DOWNGRADING SCHEDULE			Unlimited				
4. PERFORMING ORGANIZATION REPORT NUMBER(S)  UIC-5 (UIC/TRL Study No. 098)			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) ATIN: 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.	PROJECT NO.	TASK NO.	WORK UNIT ACCESSION NO.
			63807A	30463807	QC	073	
11. TITLE (Include Security Classification) THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS							
12. PERSONAL AUTHOR(S) Levine, Barry S.; Tomlinson, Michael J. (Pathology Associates, Inc.)							
13a. TYPE OF REPORT DRAFT		13b. TIME COVERED FROM 9/1/92 TO		14. DATE OF REPORT (Year, Month, Day)		15. PAGE COUNT	
16. SUPPLEMENTARY NOTATION							
17. COSATI CODES			18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)				
FIELD	GROUP	SUB-GROUP	WR 238605		Hemolytic anemia		
			Toxicology		Antimalarial		
19. ABSTRACT (Continue on reverse if necessary and identify by block number)							
<p>This study evaluated the toxicity of WR238605 in rats 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), 0.5, 6 and 18 mg base/kg/day. The primary toxic affects were seen in the RBCs, lungs, and liver. Significant methemoglobin production was observed in mid and high dose animals, but was reversible. Microscopic lesions in the spleen, kidney, and bone marrow were secondary to mild hemolytic anemia. Toxicity again was limited to the two highest dose levels. Decreased food consumption, decreased body weight gains, methemoglobin production and mild anemia were observed at the mid and high dose levels, but were readily reversible after treatment cessation. Increases in serum ALT, AST, and/or LDH and decreased A/G ratios in high dose animals and possibly mid dose males suggested mild hepatotoxicity, however histopathologic lesions were not seen. Leukocytosis possibly secondary to stress and consisting of increased number of lymphocytes, mature neutrophils, and/or monocytes was seen in the treatment period at the two highest dose levels and was reversible after cessation of treatment. Because the aforementioned toxic responses were limited to mid and high dose animals, a no-adverse effect level of WR238605 was assessed to be 0.5 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		

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Contract No.: DAMD17-92-C2001  
Task Order No.: UIC-5B  
UIC/TRL Study No.: 098

VOLUME 3

APPENDICES (Contd.)

7	Individual Hematology Data .....	7-1
8	Ophthalmology Report .....	8-1
9	Individual Organ Weights .....	9-1
10	Pathology Report .....	10-1
11	Pre-test Clinical Pathology Data .....	11-1
12	Protocol and Protocol Amendments .....	12-1
13	Study Deviations .....	13-1

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APPENDIX 7

Individual Hematology Data

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

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Erythrocytes

STUDY ID: 098  
ABBR: RBC

SEX: MALE  
UNITS: 10<sup>6</sup>/cm<sup>3</sup>

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
801	7.64	7.98	8.57	8.56	8.42	9.04	8.40
802	7.47	8.08	8.47	8.48	8.49	8.68	8.83
803	--	--	--	--	--	--	--
804	--	--	--	--	--	--	--
805	--	--	--	--	--	--	--
806	7.89	8.28	8.49	8.39	8.73	9.09	8.90
807	7.34	7.75	8.28	8.34	8.14	8.33	8.32
808	--	--	--	--	--	--	--
809	7.56	8.02	8.07	8.61	8.13	8.43	8.23
810	6.68	7.00	7.58	8.04	7.84	8.68	7.22
811	7.04	7.78	7.84	8.15	8.94	8.80	8.22
812	--	--	--	7.77	--	--	--
813	--	--	--	--	--	--	--
814	7.43	7.56	8.32	7.94	7.84	8.44	8.27
815	6.77	7.19	7.65	7.28	7.89	7.71	7.83
816	7.16	7.13	7.64	7.66	7.54	8.28	7.68
817	--	--	--	--	--	--	--
818	--	--	--	--	--	--	--
819	--	--	--	--	--	--	--
820	--	--	--	--	--	--	--
MEAN	7.30	7.68	8.09	8.11	8.20	8.55	8.19
SD	0.385	0.442	0.386	0.420	0.442	0.406	0.507
N	10	10	10	11	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
841	--	--	--	--	--	--	--
842	--	--	--	--	--	--	--
843	--	--	--	--	--	--	--
844	7.32	8.13	8.20	8.68	8.06	8.28	8.55
845	--	--	--	--	--	--	--
846	7.47	7.61	8.00	8.28	7.80	8.30	8.27
847	--	--	--	--	--	--	--
848	7.27	7.40	8.23	8.65	8.21	8.56	8.65
849	--	--	--	--	--	--	--
850	7.69	8.29	8.27	8.57	8.00	9.19	8.64
851	7.07	7.64	8.15	6.61	7.89	8.15	8.15
852	7.30	7.30	7.83	7.79	7.76	7.92	7.92
853	6.79	7.05	8.15	8.15	8.20	8.64	8.35
854	--	--	--	--	--	--	--
855	--	--	--	--	--	--	--
856	--	--	--	--	--	--	--
857	--	--	--	--	--	--	--
858	7.21	7.71	8.20	8.51	8.09	8.83	8.42
859	7.28	7.54	8.50	8.21	8.09	8.05	7.98
860	6.71	6.68	7.55	7.84	7.85	7.93	7.79
MEAN	7.21	7.54	8.11	8.13	8.00	8.39	8.27
SD	0.293	0.473	0.262	0.619	0.162	0.415	0.305
N	10	10	10	10	10	10	10

(--)-Data Unavailable

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

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Erythrocytes

STUDY ID: 098  
ABBR: RBC

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
881	--	--	--	--	--	--	--
882	--	--	--	--	--	--	--
883	--	--	--	--	--	--	--
884	7.21	7.36	7.92	8.61	8.23	8.78	7.68
885	--	--	--	--	--	--	--
886	--	--	--	--	--	--	--
887	7.26	7.35	7.64	--	7.85	9.52	8.33
888	--	--	--	--	--	--	--
889	6.97	7.40	7.59	7.78	8.01	9.11	8.68
890	6.95	7.26	7.84	7.34	7.97	9.09	8.56
891	--	--	--	--	--	--	--
892	--	--	--	--	--	--	--
893	7.14	6.94	7.40	7.95	6.71	8.75	8.87
894	--	--	--	--	--	--	--
895	6.47	7.06	7.72	8.35	8.11	9.11	8.15
896	7.75	7.40	8.21	8.55	8.61	8.97	8.83
897	7.21	7.18	8.20	8.00	8.40	8.19	8.54
898	--	--	--	--	--	--	--
899	8.29	7.82	7.21	7.66	8.02	8.57	8.46
900	6.94	7.20	8.04	7.75	8.82	9.32	8.39
MEAN	7.22	7.30	7.78	8.00	8.07	8.94	8.45
SD	0.496	0.238	0.330	0.427	0.568	0.383	0.349
N	10	10	10	9	10	10	10

GROUP: 18.0:18.0 mg base/kg/day							
921	--	--	--	--	--	--	--
922	--	--	--	7.72	8.54	8.71	8.85
923	6.23	7.20	7.50	8.37	8.02	8.98	8.43
924	--	--	--	--	--	--	--
925	--	--	--	--	--	--	--
926	--	--	--	--	--	--	--
927	7.35	7.23	8.49	7.82	8.29	8.96	8.20
928	--	--	--	--	--	--	--
929	7.20	8.33	8.07	8.04	8.25	9.36	9.16
930	5.92	6.25	7.41	8.18	7.94	8.51	7.87
931	--	--	--	--	--	--	--
932	--	7.01	7.55	8.01	7.42	8.36	8.50
933	6.32	7.15	7.95	7.99	8.75	9.90	9.33
934	6.44	7.12	7.98	--	--	--	--
935	6.02	7.16	7.18	7.45	7.56	8.41	7.66
936	--	--	--	--	--	--	--
937	7.30	--	--	--	--	--	--
938	--	--	--	--	--	--	--
939	6.25	7.00	7.95	7.26	7.11	8.04	7.92
940	6.51	7.15	7.54	7.73	7.63	8.65	8.30
MEAN	6.56	7.16	7.76	7.86	7.95	8.79	8.42
SD	0.533	0.500	0.390	0.333	0.521	0.539	0.554
N	10	10	10	10	10	10	10

(--)-Data Unavailable

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

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Hemoglobin

STUDY ID: 098  
ABBR: THGB

SEX: MALE  
UNITS: g/dL

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
881	--	--	--	--	--	--	--
882	--	--	--	--	--	--	--
883	--	--	--	--	--	--	--
884	14.9	14.7	15.0	16.2	15.5	15.8	14.5
885	--	--	--	--	--	--	--
886	--	--	--	--	--	--	--
887	15.3	15.6	15.5	--	15.4	17.6	16.2
888	--	--	--	--	--	--	--
889	15.1	15.6	14.9	15.3	15.2	16.6	15.9
890	14.8	15.2	15.2	14.5	14.9	16.2	15.6
891	--	--	--	--	--	--	--
892	--	--	--	--	--	--	--
893	15.4	14.9	14.6	15.4	14.2	16.1	16.3
894	--	--	--	--	--	--	--
895	14.2	14.5	14.8	15.3	14.8	16.1	14.8
896	16.0	15.4	16.0	16.2	16.4	17.1	16.5
897	15.5	14.8	15.8	14.8	15.7	14.7	15.7
898	--	--	--	--	--	--	--
899	17.0	16.4	14.5	15.1	15.6	15.5	16.0
900	15.5	16.0	16.0	14.8	16.8	16.6	16.0
MEAN	15.4	15.3	15.2	15.3	15.5	16.2	15.8
SD	0.75	0.61	0.56	0.59	0.76	0.82	0.64
N	10	10	10	9	10	10	10

GROUP: 18.0:18.0 mg base/kg/day							
921	--	--	--	--	--	--	--
922	--	--	--	14.6	16.1	15.8	16.0
923	13.8	14.9	13.7	14.8	14.9	16.5	16.0
924	--	--	--	--	--	--	--
925	--	--	--	--	--	--	--
926	--	--	--	--	--	--	--
927	14.9	14.2	15.2	13.8	15.4	15.9	15.1
928	--	--	--	--	--	--	--
929	14.2	15.4	13.6	13.9	14.9	16.8	16.8
930	12.9	13.1	14.8	15.1	15.6	15.9	15.2
931	--	--	--	--	--	--	--
932	--	14.1	15.4	15.4	15.2	16.0	16.0
933	12.5	13.8	13.9	13.1	14.6	16.2	16.0
934	14.3	15.3	15.4	--	--	--	--
935	13.2	14.9	13.5	14.5	15.0	16.3	15.5
936	--	--	--	--	--	--	--
937	14.5	--	--	--	--	--	--
938	--	--	--	--	--	--	--
939	13.2	14.3	14.9	13.3	14.1	15.2	15.0
940	13.1	13.6	14.0	13.3	13.8	15.3	15.2
MEAN	13.7	14.4	14.4	14.2	15.0	16.0	15.7
SD	0.79	0.75	0.77	0.81	0.68	0.50	0.57
N	10	10	10	10	10	10	10

(--)-Data Unavailable

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Hematocrit

STUDY ID: 098  
ABBR: HCT

SEX: MALE  
UNITS: %

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
801	44.4	45.5	45.2	42.5	42.4	44.9	41.0
802	44.9	47.6	46.2	42.9	43.6	43.7	44.2
803	--	--	--	--	--	--	--
804	--	--	--	--	--	--	--
805	--	--	--	--	--	--	--
806	46.6	47.3	44.6	42.5	45.4	45.8	45.1
807	46.0	47.7	48.1	47.1	47.0	48.0	46.8
808	--	--	--	--	--	--	--
809	46.3	47.8	45.1	46.3	44.6	45.3	44.6
810	40.8	41.4	40.3	40.7	40.6	43.9	35.6
811	42.9	46.1	43.0	43.0	47.7	45.8	42.3
812	--	--	--	40.4	--	--	--
813	--	--	--	--	--	--	--
814	47.4	46.6	49.2	45.7	45.6	48.4	46.6
815	43.6	45.2	44.1	40.5	43.9	42.2	41.9
816	43.8	42.7	42.6	41.3	40.8	43.4	39.6
817	--	--	--	--	--	--	--
818	--	--	--	--	--	--	--
819	--	--	--	--	--	--	--
820	--	--	--	--	--	--	--
MEAN	44.7	45.8	44.8	43.0	44.2	45.1	42.8
SD	1.99	2.19	2.61	2.38	2.40	1.97	3.45
N	10	10	10	11	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
841	--	--	--	--	--	--	--
842	--	--	--	--	--	--	--
843	--	--	--	--	--	--	--
844	44.5	47.0	44.2	45.5	43.7	44.2	44.5
845	--	--	--	--	--	--	--
846	46.0	46.0	45.2	45.5	43.0	45.4	44.4
847	--	--	--	--	--	--	--
848	47.2	46.6	49.2	50.1	47.9	49.2	49.1
849	--	--	--	--	--	--	--
850	45.4	48.0	45.8	45.2	43.1	47.9	44.8
851	43.6	45.9	46.5	36.5	43.2	44.3	44.2
852	46.0	45.0	44.8	43.4	43.1	42.9	42.6
853	41.6	43.1	45.9	44.3	44.8	46.2	43.9
854	--	--	--	--	--	--	--
855	--	--	--	--	--	--	--
856	--	--	--	--	--	--	--
857	--	--	--	--	--	--	--
858	43.5	45.4	45.3	45.2	43.0	46.4	43.1
859	43.0	43.1	45.8	43.6	43.6	43.1	42.0
860	42.2	40.5	42.8	42.5	43.1	42.6	41.2
MEAN	44.3	45.1	45.6	44.2	43.9	45.2	44.0
SD	1.82	2.24	1.65	3.39	1.53	2.21	2.15
N	10	10	10	10	10	10	10

(--)-Data Unavailable

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

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Hematocrit

STUDY ID: 098  
ABBR: HCT

SEX: MALE  
UNITS: %

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
881	--	--	--	--	--	--	--
882	--	--	--	--	--	--	--
883	--	--	--	--	--	--	--
884	42.2	41.1	42.4	44.4	43.5	44.2	39.8
885	--	--	--	--	--	--	--
886	--	--	--	--	--	--	--
887	43.8	44.4	42.2	--	43.0	49.4	44.1
888	--	--	--	--	--	--	--
889	42.2	43.4	41.7	41.9	42.9	46.5	45.0
890	42.6	43.1	43.0	38.8	41.7	45.4	43.0
891	--	--	--	--	--	--	--
892	--	--	--	--	--	--	--
893	44.3	42.7	42.0	42.9	36.6	44.6	44.8
894	--	--	--	--	--	--	--
895	41.3	42.1	42.2	43.4	42.3	45.6	41.2
896	47.1	44.1	45.5	45.3	46.7	47.4	47.3
897	44.1	42.6	44.6	41.2	43.9	40.9	43.2
898	--	--	--	--	--	--	--
899	49.6	47.5	43.0	41.1	44.6	43.8	44.6
900	44.0	44.5	44.8	41.8	47.4	48.0	43.5
MEAN	44.1	43.6	43.1	42.3	43.3	45.6	43.7
SD	2.51	1.75	1.34	1.95	2.97	2.42	2.08
N	10	10	10	9	10	10	10

GROUP: 18.0:18.0 mg base/kg/day							
921	--	--	--	--	--	--	--
922	--	--	--	40.7	44.8	43.6	44.6
923	38.9	43.3	39.7	41.9	42.7	47.1	44.8
924	--	--	--	--	--	--	--
925	--	--	--	--	--	--	--
926	--	--	--	--	--	--	--
927	43.1	41.0	43.7	39.3	43.0	44.4	41.7
928	--	--	--	--	--	--	--
929	41.6	44.9	40.3	39.6	42.5	47.5	47.0
930	37.4	38.9	42.0	43.3	45.0	44.6	42.5
931	--	--	--	--	--	--	--
932	--	42.2	43.9	45.5	43.2	44.2	44.7
933	36.0	39.5	38.2	36.8	40.7	45.3	43.9
934	39.5	42.9	43.4	--	--	--	--
935	38.2	43.2	39.6	40.1	43.4	45.0	42.9
936	--	--	--	--	--	--	--
937	42.6	--	--	--	--	--	--
938	--	--	--	--	--	--	--
939	38.0	41.2	42.5	39.0	38.7	41.5	41.3
940	36.8	40.7	40.0	38.4	39.8	42.4	42.2
MEAN	39.2	41.8	41.3	40.5	42.4	44.6	43.6
SD	2.46	1.86	2.02	2.53	2.05	1.85	1.76
N	10	10	10	10	10	10	10

(--)-Data Unavailable

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Mean Corpuscular Volume

STUDY ID: 098  
ABBR: MCV

SEX: MALE  
UNITS: fL

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
801	58.1	57.0	52.7	49.6	50.4	49.7	48.8
802	60.1	58.9	54.5	50.6	51.4	50.3	50.1
803	--	--	--	--	--	--	--
804	--	--	--	--	--	--	--
805	--	--	--	--	--	--	--
806	59.1	57.1	52.5	50.7	52.0	50.4	50.7
807	62.7	61.5	58.1	56.5	57.7	57.6	56.3
808	--	--	--	--	--	--	--
809	61.2	59.6	55.9	53.8	54.9	53.7	54.2
810	61.1	59.1	53.2	50.6	51.8	50.6	49.3
811	60.9	59.3	54.8	52.8	53.4	52.0	51.5
812	--	--	--	52.0	--	--	--
813	--	--	--	--	--	--	--
814	63.8	61.6	59.1	57.6	58.2	57.3	56.3
815	64.4	62.9	57.6	55.6	55.6	54.7	53.5
816	61.2	59.9	55.8	53.9	54.1	52.4	51.6
817	--	--	--	--	--	--	--
818	--	--	--	--	--	--	--
819	--	--	--	--	--	--	--
820	--	--	--	--	--	--	--
MEAN	61.3	59.7	55.4	53.1	54.0	52.9	52.2
SD	1.96	1.90	2.31	2.66	2.66	2.89	2.72
N	10	10	10	11	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
841	--	--	--	--	--	--	--
842	--	--	--	--	--	--	--
843	--	--	--	--	--	--	--
844	60.8	57.8	53.9	52.4	54.2	53.4	52.0
845	--	--	--	--	--	--	--
846	61.6	60.4	56.5	55.0	55.1	54.7	53.7
847	--	--	--	--	--	--	--
848	64.9	63.0	59.8	57.9	58.3	57.5	56.8
849	--	--	--	--	--	--	--
850	59.0	57.9	55.4	52.7	53.9	52.1	51.9
851	61.7	60.1	57.1	55.2	54.8	54.4	54.2
852	63.0	61.6	57.2	55.7	55.5	54.2	53.8
853	61.3	61.1	56.3	54.4	54.6	53.5	52.6
854	--	--	--	--	--	--	--
855	--	--	--	--	--	--	--
856	--	--	--	--	--	--	--
857	--	--	--	--	--	--	--
858	60.3	58.9	55.2	53.1	53.2	52.5	51.2
859	59.1	57.2	53.9	53.1	53.9	53.5	52.6
860	62.9	60.6	56.7	54.2	54.9	53.7	52.9
MEAN	61.5	59.9	56.2	54.4	54.8	54.0	53.2
SD	1.82	1.87	1.74	1.67	1.39	1.48	1.58
N	10	10	10	10	10	10	10

(--)-Data Unavailable

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

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Mean Corpuscular Volume

STUDY ID: 098  
ABBR: MCV

SEX: MALE  
UNITS: fL

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
881	--	--	--	--	--	--	--
882	--	--	--	--	--	--	--
883	--	--	--	--	--	--	--
884	58.5	55.8	53.5	51.6	52.9	50.3	51.8
885	--	--	--	--	--	--	--
886	--	--	--	--	--	--	--
887	60.3	60.4	55.2	--	54.8	51.9	52.9
888	--	--	--	--	--	--	--
889	60.5	58.6	54.9	53.9	53.6	51.0	51.8
890	61.3	59.4	54.8	52.9	52.3	49.9	50.2
891	--	--	--	--	--	--	--
892	--	--	--	--	--	--	--
893	62.0	61.5	56.8	54.0	54.5	51.0	50.5
894	--	--	--	--	--	--	--
895	63.8	59.6	54.7	52.0	52.2	50.1	50.6
896	60.8	59.6	55.4	53.0	54.2	52.8	53.6
897	61.2	59.3	54.4	51.5	52.3	49.9	50.6
898	--	--	--	--	--	--	--
899	59.8	60.7	59.6	53.7	55.6	51.1	52.7
900	63.4	61.8	55.7	53.9	53.7	51.5	51.8
MEAN	61.2	59.7	55.5	52.9	53.6	51.0	51.7
SD	1.60	1.69	1.68	1.02	1.18	0.94	1.16
N	10	10	10	9	10	10	10

GROUP: 18.0:18.0 mg base/kg/day							
921	--	--	--	--	--	--	--
922	--	--	--	52.7	52.5	50.1	50.4
923	62.4	60.1	52.9	50.1	53.2	52.4	53.1
924	--	--	--	--	--	--	--
925	--	--	--	--	--	--	--
926	--	--	--	--	--	--	--
927	58.6	56.7	51.5	50.3	51.9	49.6	50.9
928	--	--	--	--	--	--	--
929	57.8	53.9	49.9	49.3	51.5	50.7	51.3
930	63.2	62.2	56.7	52.9	56.7	52.4	54.0
931	--	--	--	--	--	--	--
932	--	60.2	58.1	56.8	58.2	52.9	52.6
933	57.0	55.2	48.1	46.1	46.5	45.8	47.1
934	61.3	60.3	54.4	--	--	--	--
935	63.5	60.3	55.2	53.8	57.4	53.5	56.0
936	--	--	--	--	--	--	--
937	58.4	--	--	--	--	--	--
938	--	--	--	--	--	--	--
939	60.7	58.9	53.5	53.7	54.4	51.6	52.1
940	56.5	56.9	53.1	49.7	52.2	49.0	50.8
MEAN	59.9	58.5	53.3	51.5	53.5	50.8	51.8
SD	2.60	2.66	3.01	3.02	3.44	2.30	2.38
N	10	10	10	10	10	10	10

(--)-Data Unavailable

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

**INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP**  
**TEST: Mean Corpuscular Hemoglobin**

STUDY ID: 098  
ABBR: TMCH

SEX: MALE  
UNITS: µg

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
801	20.5	19.9	19.0	18.0	18.5	17.8	17.6
802	21.0	20.9	20.1	18.5	18.7	18.1	17.8
803	--	--	--	--	--	--	--
804	--	--	--	--	--	--	--
805	--	--	--	--	--	--	--
806	20.9	20.4	19.1	18.8	18.8	18.6	18.0
807	22.2	21.9	21.3	21.0	21.5	20.6	20.6
808	--	--	--	--	--	--	--
809	21.6	21.1	21.3	19.5	20.3	19.6	19.8
810	21.4	21.0	19.1	18.4	18.8	18.0	20.1
811	21.6	21.0	19.9	19.8	19.0	18.6	19.1
812	--	--	--	21.0	--	--	--
813	--	--	--	--	--	--	--
814	21.4	20.8	20.9	20.2	21.4	19.7	19.6
815	22.7	22.7	20.7	20.6	20.5	19.8	19.3
816	21.1	21.7	20.0	19.8	19.6	18.7	19.1
817	--	--	--	--	--	--	--
818	--	--	--	--	--	--	--
819	--	--	--	--	--	--	--
820	--	--	--	--	--	--	--
MEAN	21.4	21.1	20.1	19.6	19.7	19.0	19.1
SD	0.64	0.79	0.89	1.06	1.14	0.92	1.01
N	10	10	10	11	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
841	--	--	--	--	--	--	--
842	--	--	--	--	--	--	--
843	--	--	--	--	--	--	--
844	21.2	20.0	19.4	19.2	19.5	19.2	18.7
845	--	--	--	--	--	--	--
846	21.4	21.2	21.0	19.8	20.4	18.8	19.6
847	--	--	--	--	--	--	--
848	21.9	21.9	21.5	20.6	20.6	20.1	19.8
849	--	--	--	--	--	--	--
850	21.2	20.3	20.1	19.0	19.5	18.6	18.9
851	21.5	21.5	20.5	11.8	19.9	19.8	20.1
852	21.6	21.6	21.1	20.3	20.1	19.8	19.7
853	20.8	21.1	20.1	19.4	19.5	19.0	18.7
854	--	--	--	--	--	--	--
855	--	--	--	--	--	--	--
856	--	--	--	--	--	--	--
857	--	--	--	--	--	--	--
858	21.6	20.6	20.0	19.2	19.7	18.8	18.3
859	20.9	20.3	19.4	19.6	19.4	19.3	19.0
860	22.1	21.4	21.1	20.0	20.1	19.3	19.6
MEAN	21.4	21.0	20.4	18.9	19.9	19.3	19.2
SD	0.41	0.65	0.74	2.54	0.42	0.50	0.59
N	10	10	10	10	10	10	10

(--)-Data Unavailable

DRAFT

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Mean Corpuscular Hemoglobin

STUDY ID: 098  
ABBR: TMCH

SEX: MALE  
UNITS: pg

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
881	--	--	--	--	--	--	--
882	--	--	--	--	--	--	--
883	--	--	--	--	--	--	--
884	20.7	20.0	18.9	18.8	18.8	18.0	18.9
885	--	--	--	--	--	--	--
886	--	--	--	--	--	--	--
887	21.1	21.2	20.3	--	19.6	18.5	19.4
888	--	--	--	--	--	--	--
889	21.7	21.1	19.6	19.7	19.0	18.2	18.3
890	21.3	20.9	19.4	19.8	18.7	17.8	18.2
891	--	--	--	--	--	--	--
892	--	--	--	--	--	--	--
893	21.6	21.5	19.7	19.4	21.2	18.4	18.4
894	--	--	--	--	--	--	--
895	21.9	20.5	19.2	18.3	18.2	17.7	18.2
896	20.6	20.8	19.5	18.9	19.0	19.1	18.7
897	21.5	20.6	19.3	18.5	18.7	17.9	18.4
898	--	--	--	--	--	--	--
899	20.5	21.0	20.1	19.7	19.5	18.1	18.9
900	22.3	22.2	19.9	19.1	19.0	17.8	19.1
MEAN	21.3	21.0	19.6	19.1	19.2	18.2	18.7
SD	0.59	0.60	0.43	0.55	0.82	0.42	0.41
N	10	10	10	9	10	10	10

GROUP: 18.0:18.0 mg base/kg/day							
921	--	--	--	--	--	--	--
922	--	--	--	18.9	18.9	18.1	18.1
923	22.2	20.7	18.3	17.7	18.6	18.4	19.0
924	--	--	--	--	--	--	--
925	--	--	--	--	--	--	--
926	--	--	--	--	--	--	--
927	20.3	19.6	17.9	17.6	18.6	17.7	18.4
928	--	--	--	--	--	--	--
929	19.7	18.5	16.9	17.3	18.1	17.9	18.3
930	21.8	21.0	20.0	18.5	19.6	18.7	19.3
931	--	--	--	--	--	--	--
932	--	20.1	20.4	19.2	20.5	19.1	18.8
933	19.8	19.3	17.5	16.4	16.7	16.4	17.1
934	22.2	21.5	19.3	--	--	--	--
935	21.9	20.8	18.8	19.5	19.8	19.4	20.2
936	--	--	--	--	--	--	--
937	19.9	--	--	--	--	--	--
938	--	--	--	--	--	--	--
939	21.1	20.4	18.7	18.3	19.8	18.9	18.9
940	20.1	19.0	18.6	17.2	18.1	17.7	18.3
MEAN	20.9	20.1	18.6	18.1	18.9	18.2	18.6
SD	1.05	0.96	1.08	0.99	1.10	0.87	0.82
N	10	10	10	10	10	10	10

(--)-Data Unavailable

DRAFT

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

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

STUDY ID: 098  
ABBR: TMCHC

SEX: MALE  
UNITS: %

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
801	35.4	34.9	36.1	36.2	36.8	35.9	36.1
802	35.0	35.5	36.8	36.6	36.5	35.9	35.5
803	--	--	--	--	--	--	--
804	--	--	--	--	--	--	--
805	--	--	--	--	--	--	--
806	35.4	35.7	36.3	37.2	36.1	36.9	35.5
807	35.4	35.6	36.6	37.2	37.2	35.8	36.5
808	--	--	--	--	--	--	--
809	35.2	35.4	38.1	36.3	37.0	36.4	36.5
810	35.0	35.5	36.0	36.4	36.2	35.5	40.7
811	35.4	35.4	36.3	37.4	35.6	35.8	37.1
812	--	--	--	40.3	--	--	--
813	--	--	--	--	--	--	--
814	33.5	33.7	35.4	35.0	36.8	34.3	34.8
815	35.3	36.1	35.8	37.0	36.9	36.3	36.0
816	34.5	36.3	35.9	36.8	36.3	35.7	37.1
817	--	--	--	--	--	--	--
818	--	--	--	--	--	--	--
819	--	--	--	--	--	--	--
820	--	--	--	--	--	--	--
MEAN	35.0	35.4	36.3	36.9	36.5	35.9	36.6
SD	0.60	0.71	0.74	1.30	0.49	0.68	1.62
N	10	10	10	11	10	10	10

GROUP: 0.5:0.5 mg. base/kg/day							
841	--	--	--	--	--	--	--
842	--	--	--	--	--	--	--
843	--	--	--	--	--	--	--
844	34.8	34.7	36.0	36.7	35.9	36.0	36.0
845	--	--	--	--	--	--	--
846	34.8	35.0	37.2	36.0	37.0	34.4	36.5
847	--	--	--	--	--	--	--
848	33.7	34.8	36.0	35.5	35.3	35.0	34.8
849	--	--	--	--	--	--	--
850	35.9	35.0	36.2	36.1	36.2	35.7	36.4
851	34.9	35.7	35.9	21.4	36.3	36.3	37.1
852	34.3	35.1	36.8	36.4	36.2	36.6	36.6
853	33.9	34.6	35.7	35.7	35.7	35.5	35.5
854	--	--	--	--	--	--	--
855	--	--	--	--	--	--	--
856	--	--	--	--	--	--	--
857	--	--	--	--	--	--	--
858	35.9	35.0	36.2	36.1	37.0	35.8	35.7
859	35.5	35.5	36.0	36.9	36.0	36.0	36.2
860	35.1	35.3	37.1	36.9	36.7	35.9	37.1
MEAN	34.9	35.1	36.3	34.8	36.2	35.7	36.2
SD	0.76	0.35	0.53	4.72	0.55	0.63	0.72
N	10	10	10	10	10	10	10

(--)-Data Unavailable

DRAFT

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

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

STUDY ID: 098  
ABBR: TMCHC

SEX: MALE  
UNITS: %

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
881	--	--	--	--	--	--	--
882	--	--	--	--	--	--	--
883	--	--	--	--	--	--	--
884	35.3	35.8	35.4	36.5	35.6	35.7	36.4
885	--	--	--	--	--	--	--
886	--	--	--	--	--	--	--
887	34.9	35.1	36.7	--	35.8	35.6	36.7
888	--	--	--	--	--	--	--
889	35.8	35.9	35.7	36.5	35.4	35.7	35.3
890	34.7	35.3	35.3	37.4	35.7	35.7	36.3
891	--	--	--	--	--	--	--
892	--	--	--	--	--	--	--
893	34.8	34.9	34.8	35.9	38.8	36.1	36.4
894	--	--	--	--	--	--	--
895	34.4	34.4	35.1	35.3	35.0	35.3	35.9
896	34.0	34.9	35.2	35.8	35.1	36.1	34.9
897	35.1	34.7	35.4	35.9	35.8	35.9	36.3
898	--	--	--	--	--	--	--
899	34.3	34.5	33.7	36.7	35.0	35.4	35.9
900	35.2	36.0	35.7	35.4	35.4	34.6	36.8
MEAN	34.9	35.2	35.3	36.2	35.8	35.6	36.1
SD	0.53	0.58	0.76	0.67	1.11	0.44	0.60
N	10	10	10	9	10	10	10

GROUP: 18.0:18.0 mg base/kg/day							
921	--	--	--	--	--	--	--
922	--	--	--	35.9	35.9	36.2	35.9
923	35.5	34.4	34.5	35.3	34.9	35.0	35.7
924	--	--	--	--	--	--	--
925	--	--	--	--	--	--	--
926	--	--	--	--	--	--	--
927	34.6	34.6	34.8	35.1	35.8	35.8	36.2
928	--	--	--	--	--	--	--
929	34.1	34.3	33.7	35.1	35.1	35.4	35.7
930	34.5	33.7	35.2	34.9	34.7	35.7	35.8
931	--	--	--	--	--	--	--
932	--	33.4	35.1	33.8	35.2	36.2	35.8
933	34.7	34.9	36.4	35.6	35.9	35.8	36.4
934	36.2	35.7	35.5	--	--	--	--
935	34.6	34.5	34.1	36.2	34.6	36.2	36.1
936	--	--	--	--	--	--	--
937	34.0	--	--	--	--	--	--
938	--	--	--	--	--	--	--
939	34.7	34.7	35.1	34.1	36.4	36.6	36.3
940	35.6	33.4	35.0	34.6	34.7	36.1	36.0
MEAN	34.9	34.4	34.9	35.1	35.3	35.9	36.0
SD	0.70	0.71	0.75	0.75	0.63	0.46	0.25
N	10	10	10	10	10	10	10

(--)-Data Unavailable

DRAFT

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Reticulocytes Count

STUDY ID: 098  
ABBR: RETICS

SEX: MALE  
UNITS: % RBCs

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
801	1.8	0.4	1.4	0.6	0.5	0.4	0.8
802	0.8	0.0	0.8	0.5	1.2	0.8	0.6
803	--	--	--	--	--	--	--
804	--	--	--	--	--	--	--
805	--	--	--	--	--	--	--
806	1.5	1.4	0.1	0.9	1.1	0.6	0.7
807	0.4	0.2	0.5	0.8	0.2	0.1	0.4
808	--	--	--	--	--	--	--
809	1.1	0.3	0.7	0.7	0.9	0.0	0.9
810	1.8	0.2	1.0	0.6	1.6	0.3	0.9
811	1.5	0.8	0.8	0.1	0.7	0.6	0.8
812	--	--	--	0.7	--	--	--
813	--	--	--	--	--	--	--
814	0.1	0.2	0.7	0.9	0.7	0.3	1.0
815	1.3	0.7	1.3	0.7	1.0	0.6	0.8
816	1.7	0.4	0.2	0.5	1.5	0.8	0.6
817	--	--	--	--	--	--	--
818	--	--	--	--	--	--	--
819	--	--	--	--	--	--	--
820	--	--	--	--	--	--	--
MEAN	1.2	0.5	0.8	0.6	0.9	0.5	0.8
SD	0.59	0.41	0.42	0.22	0.44	0.28	0.18
N	10	10	10	11	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
841	--	--	--	--	--	--	--
842	--	--	--	--	--	--	--
843	--	--	--	--	--	--	--
844	3.0	0.6	0.7	0.8	1.0	0.5	0.4
845	--	--	--	--	--	--	--
846	1.7	0.5	0.7	0.4	0.0	0.1	0.7
847	--	--	--	--	--	--	--
848	2.0	1.0	0.4	1.1	1.3	0.8	0.6
849	--	--	--	--	--	--	--
850	1.8	1.2	0.8	0.3	0.5	1.0	0.2
851	0.9	1.3	2.7	0.1	0.1	0.0	0.5
852	1.5	0.5	0.7	1.0	0.6	0.3	0.5
853	1.9	0.9	0.5	1.0	0.5	0.3	1.2
854	--	--	--	--	--	--	--
855	--	--	--	--	--	--	--
856	--	--	--	--	--	--	--
857	--	--	--	--	--	--	--
858	1.9	1.3	QNS	1.5	0.6	0.9	0.6
859	2.4	1.5	0.7	0.4	0.9	0.1	0.7
860	1.1	1.1	0.9	1.3	1.0	0.4	0.4
MEAN	1.8	1.0	0.9	0.8	0.7	0.4	0.6
SD	0.60	0.36	0.69	0.47	0.41	0.35	0.27
N	10	10	9	10	10	10	10

(--)-Data Unavailable

QNS-Quantity Not Sufficient

DRAFT

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Reticulocytes Count

STUDY ID: 098  
ABBR: RETICS

SEX: MALE  
UNITS: % RBCs

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
881	--	--	--	--	--	--	--
882	--	--	--	--	--	--	--
883	--	--	--	--	--	--	--
884	0.5	0.5	1.0	2.6	0.8	0.2	0.2
885	--	--	--	--	--	--	--
886	--	--	--	--	--	--	--
887	0.3	0.3	0.9	--	0.9	0.2	0.6
888	--	--	--	--	--	--	--
889	0.2	1.9	1.8	1.1	1.9	0.3	1.0
890	1.0	0.6	1.5	1.0	1.1	0.7	1.5
891	--	--	--	--	--	--	--
892	--	--	--	--	--	--	--
893	1.8	0.7	1.2	1.0	0.5	0.2	1.0
894	--	--	--	--	--	--	--
895	2.3	1.2	2.1	3.4	1.6	0.0	1.0
896	2.2	0.9	0.4	0.8	0.9	0.1	0.2
897	1.2	0.6	2.6	1.1	0.6	0.9	0.7
898	--	--	--	--	--	--	--
899	2.3	0.7	2.5	0.8	2.0	0.4	0.6
900	2.7	0.5	1.9	2.1	0.7	0.0	0.5
MEAN	1.5	0.8	1.6	1.5	1.1	0.3	0.7
SD	0.93	0.46	0.72	0.93	0.54	0.29	0.40
N	10	10	10	9	10	10	10

GROUP: 18.0:18.0 mg base/kg/day							
921	--	--	--	--	--	--	--
922	--	--	--	1.9	0.3	0.2	1.3
923	3.6	1.5	3.3	2.3	1.2	0.3	0.4
924	--	--	--	--	--	--	--
925	--	--	--	--	--	--	--
926	--	--	--	--	--	--	--
927	5.3	2.6	1.2	0.6	0.4	0.0	0.8
928	--	--	--	--	--	--	--
929	5.7	0.5	2.4	1.1	1.4	0.4	0.6
930	5.3	1.0	1.6	1.2	0.9	0.3	0.6
931	--	--	--	--	--	--	--
932	--	4.4	2.8	2.1	1.0	0.3	0.6
933	4.7	1.9	2.6	1.6	1.2	0.4	0.5
934	1.8	3.2	4.1	--	--	--	--
935	2.8	0.3	3.4	1.7	0.8	0.6	0.0
936	--	--	--	--	--	--	--
937	3.0	--	--	--	--	--	--
938	--	--	--	--	--	--	--
939	4.5	2.2	1.5	2.9	1.0	0.0	0.6
940	3.5	1.1	1.3	2.2	1.4	0.2	1.0
MEAN	4.0	1.9	2.4	1.8	1.0	0.3	0.6
SD	1.28	1.28	1.00	0.67	0.38	0.18	0.35
N	10	10	10	10	10	10	10

(--)-Data Unavailable

DRAFT

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Nucleated Red Cells

STUDY ID: 098  
ABBR: NRBC

SEX: MALE  
UNITS: COLNT

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
801	0	0	0	0	0	0	0
802	0	0	0	0	0	0	0
803	--	--	--	--	--	--	--
804	--	--	--	--	--	--	--
805	--	--	--	--	--	--	--
806	0	0	0	0	0	0	0
807	0	0	0	0	0	0	0
808	--	--	--	--	--	--	--
809	0	0	0	0	0	0	0
810	0	0	0	0	0	0	0
811	0	0	0	0	0	0	0
812	--	--	--	0	--	--	--
813	--	--	--	--	--	--	--
814	0	0	0	0	0	0	0
815	0	0	0	0	0	0	0
816	0	0	0	0	0	0	0
817	--	--	--	--	--	--	--
818	--	--	--	--	--	--	--
819	--	--	--	--	--	--	--
820	--	--	--	--	--	--	--
MEAN	0	0	0	0	0	0	0
SD	0.0	0.0	0.0	0.0	0.0	0.0	0.0
N	10	10	10	11	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
841	--	--	--	--	--	--	--
842	--	--	--	--	--	--	--
843	--	--	--	--	--	--	--
844	0	0	0	0	0	0	0
845	--	--	--	--	--	--	--
846	0	0	0	0	0	0	0
847	--	--	--	--	--	--	--
848	0	0	0	0	0	0	0
849	--	--	--	--	--	--	--
850	0	0	0	0	0	0	0
851	0	0	0	0	0	0	0
852	0	0	0	0	0	0	0
853	0	0	0	0	0	0	0
854	--	--	--	--	--	--	--
855	--	--	--	--	--	--	--
856	--	--	--	--	--	--	--
857	--	--	--	--	--	--	--
858	0	0	0	0	0	0	0
859	0	0	0	0	0	0	0
860	0	0	0	0	0	0	0
MEAN	0	0	0	0	0	0	0
SD	0.0	0.0	0.0	0.0	0.0	0.0	0.0
N	10	10	10	10	10	10	10

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Nucleated Red Cells

STUDY ID: 098  
ABBR: NRBC

SEX: MALE  
UNITS: COUNT

ANIMAL ID    Week 2    Week 4    Week 8    Week 13    Week 16    Week 21    Week 27

GROUP: 6.0:6.0 mg base/kg/day

881	--	--	--	--	--	--	--
882	--	--	--	--	--	--	--
883	--	--	--	--	--	--	--
884	0	0	0	0	0	0	0
885	--	--	--	--	--	--	--
886	--	--	--	--	--	--	--
887	0	0	0	--	0	0	0
888	--	--	--	--	--	--	--
889	0	0	0	0	0	0	0
890	0	0	0	0	0	0	0
891	--	--	--	--	--	--	--
892	--	--	--	--	--	--	--
893	0	0	0	0	0	0	0
894	--	--	--	--	--	--	--
895	0	0	0	0	0	0	0
896	0	0	0	0	0	0	0
897	0	0	0	0	0	0	1
898	--	--	--	--	--	--	--
899	0	0	0	0	0	0	0
900	0	0	0	0	0	0	0
MEAN	0	0	0	0	0	0	0
SD	0.0	0.0	0.0	0.0	0.0	0.0	0.3
N	10	10	10	9	10	10	10

GROUP: 18.0:18.0 mg base/kg/day

921	--	--	--	--	--	--	--
922	--	--	--	0	0	0	0
923	0	0	0	0	0	0	0
924	--	--	--	--	--	--	--
925	--	--	--	--	--	--	--
926	--	--	--	--	--	--	--
927	0	0	0	0	0	0	0
928	--	--	--	--	--	--	--
929	0	0	0	0	0	0	0
930	0	0	1	0	0	0	0
931	--	--	--	--	--	--	--
932	--	0	1	1	0	0	0
933	0	0	0	0	0	0	0
934	0	0	0	--	--	--	--
935	0	0	0	0	0	0	0
936	--	--	--	--	--	--	--
937	1	--	--	--	--	--	--
938	--	--	--	--	--	--	--
939	0	0	0	0	0	0	0
940	0	0	0	0	0	0	0
MEAN	0	0	0	0	0	0	0
SD	0.3	0.0	0.4	0.3	0.0	0.0	0.0
N	10	10	10	10	10	10	10

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

DRAFT

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Heinz Bodies

STUDY ID: 098  
ABBR: HB

SEX: MALE  
UNITS: %

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
801	0.0	0.0	0.1	0.0	0.0	0.0	0.0
802	0.0	0.0	0.0	0.0	0.0	0.0	0.0
803	--	--	--	--	--	--	--
804	--	--	--	--	--	--	--
805	--	--	--	--	--	--	--
806	0.0	0.0	0.2	0.0	0.0	0.0	0.0
807	0.0	0.0	1.0	0.0	0.0	0.0	0.0
808	--	--	--	--	--	--	--
809	0.0	0.0	0.0	0.0	0.0	0.0	0.0
810	0.0	0.0	0.0	0.0	0.0	0.0	0.0
811	0.0	0.0	0.0	0.0	0.0	0.0	0.0
812	--	--	--	0.0	--	--	--
813	--	--	--	--	--	--	--
814	0.0	0.0	0.0	0.0	0.0	0.0	0.0
815	0.0	0.0	0.0	0.0	0.0	0.0	0.0
816	0.0	0.0	0.0	0.0	0.0	0.0	0.0
817	--	--	--	--	--	--	--
818	--	--	--	--	--	--	--
819	--	--	--	--	--	--	--
820	--	--	--	--	--	--	--
MEAN	0.0	0.0	0.1	0.0	0.0	0.0	0.0
SD	0.00	0.00	0.31	0.00	0.00	0.00	0.00
N	10	10	10	11	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
841	--	--	--	--	--	--	--
842	--	--	--	--	--	--	--
843	--	--	--	--	--	--	--
844	0.0	0.0	0.0	0.0	0.0	0.0	0.0
845	--	--	--	--	--	--	--
846	0.0	0.0	0.0	0.0	0.0	0.0	0.0
847	--	--	--	--	--	--	--
848	0.0	0.0	0.0	0.0	0.0	0.0	0.0
849	--	--	--	--	--	--	--
850	0.0	0.1	0.2	0.0	0.0	0.0	0.0
851	0.0	0.0	0.3	0.0	0.0	0.0	0.0
852	0.0	0.0	0.0	0.0	0.0	0.0	0.0
853	0.0	0.2	0.0	0.0	0.0	0.0	0.0
854	--	--	--	--	--	--	--
855	--	--	--	--	--	--	--
856	--	--	--	--	--	--	--
857	--	--	--	--	--	--	--
858	0.1	0.1	0.0	0.0	0.0	0.0	0.0
859	0.0	0.7	0.0	0.0	0.0	0.0	0.0
860	0.0	0.0	0.2	0.0	0.0	0.0	0.0
MEAN	0.0	0.1	0.1	0.0	0.0	0.0	0.0
SD	0.03	0.22	0.12	0.00	0.00	0.00	0.00
N	10	10	10	10	10	10	10

(--)-Data Unavailable

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Heinz Bodies

STUDY ID: 098  
ABBR: HB

SEX: MALE  
UNITS: %

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
881	--	--	--	--	--	--	--
882	--	--	--	--	--	--	--
883	--	--	--	--	--	--	--
884	0.0	0.0	0.2	0.0	0.0	0.0	0.0
885	--	--	--	--	--	--	--
886	--	--	--	--	--	--	--
887	0.0	0.3	0.0	--	0.0	0.0	0.0
888	--	--	--	--	--	--	--
889	0.0	1.8	0.0	0.5	0.0	0.0	0.0
890	0.1	0.5	0.0	0.3	0.0	0.0	0.0
891	--	--	--	--	--	--	--
892	--	--	--	--	--	--	--
893	0.0	0.0	0.2	0.0	0.0	0.0	0.0
894	--	--	--	--	--	--	--
895	0.1	1.4	0.0	0.3	0.0	0.0	0.0
896	0.0	1.6	0.1	0.2	0.0	0.0	0.0
897	0.0	0.1	0.1	0.4	0.0	0.0	0.0
898	--	--	--	--	--	--	--
899	0.1	0.0	0.0	0.0	0.0	0.0	0.0
900	0.0	0.0	0.0	1.0	0.0	0.0	0.0
MEAN	0.0	0.6	0.1	0.3	0.0	0.0	0.0
SD	0.05	0.73	0.08	0.32	0.00	0.00	0.00
N	10	10	10	9	10	10	10

GROUP: 18.0:18.0 mg base/kg/day							
921	--	--	--	--	--	--	--
922	--	--	--	0.4	0.0	0.0	0.0
923	3.5	0.7	0.2	0.7	0.0	0.3	0.0
924	--	--	--	--	--	--	--
925	--	--	--	--	--	--	--
926	--	--	--	--	--	--	--
927	2.0	0.7	0.3	1.0	0.0	0.0	0.0
928	--	--	--	--	--	--	--
929	2.8	0.2	0.4	0.8	0.1	0.0	0.0
930	1.4	0.8	0.3	1.2	0.0	0.0	0.0
931	--	--	--	--	--	--	--
932	--	0.7	0.0	1.2	0.0	0.0	0.0
933	0.7	1.2	0.4	0.3	0.1	0.0	0.0
934	3.1	0.0	0.0	--	--	--	--
935	1.8	0.5	1.1	0.8	0.0	0.0	0.0
936	--	--	--	--	--	--	--
937	3.3	--	--	--	--	--	--
938	--	--	--	--	--	--	--
939	2.3	0.0	0.0	0.4	0.0	0.0	0.0
940	1.7	0.7	0.4	0.7	0.0	0.0	0.0
MEAN	2.3	0.6	0.3	0.8	0.0	0.0	0.0
SD	0.91	0.38	0.32	0.32	0.04	0.09	0.00
N	10	10	10	10	10	10	10

(--)-Data Unavailable



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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: % Methemoglobin

STUDY ID: 098  
ABBR: %METHGB

SEX: MALE  
UNITS: %

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
801	0.0	0.0	1.0	--	0.0	0.7	0.4
802	0.6	0.3	0.4	1.3	0.7	0.0	0.1
803	--	--	--	--	--	--	--
804	--	--	--	--	--	--	--
805	--	--	--	--	--	--	--
806	0.0	0.4	0.2	0.4	0.2	0.7	0.2
807	0.4	0.7	1.1	0.6	0.3	0.5	0.9
808	--	--	--	--	--	--	--
809	0.9	0.5	0.1	0.5	0.0	0.0	0.5
810	0.2	0.1	0.0	0.8	0.1	1.1	0.7
811	0.2	0.5	0.4	0.4	0.5	0.6	0.4
812	--	--	--	0.5	--	--	--
813	--	--	--	--	--	--	--
814	0.7	2.5	0.4	0.6	1.0	0.2	0.2
815	1.3	1.0	0.2	0.3	0.0	0.0	0.0
816	0.1	0.6	0.4	0.0	0.0	0.0	0.0
817	--	--	--	--	--	--	--
818	--	--	--	--	--	--	--
819	--	--	--	--	--	--	--
820	--	--	--	--	--	--	--
MEAN	0.4	0.7	0.4	0.5	0.3	0.4	0.3
SD	0.43	0.71	0.36	0.34	0.35	0.39	0.30
N	10	10	10	10	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
841	--	--	--	--	--	--	--
842	--	--	--	--	--	--	--
843	--	--	--	--	--	--	--
844	1.4	0.7	1.1	0.1	0.0	0.9	0.5
845	--	--	--	--	--	--	--
846	0.2	0.8	0.7	0.2	0.7	0.5	0.9
847	--	--	--	--	--	--	--
848	0.3	0.0	0.0	1.1	0.0	0.4	0.5
849	--	--	--	--	--	--	--
850	0.7	0.5	0.7	0.5	0.0	0.3	0.8
851	0.4	0.7	0.2	0.2	0.2	0.1	0.3
852	0.3	0.6	0.4	0.3	0.0	0.0	0.3
853	0.4	0.5	0.4	0.5	0.6	0.6	1.0
854	--	--	--	--	--	--	--
855	--	--	--	--	--	--	--
856	--	--	--	--	--	--	--
857	--	--	--	--	--	--	--
858	0.4	0.1	0.4	0.5	0.9	0.8	1.1
859	0.0	0.1	0.3	0.4	0.4	0.5	0.5
860	0.5	0.3	0.6	1.1	0.4	1.0	0.6
MEAN	0.5	0.4	0.5	0.5	0.3	0.5	0.7
SD	0.38	0.29	0.31	0.35	0.33	0.33	0.28
N	10	10	10	10	10	10	10

(--)-Data Unavailable



DRAFT

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: % Methemoglobin

STUDY ID: 098  
ABBR: %METHGB

SEX: MALE  
UNITS: %

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
881	--	--	--	--	--	--	--
882	--	--	--	--	--	--	--
883	--	--	--	--	--	--	--
884	4.6	4.5	7.6	7.0	0.2	2.6	0.5
885	--	--	--	--	--	--	--
886	--	--	--	--	--	--	--
887	1.9	4.5	7.6	--	0.4	0.5	1.3
888	--	--	--	--	--	--	--
889	2.3	5.4	6.7	8.9	0.0	0.2	0.5
890	0.5	3.0	4.9	6.4	0.5	0.2	0.5
891	--	--	--	--	--	--	--
892	--	--	--	--	--	--	--
893	3.2	5.3	6.3	5.6	0.8	0.4	1.0
894	--	--	--	--	--	--	--
895	1.4	4.6	7.1	7.4	0.9	0.8	1.8
896	2.2	4.5	7.1	7.8	0.0	0.1	0.9
897	1.3	3.8	7.4	7.4	0.0	0.4	0.6
898	--	--	--	--	--	--	--
899	1.7	3.3	6.0	5.7	0.0	0.2	0.0
900	1.3	4.7	5.9	6.4	0.7	0.4	1.6
MEAN	2.0	4.4	6.7	7.0	0.4	0.6	0.9
SD	1.15	0.78	0.88	1.06	0.36	0.74	0.56
N	10	10	10	9	10	10	10

GROUP: 18.0:18.0 mg base/kg/day

921	--	--	--	--	--	--	--
922	--	--	--	11.4	1.8	0.5	0.4
923	14.3	14.7	11.1	12.0	2.4	1.6	0.6
924	--	--	--	--	--	--	--
925	--	--	--	--	--	--	--
926	--	--	--	--	--	--	--
927	12.6	10.9	9.8	13.3	2.9	1.0	1.4
928	--	--	--	--	--	--	--
929	17.3	8.9	12.0	12.5	1.2	0.4	0.8
930	8.6	6.1	7.1	9.3	0.7	0.0	1.3
931	--	--	--	--	--	--	--
932	--	12.2	7.7	12.6	0.6	0.5	0.8
933	10.5	7.8	9.0	13.3	1.8	0.0	0.4
934	11.6	7.3	9.6	--	--	--	--
935	9.3	8.8	9.6	11.7	1.0	0.1	0.4
936	--	--	--	--	--	--	--
937	40.5	--	--	--	--	--	--
938	--	--	--	--	--	--	--
939	15.2	10.9	10.6	12.6	0.1	0.6	0.6
940	15.1	9.2	8.9	11.6	0.8	0.0	0.7
MEAN	15.5	9.7	9.5	12.0	1.3	0.5	0.7
SD	9.22	2.54	1.48	1.17	0.88	0.51	0.36
N	10	10	10	10	10	10	10

(--)-Data Unavailable

DRAFT

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Platelets

STUDY ID: 098  
ABBR: PLT

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
801	1018	1070	1045	810	897	681	810
802	1301	1193	1178	983	1065	1035	1136
803	--	--	--	--	--	--	--
804	--	--	--	--	--	--	--
805	--	--	--	--	--	--	--
806	1280	1204	1248	1203	1074	1247	1164
807	1250	1225	1185	1193	1050	899	1076
808	--	--	--	--	--	--	--
809	1199	1142	1173	1091	1155	1233	1210
810	1245	1250	1098	1094	1076	884	794
811	1216	1186	1068	797	1046	1061	1149
812	--	--	--	982	--	--	--
813	--	--	--	--	--	--	--
814	1309	906	1198	1161	461	1152	1268
815	1008	1206	1180	1114	1180	1137	1160
816	1264	1076	1030	1031	1046	1047	1141
817	--	--	--	--	--	--	--
818	--	--	--	--	--	--	--
819	--	--	--	--	--	--	--
820	--	--	--	--	--	--	--
MEAN	1209	1146	1140	1042	1005	1038	1091
SD	108.8	103.3	74.0	139.4	205.3	175.0	160.2
N	10	10	10	11	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
841	--	--	--	--	--	--	--
842	--	--	--	--	--	--	--
843	--	--	--	--	--	--	--
844	1563	1134	1251	1315	1240	1275	1290
845	--	--	--	--	--	--	--
846	1172	1127	1093	790	1014	926	1071
847	--	--	--	--	--	--	--
848	1250	1296	1293	1218	942	1112	1229
849	--	--	--	--	--	--	--
850	1254	1222	1178	1224	1124	1243	1193
851	1308	1303	963	937	623	711	944
852	1371	1326	1295	1312	1262	1316	1440
853	1325	1211	1229	1311	1126	1086	1123
854	--	--	--	--	--	--	--
855	--	--	--	--	--	--	--
856	--	--	--	--	--	--	--
857	--	--	--	--	--	--	--
858	1248	1238	1162	1077	906	1037	610
859	1033	1058	945	872	882	857	953
860	1159	813	1116	866	1128	1174	1113
MEAN	1268	1173	1153	1092	1025	1074	1097
SD	141.3	152.7	124.8	209.3	193.3	194.7	227.2
N	10	10	10	10	10	10	10

(--)-Data Unavailable

DRAFT

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Platelets

STUDY ID: 098  
ABBR: PLT

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
881	--	--	--	--	--	--	--
882	--	--	--	--	--	--	--
883	--	--	--	--	--	--	--
884	1295	1011	977	910	1044	983	659
885	--	--	--	--	--	--	--
886	--	--	--	--	--	--	--
887	1263	1318	1160	--	724	1276	1179
888	--	--	--	--	--	--	--
889	1133	1141	1018	988	1059	1089	1078
890	1274	1250	1192	1147	869	1205	1177
891	--	--	--	--	--	--	--
892	--	--	--	--	--	--	--
893	1131	1162	1080	1214	572	1128	1136
894	--	--	--	--	--	--	--
895	1156	954	962	935	832	944	947
896	948	1203	1230	1121	1146	1053	1050
897	1084	1271	1138	1075	1170	1006	1107
898	--	--	--	--	--	--	--
899	1035	1146	1111	745	1095	1062	1107
900	877	1236	1199	987	1129	1164	1075
MEAN	1120	1169	1107	1014	964	1091	1052
SD	138.9	114.2	95.0	143.0	203.6	103.7	153.3
N	10	10	10	9	10	10	10

GROUP: 18.0:18.0 mg base/kg/day							
921	--	--	--	--	--	--	--
922	--	--	--	911	990	892	1011
923	1321	888	1179	656	909	872	941
924	--	--	--	--	--	--	--
925	--	--	--	--	--	--	--
926	--	--	--	--	--	--	--
927	1493	1396	1332	1204	1178	1068	1169
928	--	--	--	--	--	--	--
929	1072	990	1106	961	879	851	958
930	1162	1047	958	930	890	871	977
931	--	--	--	--	--	--	--
932	--	763	1041	1072	876	1002	1057
933	1329	1144	939	916	899	943	992
934	1032	1117	1063	--	--	--	--
935	1109	925	801	892	779	785	887
936	--	--	--	--	--	--	--
937	461	--	--	--	--	--	--
938	--	--	--	--	--	--	--
939	1123	1100	1063	959	1073	970	1036
940	1858	1321	1127	996	1142	1039	1029
MEAN	1196	1069	1061	950	962	929	1006
SD	358.4	192.4	144.2	139.3	129.9	90.3	76.3
N	10	10	10	10	10	10	10

(--)-Data Unavailable

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

DRAFT

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

STUDY ID: 098  
ABBR: APTT

SEX: MALE  
UNITS: sec

ANIMAL ID	Week 14	Week 27
GROUP: 0:0 mg base/kg/day		
801	--	14.8
802	--	12.6
803	19.9	--
804	17.1	--
805	12.8	--
806	--	15.6
807	--	15.4
808	15.7	--
809	--	15.4
810	--	12.4
811	--	16.6
812	18.3	--
813	13.6	--
814	--	18.3
815	--	13.8
816	--	15.7
817	14.7	--
818	15.9	--
819	16.9	--
820	16.8	--
MEAN	16.2	15.1
SD	2.13	1.78
N	10	10

GROUP: 0.5:0.5 mg base/kg/day		
841	16.9	--
842	13.1	--
843	15.2	--
844	--	15.7
845	16.8	--
846	--	15.3
847	13.4	--
848	--	15.0
849	12.0	--
850	--	13.7
851	--	13.9
852	--	12.7
853	--	12.9
854	17.5	--
855	12.8	--
856	18.0	--
857	17.2	--
858	--	18.3
859	--	16.1
860	--	11.5
MEAN	15.3	14.5
SD	2.26	1.98
N	10	10

(--)-Data Unavailable

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

DRAFT

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

STUDY ID: 098  
PBR: APTT

SEX: MALE  
UNITS: sec

ANIMAL ID    Week 14    Week 27

GROUP: 6.0:6.0 mg base/kg/day

881	14.8	--
882	15.5	--
883	13.7	--
884	--	16.4
885	9.4	--
886	11.9	--
887	--	16.3
888	16.2	--
889	--	12.6
890	--	15.5
891	13.6	--
892	13.5	--
893	--	13.8
894	14.0	--
895	--	16.0
896	--	12.7
897	--	19.4
898	15.1	--
899	--	13.8
900	--	17.5
MEAN	13.8	15.4
SD	1.96	2.18
N	10	10

GROUP: 18.0:18.0 mg base/kg/day

921	--	--
922	--	13.1
923	--	11.7
924	18.0	--
925	18.9	--
926	--	--
927	--	18.1
928	13.5	--
929	--	16.5
930	--	18.3
931	19.0	--
932	--	13.2
933	--	13.2
934	--	--
935	--	14.9
936	--	--
937	--	--
938	9.8	--
939	--	14.7
940	--	14.7
MEAN	15.8	14.8
SD	4.06	2.20
N	5	10

(--)-Data Unavailable

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Leukocytes

STUDY ID: 098  
ABBR: WBC

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
801	14.0	13.5	12.9	12.7	11.4	13.7	9.0
802	13.6	14.9	15.6	11.8	11.4	8.6	12.0
803	--	--	--	--	--	--	--
804	--	--	--	--	--	--	--
805	--	--	--	--	--	--	--
806	18.9	20.6	15.2	14.8	13.0	13.2	13.0
807	17.4	16.3	18.2	14.7	14.5	13.2	13.0
808	--	--	--	--	--	--	--
809	26.1	20.8	20.9	16.4	16.5	16.2	17.1
810	19.4	22.3	20.1	16.5	17.9	19.6	16.5
811	12.9	14.4	12.8	12.0	12.3	12.4	11.3
812	--	--	--	12.2	--	--	--
813	--	--	--	--	--	--	--
814	15.4	12.6	19.7	12.7	9.3	11.2	11.7
815	20.0	20.5	18.2	18.0	18.2	19.2	13.4
816	19.8	19.6	14.9	14.3	13.5	13.7	11.7
817	--	--	--	--	--	--	--
818	--	--	--	--	--	--	--
819	--	--	--	--	--	--	--
820	--	--	--	--	--	--	--
MEAN	17.8	17.6	16.9	14.2	13.8	14.1	12.9
SD	3.99	3.57	2.96	2.10	2.96	3.40	2.41
N	10	10	10	11	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
841	--	--	--	--	--	--	--
842	--	--	--	--	--	--	--
843	--	--	--	--	--	--	--
844	23.0	11.2	10.6	15.3	8.6	14.2	10.3
845	--	--	--	--	--	--	--
846	24.0	22.7	19.9	17.5	14.7	15.5	14.9
847	--	--	--	--	--	--	--
848	16.3	12.1	14.8	14.6	9.8	12.5	11.6
849	--	--	--	--	--	--	--
850	20.9	19.0	20.1	17.3	15.4	15.6	16.6
851	15.7	17.1	13.9	10.4	11.9	12.3	14.9
852	16.0	14.5	17.9	14.1	11.4	13.4	15.5
853	13.2	10.3	12.4	11.1	10.9	10.6	10.0
854	--	--	--	--	--	--	--
855	--	--	--	--	--	--	--
856	--	--	--	--	--	--	--
857	--	--	--	--	--	--	--
858	20.2	20.0	20.8	16.1	12.6	13.9	13.0
859	14.5	13.5	13.0	11.0	12.3	10.7	9.9
860	27.1	17.8	22.7	19.2	18.4	19.9	24.6
MEAN	19.1	15.8	16.6	14.7	12.6	13.9	14.1
SD	4.63	4.13	4.17	3.03	2.88	2.74	4.42
N	10	10	10	10	10	10	10

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

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

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Leukocytes

STUDY ID: 098  
ABBR: WBC

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
881	--	--	--	--	--	--	--
882	--	--	--	--	--	--	--
883	--	--	--	--	--	--	--
884	21.7	27.3	24.7	21.8	12.8	13.7	10.5
885	--	--	--	--	--	--	--
886	--	--	--	--	--	--	--
887	21.2	21.8	21.4	--	11.2	9.2	13.0
888	--	--	--	--	--	--	--
889	16.1	27.2	19.8	24.1	13.7	13.9	12.1
890	22.3	20.7	23.5	20.0	13.4	16.2	16.4
891	--	--	--	--	--	--	--
892	--	--	--	--	--	--	--
893	22.3	20.7	17.5	17.6	11.2	11.9	13.6
894	--	--	--	--	--	--	--
895	25.1	25.7	25.8	29.9	17.8	15.3	15.1
896	20.1	19.8	22.2	25.3	12.8	9.6	10.3
897	18.2	26.3	28.5	27.3	15.7	14.6	13.7
898	--	--	--	--	--	--	--
899	21.7	24.3	21.5	22.6	12.6	13.6	13.0
900	17.3	26.5	24.2	22.3	14.7	12.0	11.0
MEAN	20.6	24.0	22.9	23.4	13.6	13.0	12.9
SD	2.71	2.98	3.14	3.73	2.03	2.31	1.97
N	10	10	10	9	10	10	10

GROUP: 18.0:18.0 mg base/kg/day							
921	--	--	--	--	--	--	--
922	--	--	--	39.7	22.2	13.7	14.7
923	29.0	24.5	18.0	19.5	28.4	17.3	18.9
924	--	--	--	--	--	--	--
925	--	--	--	--	--	--	--
926	--	--	--	--	--	--	--
927	37.5	28.5	26.7	34.7	19.6	16.3	14.5
928	--	--	--	--	--	--	--
929	28.4	27.0	21.5	26.2	13.7	10.0	10.9
930	23.5	20.8	23.5	30.8	23.0	15.7	15.8
931	--	--	--	--	--	--	--
932	--	23.8	23.7	21.5	16.2	16.1	15.5
933	16.6	23.6	20.1	16.6	16.5	13.9	11.6
934	39.0	22.8	22.5	--	--	--	--
935	21.9	23.5	19.2	34.6	17.9	16.9	11.8
936	--	--	--	--	--	--	--
937	20.6	--	--	--	--	--	--
938	--	--	--	--	--	--	--
939	30.3	24.2	21.5	25.9	10.7	12.1	11.6
940	33.5	26.5	28.5	26.5	17.7	11.9	14.4
MEAN	28.0	24.5	22.5	27.6	18.6	14.4	14.0
SD	7.38	2.24	3.25	7.35	5.02	2.46	2.50
N	10	10	10	10	10	10	10

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

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

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: M. Neutrophils

STUDY ID: 098  
ABBR: M. Neutrop

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

ANIMAL ID    Week 2    Week 4    Week 8    Week 13    Week 16    Week 21    Week 27

GROUP: 0:0 mg base/kg/day

801	1.1	1.1	2.2	1.5	1.4	1.5	1.0
802	1.1	1.3	1.7	2.5	1.3	1.1	1.8
803	--	--	--	--	--	--	--
804	--	--	--	--	--	--	--
805	--	--	--	--	--	--	--
806	2.6	1.4	2.1	3.1	1.3	1.5	1.0
807	0.9	1.8	2.7	1.6	1.0	1.5	1.8
808	--	--	--	--	--	--	--
809	1.8	1.0	2.7	1.8	1.3	2.1	1.5
810	2.9	2.0	0.8	1.8	1.8	1.8	3.3
811	1.5	1.6	2.0	1.6	2.3	1.6	2.1
812	--	--	--	1.0	--	--	--
813	--	--	--	--	--	--	--
814	1.1	0.3	6.9	3.0	1.0	0.6	0.9
815	1.4	2.1	1.3	0.4	0.4	1.0	1.3
816	1.6	1.2	1.5	1.9	1.4	1.1	1.9
817	--	--	--	--	--	--	--
818	--	--	--	--	--	--	--
819	--	--	--	--	--	--	--
820	--	--	--	--	--	--	--
MEAN	1.6	1.4	2.4	1.8	1.3	1.4	1.7
SD	0.67	0.53	1.69	0.80	0.50	0.43	0.71
N	10	10	10	11	10	10	10

GROUP: 0.5:0.5 mg base/kg/day

841	--	--	--	--	--	--	--
842	--	--	--	--	--	--	--
843	--	--	--	--	--	--	--
844	3.0	2.0	0.5	1.7	1.7	2.4	1.5
845	--	--	--	--	--	--	--
846	0.7	1.8	1.6	2.3	0.4	1.6	2.7
847	--	--	--	--	--	--	--
848	1.1	1.7	1.2	1.3	1.0	1.3	1.3
849	--	--	--	--	--	--	--
850	2.7	1.5	2.6	2.1	1.5	14.0	1.0
851	2.0	2.2	1.3	2.1	0.8	1.8	1.8
852	0.8	1.7	3.0	2.7	0.8	1.7	3.7
853	2.8	0.4	1.6	1.8	1.9	1.3	1.7
854	--	--	--	--	--	--	--
855	--	--	--	--	--	--	--
856	--	--	--	--	--	--	--
857	--	--	--	--	--	--	--
858	2.0	2.4	2.3	2.4	1.0	1.0	2.0
859	1.9	1.2	0.8	1.2	1.6	0.6	0.6
860	1.6	1.1	1.8	2.7	1.5	2.0	6.4
MEAN	1.9	1.6	1.7	2.0	1.2	2.8	2.3
SD	0.82	0.58	0.78	0.53	0.48	3.98	1.69
N	10	10	10	10	10	10	10

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: M. Neutrophils

STUOY ID: 098  
ABBR: M. Neutrop

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

ANIMAL IO	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
881	--	--	--	--	--	--	--
882	--	--	--	--	--	--	--
883	--	--	--	--	--	--	--
884	3.9	2.7	3.0	2.6	1.4	1.5	0.4
885	--	--	--	--	--	--	--
886	--	--	--	--	--	--	--
887	4.2	4.4	2.8	--	1.8	0.6	1.6
888	--	--	--	--	--	--	--
889	1.3	2.4	2.4	2.4	1.5	1.0	1.8
890	2.5	3.7	4.5	2.6	2.5	1.8	2.1
891	--	--	--	--	--	--	--
892	--	--	--	--	--	--	--
893	3.1	2.1	3.2	3.7	2.0	1.3	2.7
894	--	--	--	--	--	--	--
895	1.5	4.6	2.3	4.5	3.2	1.4	2.0
896	3.0	4.8	3.1	3.3	2.2	0.6	1.0
897	1.8	2.4	3.1	3.3	1.3	1.5	2.6
898	--	--	--	--	--	--	--
899	2.0	1.9	2.2	3.2	0.9	1.9	2.2
900	1.6	4.5	2.2	3.6	2.6	1.7	1.2
MEAN	2.5	3.4	2.9	3.2	1.9	1.3	1.8
SD	1.02	1.16	0.69	0.66	0.70	0.46	0.72
N	10	10	10	9	10	10	10

GROUP: 18.0:18.0 mg base/kg/day							
921	--	--	--	--	--	--	--
922	--	--	--	4.8	4.2	1.2	3.1
923	6.1	3.4	2.2	5.5	2.3	1.9	2.8
924	--	--	--	--	--	--	--
925	--	--	--	--	--	--	--
926	--	--	--	--	--	--	--
927	5.3	2.9	2.4	5.6	2.5	1.1	2.5
928	--	--	--	--	--	--	--
929	3.1	2.7	1.5	3.4	1.0	0.3	0.7
930	3.5	1.7	4.2	5.9	18.6	1.9	2.2
931	--	--	--	--	--	--	--
932	--	2.9	4.7	4.5	3.4	3.1	2.5
933	2.3	3.1	6.2	3.7	2.3	1.9	1.9
934	5.1	2.5	2.7	--	--	--	--
935	3.1	1.9	2.3	3.8	3.0	1.4	1.2
936	--	--	--	--	--	--	--
937	11.5	--	--	--	--	--	--
938	--	--	--	--	--	--	--
939	5.2	1.7	3.0	3.9	2.1	2.8	0.3
940	11.1	0.8	1.7	4.5	1.9	1.0	0.9
MEAN	5.6	2.4	3.1	4.6	4.1	1.7	1.8
SD	3.22	0.81	1.49	0.88	5.16	0.84	0.97
N	10	10	10	10	10	10	10

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

DRAFT

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: I. Neutrophils

STUDY ID: 098  
ABBR: I. Neutrop

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

ANIMAL ID    Week 2    Week 4    Week 8    Week 13    Week 16    Week 21    Week 27

GROUP: 0:0 mg base/kg/day

801	0.0	0.0	0.0	0.0	0.0	0.0	0.0
802	0.0	0.0	0.0	0.0	0.0	0.0	0.0
803	--	--	--	--	--	--	--
804	--	--	--	--	--	--	--
805	--	--	--	--	--	--	--
806	0.0	0.0	0.0	0.0	0.0	0.0	0.0
807	0.0	0.0	0.0	0.0	0.0	0.0	0.0
808	--	--	--	--	--	--	--
809	0.0	0.0	0.0	0.0	0.0	0.0	0.0
810	0.0	0.0	0.0	0.0	0.0	0.0	0.0
811	0.0	0.0	0.0	0.0	0.0	0.0	0.0
812	--	--	--	0.0	--	--	--
813	--	--	--	--	--	--	--
814	0.0	0.0	0.0	0.0	0.0	0.0	0.0
815	0.0	0.0	0.0	0.0	0.0	0.0	0.0
816	0.0	0.0	0.0	0.0	0.0	0.0	0.0
817	--	--	--	--	--	--	--
818	--	--	--	--	--	--	--
819	--	--	--	--	--	--	--
820	--	--	--	--	--	--	--
MEAN	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
N	10	10	10	11	10	10	10

GROUP: 0.5:0.5 mg base/kg/day

841	--	--	--	--	--	--	--
842	--	--	--	--	--	--	--
843	--	--	--	--	--	--	--
844	0.0	0.0	0.0	0.0	0.0	0.0	0.0
845	--	--	--	--	--	--	--
846	0.0	0.0	0.0	0.0	0.0	0.0	0.0
847	--	--	--	--	--	--	--
848	0.0	0.0	0.0	0.0	0.0	0.0	0.0
849	--	--	--	--	--	--	--
850	0.0	0.0	0.0	0.0	0.0	0.0	0.0
851	0.0	0.0	0.0	0.0	0.0	0.0	0.0
852	0.0	0.1	0.0	0.0	0.0	0.0	0.0
853	0.0	0.1	0.0	0.0	0.0	0.0	0.0
854	--	--	--	--	--	--	--
855	--	--	--	--	--	--	--
856	--	--	--	--	--	--	--
857	--	--	--	--	--	--	--
858	0.0	0.0	0.0	0.0	0.0	0.0	0.0
859	0.0	0.0	0.0	0.0	0.0	0.0	0.0
860	0.0	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
SD	0.00	0.04	0.00	0.00	0.00	0.00	0.00
N	10	10	10	10	10	10	10

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

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

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: I. Neutrophils

STUDY ID: 098  
ABBR: I. Neutrop

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
881	--	--	--	--	--	--	--
882	--	--	--	--	--	--	--
883	--	--	--	--	--	--	--
884	0.0	0.0	0.0	0.0	0.0	0.0	0.0
885	--	--	--	--	--	--	--
886	--	--	--	--	--	--	--
887	0.0	0.0	0.0	--	0.0	0.0	0.0
888	--	--	--	--	--	--	--
889	0.0	0.0	0.0	0.0	0.0	0.0	0.0
890	0.0	0.0	0.0	0.0	0.0	0.0	0.0
891	--	--	--	--	--	--	--
892	--	--	--	--	--	--	--
893	0.0	0.0	0.0	0.0	0.0	0.0	0.0
894	--	--	--	--	--	--	--
895	0.0	0.0	0.0	0.0	0.0	0.0	0.0
896	0.0	0.0	0.0	0.0	0.0	0.0	0.0
897	0.0	0.0	0.0	0.0	0.0	0.0	0.0
898	--	--	--	--	--	--	--
899	0.0	0.0	0.0	0.0	0.0	0.0	0.0
900	0.0	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
SD	0.00	0.00	0.00	0.00	0.00	0.00	0.00
N	10	10	10	9	10	10	10

GROUP: 18.0:18.0 mg base/kg/day							
921	--	--	--	--	--	--	--
922	--	--	--	0.0	0.0	0.0	0.0
923	0.0	0.0	0.0	0.0	0.0	0.0	0.0
924	--	--	--	--	--	--	--
925	--	--	--	--	--	--	--
926	--	--	--	--	--	--	--
927	0.0	0.0	0.0	0.0	0.0	0.0	0.0
928	--	--	--	--	--	--	--
929	0.0	0.0	0.0	0.0	0.0	0.0	0.0
930	0.0	0.0	0.0	0.0	0.0	0.0	0.0
931	--	--	--	--	--	--	--
932	--	0.0	0.0	0.0	0.0	0.0	0.0
933	0.0	0.0	0.0	0.0	0.0	0.0	0.0
934	0.0	0.0	0.0	--	--	--	--
935	0.0	0.0	0.0	0.0	0.0	0.0	0.0
936	--	--	--	--	--	--	--
937	0.0	--	--	--	--	--	--
938	--	--	--	--	--	--	--
939	0.0	0.0	0.0	0.0	0.0	0.0	0.0
940	0.0	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
SD	0.00	0.00	0.00	0.00	0.00	0.00	0.00
N	10	10	10	10	10	10	10

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

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

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Lymphocytes

STUDY ID: 098  
ABBR: Lymphocyte

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
801	12.2	12.0	10.3	10.2	9.7	12.1	7.5
802	12.0	13.0	12.6	8.5	9.3	6.8	10.0
803	--	--	--	--	--	--	--
804	--	--	--	--	--	--	--
805	--	--	--	--	--	--	--
806	15.7	19.0	11.7	11.2	11.3	11.6	11.3
807	16.4	14.2	14.2	12.2	13.1	11.0	10.8
808	--	--	--	--	--	--	--
809	24.0	19.1	17.1	14.1	14.5	12.8	14.5
810	16.1	20.3	18.5	14.2	15.0	17.2	12.5
811	11.0	12.7	9.1	10.0	9.5	9.7	8.1
812	--	--	--	10.5	--	--	--
813	--	--	--	--	--	--	--
814	14.0	12.0	11.4	8.6	7.9	9.6	10.2
815	18.4	17.4	16.4	16.2	16.9	18.0	11.5
816	17.8	18.4	13.1	12.2	11.9	11.5	9.2
817	--	--	--	--	--	--	--
818	--	--	--	--	--	--	--
819	--	--	--	--	--	--	--
820	--	--	--	--	--	--	--
MEAN	15.8	15.8	13.4	11.6	11.9	12.0	10.6
SD	3.83	3.33	3.07	2.44	2.92	3.39	2.07
N	10	10	10	11	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
841	--	--	--	--	--	--	--
842	--	--	--	--	--	--	--
843	--	--	--	--	--	--	--
844	17.9	8.7	8.9	12.7	5.7	11.5	8.4
845	--	--	--	--	--	--	--
846	22.8	20.7	16.7	14.9	13.7	13.0	11.0
847	--	--	--	--	--	--	--
848	14.2	9.8	12.6	13.0	8.6	10.8	9.9
849	--	--	--	--	--	--	--
850	17.6	16.9	15.7	15.1	12.2	1.1	14.6
851	12.9	14.4	12.2	7.9	10.1	10.1	12.5
852	14.2	11.9	13.1	10.9	10.0	10.7	10.5
853	10.2	9.5	10.3	8.8	8.8	8.7	7.5
854	--	--	--	--	--	--	--
855	--	--	--	--	--	--	--
856	--	--	--	--	--	--	--
857	--	--	--	--	--	--	--
858	16.8	17.2	17.5	13.2	10.8	11.8	11.1
859	11.7	12.0	11.6	9.0	9.6	9.7	9.2
860	24.9	16.6	19.7	15.9	15.5	17.1	16.7
MEAN	16.3	13.8	13.8	12.1	10.5	10.5	11.1
SD	4.71	4.00	3.43	2.85	2.77	4.01	2.81
N	10	10	10	10	10	10	10

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

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

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Lymphocytes

STUDY ID: 098  
ABBR: Lymphocyte

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
881	--	--	--	--	--	--	--
882	--	--	--	--	--	--	--
883	--	--	--	--	--	--	--
884	16.7	22.7	20.3	18.1	11.3	11.8	9.9
885	--	--	--	--	--	--	--
886	--	--	--	--	--	--	--
887	15.7	17.0	18.2	--	8.4	8.2	9.9
888	--	--	--	--	--	--	--
889	14.3	22.6	16.4	21.2	11.8	12.8	9.8
890	19.6	15.7	18.1	17.0	10.1	14.3	13.9
891	--	--	--	--	--	--	--
892	--	--	--	--	--	--	--
893	19.0	17.0	14.0	12.7	8.2	9.9	9.4
894	--	--	--	--	--	--	--
895	22.6	18.8	20.6	22.7	14.2	12.9	11.8
896	16.7	14.7	17.3	20.7	10.1	8.9	9.1
897	15.1	20.8	23.7	22.1	13.7	11.8	10.7
898	--	--	--	--	--	--	--
899	19.3	21.9	17.8	18.8	11.1	11.0	10.0
900	14.9	18.8	18.9	15.8	11.0	9.8	8.7
MEAN	17.4	19.0	18.5	18.8	11.0	11.1	10.3
SD	2.65	2.90	2.62	3.27	1.96	1.94	1.52
N	10	10	10	9	10	10	10

GROUP: 18.0:18.0 mg base/kg/day							
921	--	--	--	--	--	--	--
922	--	--	--	31.0	16.9	12.2	11.3
923	21.5	18.4	14.8	12.3	23.9	14.7	14.7
924	--	--	--	--	--	--	--
925	--	--	--	--	--	--	--
926	--	--	--	--	--	--	--
927	31.5	23.7	21.6	25.3	16.3	14.5	11.6
928	--	--	--	--	--	--	--
929	23.0	16.5	17.6	21.5	11.1	8.9	9.9
930	20.0	15.8	16.2	22.5	2.1	13.3	12.6
931	--	--	--	--	--	--	--
932	--	18.8	15.9	14.8	11.8	12.6	12.4
933	12.1	18.9	12.5	10.6	13.4	11.7	8.8
934	33.2	18.0	18.0	--	--	--	--
935	16.9	21.4	15.4	28.0	14.3	14.5	10.1
936	--	--	--	--	--	--	--
937	8.0	--	--	--	--	--	--
938	--	--	--	--	--	--	--
939	21.8	15.7	15.5	18.6	7.5	8.7	10.9
940	22.4	19.3	23.9	17.2	15.4	10.7	13.0
MEAN	21.0	18.7	17.1	20.2	13.3	12.2	11.5
SD	7.69	2.48	3.36	6.71	5.83	2.21	1.72
N	10	10	10	10	10	10	10

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

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

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Monocytes

STUDY ID: 098  
ABBR: Monocytes

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
801	0.7	0.3	0.3	1.0	0.2	0.1	0.5
802	0.5	0.4	1.2	0.7	0.7	0.7	0.1
803	--	--	--	--	--	--	--
804	--	--	--	--	--	--	--
805	--	--	--	--	--	--	--
806	0.6	0.2	1.4	0.4	0.4	0.0	0.4
807	0.0	0.3	1.1	0.4	0.4	0.5	0.3
808	--	--	--	--	--	--	--
809	0.3	0.2	0.6	0.2	0.7	1.0	0.5
810	0.2	0.0	0.8	0.3	1.1	0.2	0.5
811	0.4	0.1	1.5	0.2	0.4	0.9	1.0
812	--	--	--	0.7	--	--	--
813	--	--	--	--	--	--	--
814	0.2	0.3	0.8	1.0	0.1	1.0	0.4
815	0.2	1.0	0.5	1.4	0.9	0.2	0.4
816	0.4	0.0	0.1	0.1	0.1	0.8	0.4
817	--	--	--	--	--	--	--
818	--	--	--	--	--	--	--
819	--	--	--	--	--	--	--
820	--	--	--	--	--	--	--
MEAN	0.4	0.3	0.8	0.6	0.5	0.5	0.5
SD	0.21	0.29	0.47	0.41	0.34	0.39	0.23
N	10	10	10	11	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
841	--	--	--	--	--	--	--
842	--	--	--	--	--	--	--
843	--	--	--	--	--	--	--
844	1.8	0.3	1.1	0.8	0.9	0.1	0.2
845	--	--	--	--	--	--	--
846	0.5	0.2	1.6	0.2	0.6	0.6	1.0
847	--	--	--	--	--	--	--
848	0.2	0.6	0.7	0.1	0.1	0.4	0.3
849	--	--	--	--	--	--	--
850	0.2	0.2	1.4	0.2	1.4	0.5	0.8
851	0.8	0.3	0.4	0.4	0.8	0.1	0.3
852	1.0	0.1	1.6	0.4	0.5	0.5	1.2
853	0.3	0.3	0.4	0.6	0.2	0.6	0.8
854	--	--	--	--	--	--	--
855	--	--	--	--	--	--	--
856	--	--	--	--	--	--	--
857	--	--	--	--	--	--	--
858	0.8	0.4	0.8	0.3	0.5	0.6	0.0
859	0.7	0.3	0.5	0.4	1.1	0.2	0.0
860	0.3	0.2	1.1	0.6	1.5	0.6	1.0
MEAN	0.7	0.3	1.0	0.4	0.8	0.4	0.6
SD	0.49	0.14	0.47	0.22	0.47	0.21	0.45
N	10	10	10	10	10	10	10

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

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

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Monocytes

STUDY ID: 098  
ABBR: Monocytes

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
881	--	--	--	--	--	--	--
882	--	--	--	--	--	--	--
883	--	--	--	--	--	--	--
884	0.7	1.6	1.2	1.1	0.0	0.3	0.1
885	--	--	--	--	--	--	--
886	--	--	--	--	--	--	--
887	1.3	0.2	0.4	--	0.8	0.4	1.3
888	--	--	--	--	--	--	--
889	0.5	1.9	0.8	0.5	0.3	0.1	0.5
890	0.2	0.8	0.7	0.4	0.4	0.2	0.3
891	--	--	--	--	--	--	--
892	--	--	--	--	--	--	--
893	0.2	1.2	0.4	1.2	1.0	0.7	1.5
894	--	--	--	--	--	--	--
895	1.0	2.1	2.8	2.7	0.4	1.1	1.2
896	0.4	0.4	1.6	1.3	0.3	0.1	0.1
897	1.1	2.9	1.4	1.9	0.6	1.3	0.4
898	--	--	--	--	--	--	--
899	0.4	0.5	1.5	0.7	0.6	0.7	0.7
900	0.9	2.9	2.9	2.7	0.9	0.4	1.0
MEAN	0.7	1.5	1.4	1.4	0.5	0.5	0.7
SD	0.39	0.99	0.89	0.87	0.31	0.41	0.51
N	10	10	10	9	10	10	10

GROUP: 18.0:18.0 mg base/kg/day							
921	--	--	--	--	--	--	--
922	--	--	--	4.0	0.9	0.1	0.1
923	1.5	2.7	1.1	1.8	2.3	0.3	1.1
924	--	--	--	--	--	--	--
925	--	--	--	--	--	--	--
926	--	--	--	--	--	--	--
927	0.8	1.7	2.7	3.8	0.6	0.5	0.1
928	--	--	--	--	--	--	--
929	2.0	7.8	2.4	1.3	1.6	0.7	0.2
930	0.0	3.3	2.6	2.5	2.3	0.5	0.6
931	--	--	--	--	--	--	--
932	--	2.1	2.8	2.2	0.8	0.2	0.6
933	2.2	1.4	1.4	2.3	0.8	0.1	0.8
934	0.8	2.3	1.6	--	--	--	--
935	1.8	0.2	1.5	2.8	0.5	1.0	0.5
936	--	--	--	--	--	--	--
937	1.0	--	--	--	--	--	--
938	--	--	--	--	--	--	--
939	3.3	6.5	2.8	3.4	1.0	0.5	0.3
940	0.0	6.4	2.9	4.8	0.2	0.2	0.6
MEAN	1.3	3.4	2.2	2.9	1.1	0.4	0.5
SD	1.03	2.55	0.70	1.09	0.73	0.29	0.32
N	10	10	10	10	10	10	10

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

DRAFT

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Eosinophils

STUDY ID: 098  
ABBR: Eosinophil

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
801	0.0	0.1	0.1	0.0	0.1	0.0	0.1
802	0.0	0.1	0.0	0.1	0.1	0.0	0.1
803	--	--	--	--	--	--	--
804	--	--	--	--	--	--	--
805	--	--	--	--	--	--	--
806	0.0	0.0	0.0	0.0	0.0	0.1	0.3
807	0.2	0.0	0.2	0.4	0.0	0.3	0.1
808	--	--	--	--	--	--	--
809	0.0	0.4	0.4	0.3	0.0	0.3	0.5
810	0.2	0.0	0.0	0.2	0.0	0.4	0.2
811	0.0	0.0	0.1	0.2	0.1	0.2	0.0
812	--	--	--	0.0	--	--	--
813	--	--	--	--	--	--	--
814	0.2	0.1	0.6	0.0	0.3	0.0	0.2
815	0.0	0.0	0.0	0.0	0.0	0.0	0.1
816	0.0	0.0	0.1	0.1	0.1	0.3	0.2
817	--	--	--	--	--	--	--
818	--	--	--	--	--	--	--
819	--	--	--	--	--	--	--
820	--	--	--	--	--	--	--
MEAN	0.1	0.1	0.2	0.1	0.1	0.2	0.2
SD	0.10	0.13	0.20	0.14	0.09	0.16	0.14
N	10	10	10	11	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
841	--	--	--	--	--	--	--
842	--	--	--	--	--	--	--
843	--	--	--	--	--	--	--
844	0.2	0.1	0.1	0.2	0.3	0.1	0.1
845	--	--	--	--	--	--	--
846	0.0	0.0	0.0	0.2	0.0	0.3	0.1
847	--	--	--	--	--	--	--
848	0.8	0.0	0.3	0.1	0.1	0.1	0.1
849	--	--	--	--	--	--	--
850	0.4	0.4	0.4	0.0	0.3	0.0	0.2
851	0.0	0.2	0.0	0.0	0.1	0.2	0.3
852	0.0	0.6	0.2	0.1	0.1	0.4	0.0
853	0.0	0.0	0.1	0.0	0.0	0.0	0.0
854	--	--	--	--	--	--	--
855	--	--	--	--	--	--	--
856	--	--	--	--	--	--	--
857	--	--	--	--	--	--	--
858	0.6	0.0	0.2	0.2	0.3	0.6	0.0
859	0.1	0.0	0.1	0.3	0.0	0.1	0.1
860	0.3	0.0	0.0	0.0	0.0	0.2	0.5
MEAN	0.2	0.1	0.1	0.1	0.1	0.2	0.1
SD	0.28	0.21	0.13	0.11	0.13	0.19	0.16
N	10	10	10	10	10	10	10

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

DRAFT

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Eosinophils

STUDY ID: 098  
ABBR: Eosinophil

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
881	--	--	--	--	--	--	--
882	--	--	--	--	--	--	--
883	--	--	--	--	--	--	--
884	0.4	0.3	0.2	0.0	0.1	0.1	0.1
885	--	--	--	--	--	--	--
886	--	--	--	--	--	--	--
887	0.0	0.2	0.0	--	0.2	0.0	0.3
888	--	--	--	--	--	--	--
889	0.0	0.3	0.2	0.0	0.1	0.0	0.0
890	0.0	0.4	0.2	0.0	0.4	0.0	0.0
891	--	--	--	--	--	--	--
892	--	--	--	--	--	--	--
893	0.0	0.4	0.0	0.0	0.0	0.0	0.0
894	--	--	--	--	--	--	--
895	0.0	0.3	0.0	0.0	0.0	0.0	0.2
896	0.0	0.0	0.2	0.0	0.3	0.0	0.1
897	0.2	0.3	0.3	0.0	0.2	0.0	0.0
898	--	--	--	--	--	--	--
899	0.0	0.0	0.0	0.0	0.0	0.0	0.1
900	0.0	0.3	0.2	0.2	0.1	0.1	0.1
MEAN	0.1	0.3	0.1	0.0	0.1	0.0	0.1
SD	0.13	0.14	0.12	0.07	0.13	0.04	0.10
N	10	10	10	9	10	10	10

GROUP: 18.0:18.0 mg base/kg/day							
921	--	--	--	--	--	--	--
922	--	--	--	0.0	0.2	0.1	0.1
923	0.0	0.0	0.0	0.0	0.0	0.3	0.2
924	--	--	--	--	--	--	--
925	--	--	--	--	--	--	--
926	--	--	--	--	--	--	--
927	0.0	0.3	0.0	0.0	0.2	0.2	0.3
928	--	--	--	--	--	--	--
929	0.3	0.0	0.0	0.0	0.0	0.1	0.1
930	0.0	0.0	0.5	0.0	0.0	0.0	0.3
931	--	--	--	--	--	--	--
932	--	0.0	0.2	0.0	0.2	0.3	0.0
933	0.0	0.2	0.0	0.0	0.0	0.1	0.1
934	0.0	0.0	0.2	--	--	--	--
935	0.2	0.0	0.0	0.0	0.0	0.0	0.0
936	--	--	--	--	--	--	--
937	0.0	--	--	--	--	--	--
938	--	--	--	--	--	--	--
939	0.0	0.2	0.2	0.0	0.1	0.1	0.0
940	0.0	0.0	0.0	0.0	0.2	0.0	0.0
MEAN	0.1	0.1	0.1	0.0	0.1	0.1	0.1
SD	0.11	0.12	0.17	0.00	0.10	0.11	0.12
N	10	10	10	10	10	10	10

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

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

D R A F T

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Basophils

STUDY ID: 098  
ABBR: Basophils

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
801	0.0	0.0	0.0	0.0	0.0	0.0	0.0
802	0.0	0.0	0.0	0.0	0.0	0.0	0.0
803	--	--	--	--	--	--	--
804	--	--	--	--	--	--	--
805	--	--	--	--	--	--	--
806	0.0	0.0	0.0	0.0	0.0	0.0	0.0
807	0.0	0.0	0.0	0.0	0.0	0.0	0.0
808	--	--	--	--	--	--	--
809	0.0	0.0	0.0	0.0	0.0	0.0	0.0
810	0.0	0.0	0.0	0.0	0.0	0.0	0.0
811	0.0	0.0	0.0	0.0	0.0	0.0	0.0
812	--	--	--	0.0	--	--	--
813	--	--	--	--	--	--	--
814	0.0	0.0	0.0	0.0	0.0	0.0	0.0
815	0.0	0.0	0.0	0.0	0.0	0.0	0.0
816	0.0	0.0	0.0	0.0	0.0	0.0	0.0
817	--	--	--	--	--	--	--
818	--	--	--	--	--	--	--
819	--	--	--	--	--	--	--
820	--	--	--	--	--	--	--
MEAN	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
N	10	10	10	11	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
841	--	--	--	--	--	--	--
842	--	--	--	--	--	--	--
843	--	--	--	--	--	--	--
844	0.0	0.0	0.0	0.0	0.0	0.0	0.0
845	--	--	--	--	--	--	--
846	0.0	0.0	0.0	0.0	0.0	0.0	0.0
847	--	--	--	--	--	--	--
848	0.0	0.0	0.0	0.0	0.0	0.0	0.0
849	--	--	--	--	--	--	--
850	0.0	0.0	0.0	0.0	0.0	0.0	0.0
851	0.0	0.0	0.0	0.0	0.0	0.0	0.0
852	0.0	0.0	0.0	0.0	0.0	0.0	0.0
853	0.0	0.0	0.0	0.0	0.0	0.0	0.0
854	--	--	--	--	--	--	--
855	--	--	--	--	--	--	--
856	--	--	--	--	--	--	--
857	--	--	--	--	--	--	--
858	0.0	0.0	0.0	0.0	0.0	0.0	0.0
859	0.0	0.0	0.0	0.0	0.0	0.0	0.0
860	0.0	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
SD	0.00	0.00	0.00	0.00	0.00	0.00	0.00
N	10	10	10	10	10	10	10

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

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

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Basophils

STUDY ID: 098  
ABBR: Basophils

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
881	--	--	--	--	--	--	--
882	--	--	--	--	--	--	--
883	--	--	--	--	--	--	--
884	0.0	0.0	0.0	0.0	0.0	0.0	0.0
885	--	--	--	--	--	--	--
886	--	--	--	--	--	--	--
887	0.0	0.0	0.0	--	0.0	0.0	0.0
888	--	--	--	--	--	--	--
889	0.0	0.0	0.0	0.0	0.0	0.0	0.0
890	0.0	0.0	0.0	0.0	0.0	0.0	0.0
891	--	--	--	--	--	--	--
892	--	--	--	--	--	--	--
893	0.0	0.0	0.0	0.0	0.0	0.0	0.0
894	--	--	--	--	--	--	--
895	0.0	0.0	0.0	0.0	0.0	0.0	0.0
896	0.0	0.0	0.0	0.0	0.0	0.0	0.0
897	0.0	0.0	0.0	0.0	0.0	0.0	0.0
898	--	--	--	--	--	--	--
899	0.0	0.0	0.0	0.0	0.0	0.0	0.0
900	0.0	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
SD	0.00	0.00	0.00	0.00	0.00	0.00	0.00
N	10	10	10	9	10	10	10

GROUP: 18.0:18.0 mg base/kg/day							
921	--	--	--	--	--	--	--
922	--	--	--	0.0	0.0	0.0	0.0
923	0.0	0.0	0.0	0.0	0.0	0.0	0.0
924	--	--	--	--	--	--	--
925	--	--	--	--	--	--	--
926	--	--	--	--	--	--	--
927	0.0	0.0	0.0	0.0	0.0	0.0	0.0
928	--	--	--	--	--	--	--
929	0.0	0.0	0.0	0.0	0.0	0.0	0.0
930	0.0	0.0	0.0	0.0	0.0	0.0	0.0
931	--	--	--	--	--	--	--
932	--	0.0	0.0	0.0	0.0	0.0	0.0
933	0.0	0.0	0.0	0.0	0.0	0.0	0.0
934	0.0	0.0	0.0	--	--	--	--
935	0.0	0.0	0.0	0.0	0.0	0.0	0.0
936	--	--	--	--	--	--	--
937	0.0	--	--	--	--	--	--
938	--	--	--	--	--	--	--
939	0.0	0.0	0.0	0.0	0.0	0.0	0.0
940	0.0	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
SD	0.00	0.00	0.00	0.00	0.00	0.00	0.00
N	10	10	10	10	10	10	10

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

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

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Erythrocytes

STUDY ID: 098  
ABBR: RBC

SEX: FEMALE  
UNITS: 10<sup>6</sup>/cm<sup>3</sup>

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
821	--	--	--	--	--	--	--
822	--	--	--	--	--	--	--
823	7.55	7.25	8.06	8.20	8.04	8.68	8.50
824	6.72	6.83	7.66	--	6.85	7.61	7.30
825	--	--	--	--	--	--	--
826	--	--	--	--	--	--	--
827	7.45	7.49	7.68	7.97	7.54	8.14	7.22
828	--	--	--	--	--	--	--
829	--	--	--	--	--	--	--
830	7.00	7.00	7.91	7.61	8.04	8.07	8.11
831	7.06	7.12	7.66	7.49	7.42	7.78	7.49
832	--	--	--	--	--	--	--
833	--	--	--	--	--	--	--
834	7.33	7.76	7.76	8.28	8.00	8.50	8.16
835	7.30	7.61	7.94	7.97	7.79	8.49	7.66
836	7.15	7.25	7.89	7.95	7.68	8.16	8.00
837	7.76	7.98	7.90	7.43	7.80	7.80	7.78
838	--	--	--	--	--	--	--
839	--	--	--	--	--	--	--
840	7.43	7.56	8.09	7.93	7.64	7.89	7.76
MEAN	7.28	7.39	7.86	7.87	7.68	8.11	7.80
SD	0.301	0.357	0.159	0.298	0.360	0.354	0.403
N	10	10	10	9	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
861	7.66	7.63	8.57	7.93	7.18	7.92	7.92
862	--	--	--	--	--	--	--
863	--	--	--	--	--	--	--
864	7.19	7.93	7.95	8.19	7.42	7.69	7.50
865	--	--	--	--	--	--	--
866	--	--	--	--	--	--	--
867	6.78	7.27	7.64	7.58	7.56	8.11	7.22
868	6.79	7.83	8.23	8.02	--	8.50	8.05
869	--	--	--	--	--	--	--
870	--	--	--	--	--	--	--
871	6.95	6.77	7.64	6.97	6.80	7.36	7.73
872	--	--	--	--	--	--	--
873	6.82	6.91	7.64	7.33	7.07	7.89	6.87
874	6.42	7.56	7.56	7.09	7.47	7.85	7.23
875	--	--	--	--	--	--	--
876	--	--	--	--	--	--	--
877	7.29	7.16	7.76	7.72	7.69	8.14	7.86
878	--	--	--	--	--	--	--
879	7.28	7.39	7.83	8.12	7.95	8.42	8.28
880	7.19	6.91	6.79	7.84	7.68	7.84	7.51
MEAN	7.04	7.34	7.76	7.68	7.42	7.97	7.62
SD	0.353	0.402	0.465	0.427	0.355	0.337	0.432
N	10	10	10	10	9	10	10

(--)-Data Unavailable

DRAFT

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Erythrocytes

STUDY ID: 098  
ABBR: RBC

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
901	6.88	6.54	7.34	7.04	7.27	8.00	7.80
902	7.16	7.37	7.06	7.34	7.28	7.58	7.61
903	--	--	--	--	--	--	--
904	7.19	7.02	7.94	7.30	--	8.49	7.73
905	--	--	--	--	--	--	--
906	--	--	--	--	--	--	--
907	--	--	--	--	--	--	--
908	6.94	6.93	7.11	8.16	7.33	8.00	7.94
909	7.07	7.36	7.65	7.19	8.02	8.58	8.16
910	--	--	--	--	--	--	--
911	--	--	--	--	--	--	--
912	7.09	7.39	6.93	--	7.99	8.04	7.86
913	--	--	--	--	--	--	--
914	--	--	--	--	--	--	--
915	6.94	6.80	7.50	6.98	7.32	7.65	7.48
916	7.37	6.71	7.05	6.93	7.56	7.79	7.37
917	--	--	--	--	--	--	--
918	6.32	6.64	6.70	6.71	6.00	7.66	7.19
919	6.84	6.97	7.32	7.44	7.73	8.25	8.16
920	--	--	--	--	--	--	--
MEAN	6.98	6.97	7.26	7.23	7.39	8.00	7.73
SD	0.282	0.313	0.367	0.416	0.599	0.349	0.322
N	10	10	10	9	9	10	10

GROUP: 18.0:18.0 mg base/kg/day							
941	5.65	6.65	7.94	6.56	7.07	8.27	7.51
942	6.01	6.43	7.01	6.83	6.94	8.59	7.70
943	--	--	--	--	--	--	--
944	6.19	6.83	7.56	6.92	7.75	8.33	8.54
945	--	--	--	--	--	--	--
946	--	--	--	--	--	--	--
947	--	--	--	--	--	--	--
948	--	--	--	--	--	--	--
949	6.59	6.55	7.35	7.63	7.94	8.16	7.94
950	--	--	--	--	--	--	--
951	--	--	--	--	--	--	--
952	--	--	--	--	--	--	--
953	6.01	7.35	7.25	5.25	7.39	8.26	7.44
954	6.18	7.00	7.55	7.25	7.61	8.46	7.98
955	--	--	--	--	--	--	--
956	6.69	6.87	8.14	5.92	7.79	--	--
957	5.79	7.13	8.04	7.56	7.99	8.56	7.83
958	--	--	--	--	--	--	--
959	6.07	6.36	7.12	6.98	7.32	7.84	7.13
960	6.70	7.43	7.48	7.57	7.71	8.15	7.86
MEAN	6.19	6.86	7.54	6.85	7.55	8.29	7.77
SD	0.365	0.370	0.388	0.769	0.358	0.233	0.398
N	10	10	10	10	10	9	9

(--)-Data Unavailable

DRAFT

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Hemoglobin

STUDY ID: 098  
ABBR: THGB

SEX: FEMALE  
UNITS: g/dL

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
821	--	--	--	--	--	--	--
822	--	--	--	--	--	--	--
823	15.7	15.3	16.5	16.6	16.8	17.3	16.6
824	15.3	15.1	16.3	--	15.3	16.1	15.8
825	--	--	--	--	--	--	--
826	--	--	--	--	--	--	--
827	16.4	16.0	16.8	15.4	15.1	17.0	15.3
828	--	--	--	--	--	--	--
829	--	--	--	--	--	--	--
830	15.9	15.7	16.5	16.0	17.4	16.8	16.8
831	15.1	15.0	15.3	14.9	15.2	15.4	14.7
832	--	--	--	--	--	--	--
833	--	--	--	--	--	--	--
834	15.5	15.9	15.4	16.5	16.1	16.8	16.0
835	15.7	15.9	17.0	16.1	16.1	16.6	15.8
836	15.8	15.8	16.3	16.8	16.4	16.8	16.1
837	16.6	16.7	16.4	15.4	16.7	16.2	16.3
838	--	--	--	--	--	--	--
839	--	--	--	--	--	--	--
840	15.6	16.0	17.0	16.3	15.8	15.9	16.0
MEAN	15.8	15.7	16.4	16.0	16.1	16.5	15.9
SD	0.46	0.50	0.59	0.64	0.76	0.58	0.61
N	10	10	10	9	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
861	15.9	15.8	17.0	16.0	15.0	15.8	15.5
862	--	--	--	--	--	--	--
863	--	--	--	--	--	--	--
864	15.2	16.5	16.9	16.3	15.1	15.8	15.4
865	--	--	--	--	--	--	--
866	--	--	--	--	--	--	--
867	15.0	15.8	16.4	16.1	16.6	17.2	15.1
868	15.5	17.2	17.9	16.8	--	16.8	17.0
869	--	--	--	--	--	--	--
870	--	--	--	--	--	--	--
871	15.5	15.0	16.5	14.9	15.9	15.3	16.0
872	--	--	--	--	--	--	--
873	15.8	16.0	17.0	16.5	16.3	17.4	16.3
874	13.8	15.8	15.7	14.7	15.5	15.7	14.7
875	--	--	--	--	--	--	--
876	--	--	--	--	--	--	--
877	16.1	15.7	16.3	15.8	16.6	16.8	15.6
878	--	--	--	--	--	--	--
879	15.0	15.2	15.8	15.9	16.1	16.3	16.1
880	15.7	15.1	15.0	15.7	15.8	15.8	15.2
MEAN	15.4	15.8	16.5	15.9	15.9	16.3	15.7
SD	0.66	0.67	0.82	0.65	0.59	0.72	0.67
N	10	10	10	10	9	10	10

(--)-Data Unavailable

DRAFT

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Hemoglobin

STUDY ID: 098  
ABBR: THGB

SEX: FEMALE  
UNITS: g/dL

ANIMAL ID    Week 2    Week 4    Week 8    Week 13    Week 16    Week 21    Week 27

GROUP: 6.0:6.0 mg base/kg/day

901	14.8	14.7	15.7	15.4	16.0	16.6	15.7
902	15.2	15.6	14.9	14.8	15.5	15.2	15.2
903	--	--	--	--	--	--	--
904	15.6	15.1	16.4	15.5	--	17.0	15.7
905	--	--	--	--	--	--	--
906	--	--	--	--	--	--	--
907	--	--	--	--	--	--	--
908	14.6	15.0	15.4	18.1	16.2	16.2	15.7
909	14.9	15.9	15.6	15.2	16.8	16.3	15.9
910	--	--	--	--	--	--	--
911	--	--	--	--	--	--	--
912	15.0	16.1	15.6	--	16.4	15.7	15.3
913	--	--	--	--	--	--	--
914	--	--	--	--	--	--	--
915	15.1	15.6	16.2	15.5	16.3	16.2	15.6
916	16.1	15.4	15.9	15.3	17.0	16.1	15.4
917	--	--	--	--	--	--	--
918	14.4	14.3	14.4	14.5	12.6	16.0	14.6
919	15.0	15.2	15.8	15.6	16.8	16.2	16.1
920	--	--	--	--	--	--	--
MEAN	15.1	15.3	15.6	15.5	16.0	16.2	15.5
SD	0.49	0.55	0.59	1.02	1.34	0.48	0.42
N	10	10	10	9	9	10	10

GROUP: 18.0:18.0 mg base/kg/day

941	11.6	14.3	16.2	13.2	15.1	16.2	15.2
942	12.9	13.2	15.3	13.2	15.5	18.2	16.4
943	--	--	--	--	--	--	--
944	13.0	13.3	15.1	13.6	15.8	16.0	15.8
945	--	--	--	--	--	--	--
946	--	--	--	--	--	--	--
947	--	--	--	--	--	--	--
948	--	--	--	--	--	--	--
949	14.3	14.1	14.5	14.6	16.0	15.8	15.5
950	--	--	--	--	--	--	--
951	--	--	--	--	--	--	--
952	--	--	--	--	--	--	--
953	13.5	15.4	15.3	11.0	15.7	16.5	15.3
954	13.1	14.0	14.3	13.6	15.2	16.0	15.7
955	--	--	--	--	--	--	--
956	13.7	13.6	15.5	13.5	15.5	--	--
957	12.0	14.0	15.3	14.6	16.2	16.3	15.9
958	--	--	--	--	--	--	--
959	13.2	13.4	14.4	13.4	15.3	15.6	14.5
960	13.9	15.7	15.7	14.7	16.1	16.1	15.9
MEAN	13.1	14.1	15.2	13.5	15.6	16.3	15.6
SD	0.82	0.85	0.61	1.07	0.38	0.76	0.54
N	10	10	10	10	10	9	9

(--)-Data Unavailable

DRAFT

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Hematocrit

STUDY ID: 098  
ABBR: HCT

SEX: FEMALE  
UNITS: %

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
821	--	--	--	--	--	--	--
822	--	--	--	--	--	--	--
823	44.1	42.7	44.6	45.4	45.0	48.1	45.8
824	40.9	41.1	44.1	--	39.9	43.2	41.9
825	--	--	--	--	--	--	--
826	--	--	--	--	--	--	--
827	44.5	44.6	44.4	43.8	44.0	45.7	40.0
828	--	--	--	--	--	--	--
829	--	--	--	--	--	--	--
830	42.5	43.5	45.3	43.1	45.9	46.4	46.2
831	41.8	41.4	42.0	40.1	40.4	42.6	40.2
832	--	--	--	--	--	--	--
833	--	--	--	--	--	--	--
834	41.9	42.8	41.2	43.5	43.0	46.0	42.8
835	42.1	43.7	43.9	43.1	43.7	46.8	43.4
836	43.6	43.3	44.3	44.4	44.4	45.9	44.5
837	44.9	46.4	44.2	41.8	44.3	43.9	43.3
838	--	--	--	--	--	--	--
839	--	--	--	--	--	--	--
840	41.8	43.1	44.7	43.0	42.6	42.8	42.5
MEAN	42.8	43.3	43.9	43.1	43.3	45.1	43.1
SD	1.36	1.51	1.27	1.51	1.92	1.88	2.08
N	10	10	10	9	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
861	44.1	43.3	46.8	42.9	40.1	43.2	42.8
862	--	--	--	--	--	--	--
863	--	--	--	--	--	--	--
864	42.3	45.6	45.0	45.8	43.0	44.0	42.2
865	--	--	--	--	--	--	--
866	--	--	--	--	--	--	--
867	42.1	44.2	44.5	43.6	44.9	47.2	41.5
868	41.5	47.4	48.6	46.1	--	49.3	46.4
869	--	--	--	--	--	--	--
870	--	--	--	--	--	--	--
871	42.3	41.2	45.0	40.7	40.3	42.7	44.0
872	--	--	--	--	--	--	--
873	43.7	44.5	46.9	44.9	44.0	48.5	45.4
874	37.6	44.2	43.3	39.3	41.6	43.6	40.2
875	--	--	--	--	--	--	--
876	--	--	--	--	--	--	--
877	42.8	43.1	44.5	42.8	44.1	46.2	43.2
878	--	--	--	--	--	--	--
879	40.8	42.3	43.5	44.1	43.8	45.6	44.2
880	42.7	40.5	39.4	42.6	43.0	43.4	41.0
MEAN	42.0	43.6	44.8	43.3	42.8	45.4	43.1
SD	1.82	2.04	2.50	2.14	1.72	2.36	1.96
N	10	10	10	10	9	10	10

(--)-Data Unavailable

DRAFT

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Hematocrit

STUDY ID: 098  
ABBR: HCT

SEX: FEMALE  
UNITS: %

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
901	40.4	39.3	43.3	40.4	42.7	44.2	42.4
902	42.6	43.7	41.9	41.3	41.6	42.4	42.2
903	--	--	--	--	--	--	--
904	41.9	41.3	44.9	42.0	--	46.5	42.3
905	--	--	--	--	--	--	--
906	--	--	--	--	--	--	--
907	--	--	--	--	--	--	--
908	39.8	41.2	41.2	47.7	43.8	44.3	42.8
909	40.0	43.1	43.4	41.1	45.5	46.1	43.7
910	--	--	--	--	--	--	--
911	--	--	--	--	--	--	--
912	42.0	44.0	41.0	--	44.0	44.3	42.0
913	--	--	--	--	--	--	--
914	--	--	--	--	--	--	--
915	41.3	41.7	43.6	41.2	43.3	43.1	42.1
916	44.5	41.9	42.5	42.4	45.5	45.6	42.7
917	--	--	--	--	--	--	--
918	38.6	40.8	40.2	39.4	36.2	43.8	40.2
919	40.2	41.7	42.3	43.1	46.2	46.0	45.1
920	--	--	--	--	--	--	--
MEAN	41.1	41.9	42.4	42.1	43.2	44.6	42.6
SD	1.69	1.41	1.41	2.37	3.01	1.37	1.25
N	10	10	10	9	9	10	10

GROUP: 18.0:18.0 mg base/kg/day							
941	33.6	40.7	45.0	37.3	41.9	44.4	41.1
942	35.2	38.5	39.5	40.3	42.3	47.9	43.5
943	--	--	--	--	--	--	--
944	35.7	38.2	40.6	35.8	42.0	42.7	44.3
945	--	--	--	--	--	--	--
946	--	--	--	--	--	--	--
947	--	--	--	--	--	--	--
948	--	--	--	--	--	--	--
949	39.4	39.6	40.6	40.5	44.2	43.1	42.0
950	--	--	--	--	--	--	--
951	--	--	--	--	--	--	--
952	--	--	--	--	--	--	--
953	36.0	44.5	41.8	30.5	44.4	46.1	42.6
954	36.0	40.7	41.3	37.7	42.8	44.7	43.0
955	--	--	--	--	--	--	--
956	38.6	38.6	43.5	30.7	43.1	--	--
957	33.4	40.9	42.7	40.1	44.5	45.2	43.1
958	--	--	--	--	--	--	--
959	36.2	37.5	39.2	37.6	41.4	42.2	38.7
960	38.3	44.7	42.2	41.1	42.9	44.0	43.2
MEAN	36.2	40.4	41.6	37.2	43.0	44.5	42.4
SD	2.01	2.50	1.80	3.85	1.10	1.78	1.65
N	10	10	10	10	10	9	9

(--)-Data Unavailable

DRAFT

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Mean Corpuscular Volume

STUDY ID: 098  
ABBR: MCV

SEX: FEMALE  
UNITS: fl.

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
821	--	--	--	--	--	--	--
822	--	--	--	--	--	--	--
823	58.4	58.9	55.3	55.4	56.0	55.4	53.9
824	60.9	60.2	57.6	--	58.2	56.8	57.4
825	--	--	--	--	--	--	--
826	--	--	--	--	--	--	--
827	59.7	59.5	57.8	55.0	58.4	56.1	55.4
828	--	--	--	--	--	--	--
829	--	--	--	--	--	--	--
830	60.7	62.1	57.3	56.6	57.1	57.5	57.0
831	59.2	58.1	54.8	53.5	54.4	54.8	53.7
832	--	--	--	--	--	--	--
833	--	--	--	--	--	--	--
834	57.2	55.2	53.1	52.5	53.8	54.1	52.5
835	57.7	57.4	55.3	54.1	56.1	55.1	56.7
836	61.0	59.7	56.1	55.8	57.8	56.3	55.6
837	57.9	58.1	55.9	56.3	56.8	56.3	55.7
838	--	--	--	--	--	--	--
839	--	--	--	--	--	--	--
840	56.3	57.0	55.3	54.2	55.8	54.2	54.8
MEAN	58.9	58.6	55.9	54.8	56.4	55.7	55.3
SD	1.66	1.91	1.44	1.36	1.53	1.12	1.57
N	10	10	10	9	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
861	57.6	56.7	54.6	54.1	55.8	54.5	54.0
862	--	--	--	--	--	--	--
863	--	--	--	--	--	--	--
864	58.8	57.5	56.6	55.9	58.0	57.2	56.3
865	--	--	--	--	--	--	--
866	--	--	--	--	--	--	--
867	62.1	60.8	58.2	57.5	59.4	58.2	57.5
868	61.1	60.5	59.1	57.5	--	58.0	57.6
869	--	--	--	--	--	--	--
870	--	--	--	--	--	--	--
871	60.9	60.9	58.9	58.4	59.3	58.0	56.9
872	--	--	--	--	--	--	--
873	64.1	64.4	61.4	61.3	62.2	61.5	66.1
874	58.6	58.5	57.3	55.4	55.7	55.5	55.6
875	--	--	--	--	--	--	--
876	--	--	--	--	--	--	--
877	58.7	60.2	57.3	55.4	57.3	56.8	55.0
878	--	--	--	--	--	--	--
879	56.0	57.2	55.6	54.3	55.1	54.2	53.4
880	59.4	58.6	58.0	54.3	56.0	55.4	54.6
MEAN	59.7	59.5	57.7	56.4	57.6	56.9	56.7
SD	2.35	2.31	1.91	2.28	2.32	2.18	3.60
N	10	10	10	10	9	10	10

(--)-Data Unavailable

DRAFT

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Mean Corpuscular Volume

STUDY ID: 098  
ABBR: MCV

SEX: FEMALE  
UNITS: fl.

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
901	58.7	60.1	59.0	57.4	58.7	55.3	54.4
902	59.5	59.3	59.3	56.3	57.1	55.9	55.5
903	--	--	--	--	--	--	--
904	58.3	58.8	56.5	57.5	--	54.8	54.7
905	--	--	--	--	--	--	--
906	--	--	--	--	--	--	--
907	--	--	--	--	--	--	--
908	57.3	59.5	57.9	58.5	59.8	55.4	53.9
909	56.6	58.6	56.7	57.2	56.7	53.7	53.6
910	--	--	--	--	--	--	--
911	--	--	--	--	--	--	--
912	59.2	59.5	59.2	--	55.1	55.1	53.4
913	--	--	--	--	--	--	--
914	--	--	--	--	--	--	--
915	59.5	61.3	58.1	59.0	59.2	56.3	56.3
916	60.4	62.4	60.3	61.2	60.2	58.5	57.9
917	--	--	--	--	--	--	--
918	61.1	61.4	60.0	58.7	60.3	57.2	55.9
919	58.8	59.8	57.8	57.9	59.8	55.8	55.3
920	--	--	--	--	--	--	--
MEAN	58.9	60.1	58.5	58.2	58.5	55.8	55.1
SD	1.34	1.24	1.30	1.41	1.83	1.33	1.39
N	10	10	10	9	9	10	10

GROUP: 18.0:18.0 mg base/kg/day							
941	59.5	61.2	56.7	56.9	59.3	53.7	54.7
942	58.6	59.9	56.3	59.0	61.0	55.8	56.5
943	--	--	--	--	--	--	--
944	57.7	55.9	53.7	51.7	54.2	51.3	51.9
945	--	--	--	--	--	--	--
946	--	--	--	--	--	--	--
947	--	--	--	--	--	--	--
948	--	--	--	--	--	--	--
949	59.8	60.5	55.2	53.1	55.7	52.8	52.9
950	--	--	--	--	--	--	--
951	--	--	--	--	--	--	--
952	--	--	--	--	--	--	--
953	59.9	60.5	57.7	58.1	60.1	55.8	57.3
954	58.3	58.1	54.4	52.0	56.2	52.8	53.9
955	--	--	--	--	--	--	--
956	57.7	56.2	53.4	51.9	55.3	--	--
957	57.7	57.4	53.1	53.0	55.7	52.8	55.0
958	--	--	--	--	--	--	--
959	59.6	59.0	55.1	53.9	56.6	53.8	54.3
960	57.2	60.2	56.4	54.3	55.6	54.0	55.0
MEAN	58.6	58.9	55.2	54.4	57.0	53.6	54.6
SD	1.02	1.89	1.55	2.67	2.30	1.46	1.66
N	10	10	10	10	10	9	9

(--)-Data Unavailable

DRAFT

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Mean Corpuscular Hemoglobin

STUDY ID: 098  
ABBR: TMCH

SEX: FEMALE  
UNITS: pg

ANIMAL ID    Week 2    Week 4    Week 8    Week 13    Week 16    Week 21    Week 27

GROUP: 0:0 mg base/kg/day

821	--	--	--	--	--	--	--
822	--	--	--	--	--	--	--
823	20.8	21.1	20.5	20.2	20.9	19.9	19.5
824	22.8	22.1	21.3	--	22.3	21.2	21.6
825	--	--	--	--	--	--	--
826	--	--	--	--	--	--	--
827	22.0	21.4	21.9	19.3	20.0	20.9	21.2
828	--	--	--	--	--	--	--
829	--	--	--	--	--	--	--
830	22.7	22.4	20.9	21.0	21.6	20.8	20.7
831	21.4	21.1	20.0	19.9	20.5	19.8	19.6
832	--	--	--	--	--	--	--
833	--	--	--	--	--	--	--
834	21.1	20.5	19.8	19.9	20.1	19.8	19.6
835	21.5	20.9	21.4	20.2	20.7	19.6	20.6
836	22.1	21.8	20.7	21.1	21.4	20.6	20.1
837	21.4	20.9	20.8	20.7	21.4	20.8	21.0
838	--	--	--	--	--	--	--
839	--	--	--	--	--	--	--
840	21.0	21.2	21.0	20.6	20.7	20.2	20.6
MEAN	21.7	21.3	20.8	20.3	21.0	20.4	20.5
SD	0.69	0.59	0.63	0.58	0.72	0.57	0.73
N	10	10	10	9	10	10	10

GROUP: 0.5:0.5 mg base/kg/day

861	20.8	20.7	19.8	20.2	20.9	19.9	19.6
862	--	--	--	--	--	--	--
863	--	--	--	--	--	--	--
864	21.1	20.8	21.3	19.9	20.4	20.5	20.5
865	--	--	--	--	--	--	--
866	--	--	--	--	--	--	--
867	22.1	21.7	21.5	21.2	22.0	21.2	20.9
868	22.8	22.0	21.7	20.9	--	19.8	21.1
869	--	--	--	--	--	--	--
870	--	--	--	--	--	--	--
871	22.3	22.2	21.6	21.4	23.4	20.8	20.7
872	--	--	--	--	--	--	--
873	23.2	23.2	22.3	22.5	23.1	22.1	23.7
874	21.5	20.9	20.8	20.7	20.7	20.0	20.3
875	--	--	--	--	--	--	--
876	--	--	--	--	--	--	--
877	22.1	21.9	21.0	20.5	21.6	20.6	19.8
878	--	--	--	--	--	--	--
879	20.6	20.6	20.2	19.6	20.3	19.4	19.4
880	21.8	21.9	22.1	20.0	20.6	20.2	20.2
MEAN	21.8	21.6	21.2	20.7	21.4	20.5	20.6
SD	0.84	0.83	0.79	0.86	1.17	0.78	1.22
N	10	10	10	10	9	10	10

(--)-Data Unavailable

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Mean Corpuscular Hemoglobin

STUDY ID: 098  
ABBR: TMCH

SEX: FEMALE  
UNITS: pg

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
901	21.5	22.5	21.4	21.9	22.0	20.8	20.1
902	21.2	21.2	21.1	20.2	21.3	20.1	20.0
903	--	--	--	--	--	--	--
904	21.7	21.5	20.7	21.2	--	20.0	20.3
905	--	--	--	--	--	--	--
906	--	--	--	--	--	--	--
907	--	--	--	--	--	--	--
908	21.0	21.6	21.7	22.2	22.1	20.3	19.8
909	21.1	21.6	20.4	21.1	20.9	19.0	19.5
910	--	--	--	--	--	--	--
911	--	--	--	--	--	--	--
912	21.2	21.8	22.5	--	20.5	19.5	19.5
913	--	--	--	--	--	--	--
914	--	--	--	--	--	--	--
915	21.8	22.9	21.6	22.2	22.3	21.2	20.9
916	21.8	23.0	22.6	22.1	22.5	20.7	20.9
917	--	--	--	--	--	--	--
918	22.8	21.5	21.5	21.6	21.0	20.9	20.3
919	21.9	21.8	21.6	21.0	21.7	19.6	19.7
920	--	--	--	--	--	--	--
MEAN	21.6	21.9	21.5	21.5	21.6	20.2	20.1
SD	0.53	0.63	0.69	0.68	0.70	0.70	0.51
N	10	10	10	9	9	10	10

GROUP: 18.0:18.0 mg base/kg/day							
941	20.5	21.5	20.4	20.1	21.4	19.6	20.2
942	21.5	20.5	21.8	19.3	22.3	21.2	21.3
943	--	--	--	--	--	--	--
944	21.0	19.5	20.0	19.7	20.4	19.2	18.5
945	--	--	--	--	--	--	--
946	--	--	--	--	--	--	--
947	--	--	--	--	--	--	--
948	--	--	--	--	--	--	--
949	21.7	21.5	19.7	19.1	20.2	19.4	19.5
950	--	--	--	--	--	--	--
951	--	--	--	--	--	--	--
952	--	--	--	--	--	--	--
953	22.5	21.0	21.1	21.0	21.2	20.0	20.6
954	21.2	20.0	18.8	18.8	20.0	18.9	19.7
955	--	--	--	--	--	--	--
956	20.5	19.8	19.0	22.8	19.9	--	--
957	20.7	19.6	19.0	19.3	20.3	19.0	20.3
958	--	--	--	--	--	--	--
959	21.7	21.1	20.2	19.2	20.9	19.9	20.3
960	20.7	21.1	21.0	19.4	20.9	19.8	20.2
MEAN	21.2	20.6	20.1	19.9	20.8	19.7	20.1
SD	0.65	0.78	1.00	1.20	0.74	0.69	0.78
N	10	10	10	10	10	9	9

(--)-Data Unavailable

DRAFT

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

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

STUDY ID: 098  
ABBR: TMCHC

SEX: FEMALE  
UNITS: %

ANIMAL ID    Week 2    Week 4    Week 8    Week 13    Week 16    Week 21    Week 27

GROUP: 0:0 mg base/kg/day

821	--	--	--	--	--	--	--
822	--	--	--	--	--	--	--
823	35.6	35.8	37.0	36.6	37.3	36.0	36.2
824	37.4	36.7	37.0	--	38.3	37.3	37.7
825	--	--	--	--	--	--	--
826	--	--	--	--	--	--	--
827	36.9	35.9	37.8	35.2	34.3	37.2	38.3
828	--	--	--	--	--	--	--
829	--	--	--	--	--	--	--
830	37.4	36.1	36.4	37.1	37.9	36.2	36.4
831	36.1	36.2	36.4	37.2	37.6	36.2	36.6
832	--	--	--	--	--	--	--
833	--	--	--	--	--	--	--
834	37.0	37.1	37.4	37.9	37.4	36.5	37.4
835	37.3	36.4	38.7	37.4	36.8	35.5	36.4
836	36.2	36.5	36.8	37.8	36.9	36.6	36.2
837	37.0	36.0	37.1	36.8	37.7	36.9	37.6
838	--	--	--	--	--	--	--
839	--	--	--	--	--	--	--
840	37.3	37.1	38.0	37.9	37.1	37.1	37.6
MEAN	36.8	36.4	37.3	37.1	37.1	36.6	37.0
SD	0.63	0.47	0.73	0.85	1.09	0.58	0.76
N	10	10	10	9	10	10	10

GROUP: 0.5:0.5 mg base/kg/day

861	36.1	36.5	36.3	37.3	37.4	36.6	36.2
862	--	--	--	--	--	--	--
863	--	--	--	--	--	--	--
864	35.9	36.2	37.6	35.6	35.1	35.9	36.5
865	--	--	--	--	--	--	--
866	--	--	--	--	--	--	--
867	35.6	35.7	36.9	36.9	37.0	36.4	36.4
868	37.3	36.3	36.8	36.4	--	34.1	36.6
869	--	--	--	--	--	--	--
870	--	--	--	--	--	--	--
871	36.6	36.4	36.7	36.6	39.5	35.8	36.4
872	--	--	--	--	--	--	--
873	36.2	36.0	36.2	36.7	37.0	35.9	35.9
874	36.7	35.7	36.3	37.4	37.3	36.0	36.6
875	--	--	--	--	--	--	--
876	--	--	--	--	--	--	--
877	37.6	36.4	36.6	36.9	37.6	36.4	36.1
878	--	--	--	--	--	--	--
879	36.8	35.9	36.3	36.1	36.8	35.7	36.4
880	36.8	37.3	38.1	36.9	36.7	36.4	37.1
MEAN	36.6	36.2	36.8	36.7	37.2	35.9	36.4
SD	0.62	0.47	0.62	0.54	1.14	0.71	0.33
N	10	10	10	10	9	10	10

(--)-Data Unavailable

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

DRAFT

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

STUDY ID: 098  
ABBR: TMCHC

SEX: FEMALE  
UNITS: %

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
901	36.6	37.4	36.3	38.1	37.5	37.6	37.0
902	35.7	35.7	35.6	35.8	37.3	35.8	36.0
903	--	--	--	--	--	--	--
904	37.2	36.6	36.5	36.9	--	36.6	37.1
905	--	--	--	--	--	--	--
906	--	--	--	--	--	--	--
907	--	--	--	--	--	--	--
908	36.7	36.4	37.4	37.9	37.0	36.6	36.7
909	37.3	36.9	35.9	37.0	36.9	35.4	36.4
910	--	--	--	--	--	--	--
911	--	--	--	--	--	--	--
912	35.7	36.6	38.0	--	37.3	35.4	36.4
913	--	--	--	--	--	--	--
914	--	--	--	--	--	--	--
915	36.6	37.4	37.2	37.6	37.6	37.6	37.1
916	36.2	36.8	37.4	36.1	37.4	35.3	36.1
917	--	--	--	--	--	--	--
918	37.3	35.0	35.8	36.8	34.8	36.5	36.3
919	37.3	36.5	37.4	36.2	36.4	35.2	35.7
920	--	--	--	--	--	--	--
MEAN	36.7	36.5	36.8	36.9	36.9	36.2	36.5
SD	0.63	0.73	0.83	0.81	0.87	0.92	0.48
N	10	10	10	9	9	10	10

GROUP: 18.0:18.0 mg base/kg/day							
941	34.5	35.1	36.0	35.4	36.0	36.5	37.0
942	36.6	34.3	38.7	32.8	36.6	38.0	37.7
943	--	--	--	--	--	--	--
944	36.4	34.8	37.2	38.0	37.6	37.5	35.7
945	--	--	--	--	--	--	--
946	--	--	--	--	--	--	--
947	--	--	--	--	--	--	--
948	--	--	--	--	--	--	--
949	36.3	35.6	35.7	36.0	36.2	36.7	36.9
950	--	--	--	--	--	--	--
951	--	--	--	--	--	--	--
952	--	--	--	--	--	--	--
953	37.5	34.6	36.6	36.1	35.4	35.8	35.9
954	36.4	34.4	34.6	36.1	35.5	35.8	36.5
955	--	--	--	--	--	--	--
956	35.5	35.2	35.6	44.0	36.0	--	--
957	35.9	34.2	35.8	36.4	36.4	36.1	36.9
958	--	--	--	--	--	--	--
959	36.5	35.7	36.7	35.6	37.0	37.0	37.5
960	36.3	35.1	37.2	35.8	37.5	36.6	36.8
MEAN	36.2	34.9	36.4	36.6	36.4	36.7	36.8
SD	0.78	0.53	1.13	2.89	0.76	0.74	0.66
N	10	10	10	10	10	9	9

(--)-Data Unavailable

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Reticulocytes Count

STUDY ID: 098  
ABBR: RETICS

SEX: FEMALE  
UNITS: % RBCs

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
821	--	--	--	--	--	--	--
822	--	--	--	--	--	--	--
823	0.3	1.3	0.7	0.7	0.4	0.0	0.5
824	1.3	1.5	0.5	--	0.3	0.8	0.3
825	--	--	--	--	--	--	--
826	--	--	--	--	--	--	--
827	0.9	1.4	0.3	1.3	0.7	0.3	0.3
828	--	--	--	--	--	--	--
829	--	--	--	--	--	--	--
830	1.2	1.9	0.4	1.1	0.4	0.3	0.9
831	1.3	1.2	0.4	0.7	0.7	0.5	1.1
832	--	--	--	--	--	--	--
833	--	--	--	--	--	--	--
834	1.0	0.1	0.1	0.8	0.1	0.0	0.0
835	1.4	0.5	0.1	0.6	1.1	0.5	0.8
836	2.9	0.4	0.3	0.7	0.7	0.2	0.5
837	0.4	0.7	0.7	0.4	1.0	0.3	0.9
838	--	--	--	--	--	--	--
839	--	--	--	--	--	--	--
840	1.5	0.7	0.6	1.1	0.5	0.4	0.3
MEAN	1.2	1.0	0.4	0.8	0.6	0.3	0.6
SD	0.72	0.57	0.22	0.29	0.31	0.24	0.35
N	10	10	10	9	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
861	2.1	0.1	0.8	0.6	0.2	0.1	0.0
862	--	--	--	--	--	--	--
863	--	--	--	--	--	--	--
864	1.9	1.0	0.9	0.5	0.3	0.2	0.9
865	--	--	--	--	--	--	--
866	--	--	--	--	--	--	--
867	2.0	0.8	0.4	0.4	0.4	0.9	0.1
868	0.1	1.5	0.3	0.6	--	0.8	0.3
869	--	--	--	--	--	--	--
870	--	--	--	--	--	--	--
871	0.7	0.6	0.4	0.8	0.1	0.8	0.8
872	--	--	--	--	--	--	--
873	0.7	0.6	0.6	1.4	1.5	0.5	1.9
874	1.2	1.1	0.5	0.6	0.7	0.2	0.3
875	--	--	--	--	--	--	--
876	--	--	--	--	--	--	--
877	0.6	1.8	0.8	0.9	0.5	0.1	0.1
878	--	--	--	--	--	--	--
879	1.1	1.0	0.4	0.7	1.0	0.1	0.7
880	1.3	1.6	1.0	0.9	0.1	0.3	0.6
MEAN	1.2	1.0	0.6	0.7	0.5	0.4	0.6
SD	0.67	0.52	0.25	0.28	0.47	0.32	0.56
N	10	10	10	10	9	10	10

(--)-Data Unavailable

DRAFT

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Reticulocytes Count

STUDY ID: 098  
ABBR: RETICS

SEX: FEMALE  
UNITS: % RBCs

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
901	0.1	1.9	0.4	0.9	0.7	0.5	0.5
902	0.0	2.2	1.7	1.7	0.8	0.3	0.0
903	--	--	--	--	--	--	--
904	0.1	0.3	1.0	0.9	--	0.0	0.1
905	--	--	--	--	--	--	--
906	--	--	--	--	--	--	--
907	--	--	--	--	--	--	--
908	1.3	2.0	1.2	0.3	0.8	0.7	0.3
909	1.5	1.2	1.2	1.1	0.0	0.3	0.3
910	--	--	--	--	--	--	--
911	--	--	--	--	--	--	--
912	0.1	0.1	0.8	--	0.8	0.2	0.2
913	--	--	--	--	--	--	--
914	--	--	--	--	--	--	--
915	0.3	1.7	0.5	0.9	1.3	0.4	0.7
916	1.1	2.1	1.2	0.6	0.3	0.6	0.0
917	--	--	--	--	--	--	--
918	0.9	2.9	0.9	1.2	1.2	0.3	0.6
919	1.1	0.2	1.3	0.2	0.1	0.2	0.6
920	--	--	--	--	--	--	--
MEAN	0.7	1.5	1.0	0.9	0.7	0.4	0.3
SD	0.58	0.97	0.39	0.46	0.45	0.21	0.26
N	10	10	10	9	9	10	10

GROUP: 18.0:18.0 mg base/kg/day							
941	5.0	1.5	2.0	4.7	0.2	0.6	1.0
942	2.8	5.0	1.1	CL	1.9	0.2	0.2
943	--	--	--	--	--	--	--
944	2.7	3.5	1.2	0.8	1.4	0.0	0.1
945	--	--	--	--	--	--	--
946	--	--	--	--	--	--	--
947	--	--	--	--	--	--	--
948	--	--	--	--	--	--	--
949	4.2	0.5	1.5	3.7	0.9	0.2	0.4
950	--	--	--	--	--	--	--
951	--	--	--	--	--	--	--
952	--	--	--	--	--	--	--
953	4.2	2.5	2.2	1.5	0.6	0.4	0.5
954	3.6	2.1	1.2	2.8	0.9	0.2	0.4
955	--	--	--	--	--	--	--
956	3.9	1.4	2.0	3.0	0.9	--	--
957	3.8	2.0	1.6	0.5	0.9	0.2	0.3
958	--	--	--	--	--	--	--
959	0.4	0.7	1.1	1.8	0.3	0.5	0.7
960	4.1	3.0	2.1	4.6	0.5	0.3	1.2
MEAN	3.5	2.2	1.6	2.6	0.9	0.3	0.5
SD	1.27	1.36	0.44	1.55	0.51	0.18	0.37
N	10	10	10	9	10	9	9

(--)-Data Unavailable

CL-Clotted

DRAFT

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Nucleated Red Cells

STUDY ID: 098  
ABBR: NRBC

SEX: FEMALE  
UNITS: COUNT

ANIMAL ID    Week 2    Week 4    Week 8    Week 13    Week 16    Week 21    Week 27

GROUP: 0:0 mg base/kg/day

821	--	--	--	--	--	--	--
822	--	--	--	--	--	--	--
823	0	0	0	0	0	0	0
824	0	0	0	--	0	0	0
825	--	--	--	--	--	--	--
826	--	--	--	--	--	--	--
827	0	0	0	0	0	0	0
828	--	--	--	--	--	--	--
829	--	--	--	--	--	--	--
830	0	0	0	0	0	0	0
831	0	0	0	0	0	0	0
832	--	--	--	--	--	--	--
833	--	--	--	--	--	--	--
834	0	0	0	0	0	0	0
835	0	0	0	0	0	0	0
836	0	0	0	0	0	0	0
837	0	0	0	0	0	0	0
838	--	--	--	--	--	--	--
839	--	--	--	--	--	--	--
840	0	0	0	0	0	0	0
MEAN	0	0	0	0	0	0	0
SD	0.0	0.0	0.0	0.0	0.0	0.0	0.0
N	10	10	10	9	10	10	10

GROUP: 0.5:0.5 mg base/kg/day

861	0	0	0	0	0	0	0
862	--	--	--	--	--	--	--
863	--	--	--	--	--	--	--
864	0	0	0	0	0	0	0
865	--	--	--	--	--	--	--
866	--	--	--	--	--	--	--
867	0	0	0	0	0	0	0
868	0	0	0	0	--	0	0
869	--	--	--	--	--	--	--
870	--	--	--	--	--	--	--
871	0	0	0	0	0	0	0
872	--	--	--	--	--	--	--
873	0	0	0	0	0	0	0
874	0	0	0	0	0	0	0
875	--	--	--	--	--	--	--
876	--	--	--	--	--	--	--
877	0	0	0	0	0	0	0
878	--	--	--	--	--	--	--
879	0	0	0	0	0	0	0
880	0	0	0	0	0	0	0
MEAN	0	0	0	0	0	0	0
SD	0.0	0.0	0.0	0.0	0.0	0.0	0.0
N	10	10	10	10	9	10	10

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

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

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Nucleated Red Cells

STUDY ID: 098  
ABBR: NRBC

SEX: FEMALE  
UNITS: COUNT

ANIMAL IO    Week 2    Week 4    Week 8    Week 13    Week 16    Week 21    Week 27

GROUP: 6.0:6.0 mg base/kg/day

901	0	0	0	1	0	0	0
902	0	0	0	0	0	0	0
903	--	--	--	--	--	--	--
904	0	0	0	0	--	0	0
905	--	--	--	--	--	--	--
906	--	--	--	--	--	--	--
907	--	--	--	--	--	--	--
908	0	0	0	0	0	0	0
909	0	0	0	0	0	0	0
910	--	--	--	--	--	--	--
911	--	--	--	--	--	--	--
912	0	0	0	--	0	0	0
913	--	--	--	--	--	--	--
914	--	--	--	--	--	--	--
915	0	0	0	0	0	0	0
916	0	0	0	0	0	0	0
917	--	--	--	--	--	--	--
918	0	0	0	0	0	0	0
919	0	0	0	0	0	0	0
920	--	--	--	--	--	--	--
MEAN	0	0	0	0	0	0	0
SO	0.0	0.0	0.0	0.3	0.0	0.0	0.0
N	10	10	10	9	9	10	10

GROUP: 18.0:18.0 mg base/kg/day

941	0	0	1	0	0	0	0
942	0	0	0	--	0	0	0
943	--	--	--	--	--	--	--
944	1	0	0	0	0	0	0
945	--	--	--	--	--	--	--
946	--	--	--	--	--	--	--
947	--	--	--	--	--	--	--
948	--	--	--	--	--	--	--
949	0	0	0	0	0	0	0
950	--	--	--	--	--	--	--
951	--	--	--	--	--	--	--
952	--	--	--	--	--	--	--
953	0	0	0	0	0	0	0
954	0	0	0	0	0	0	0
955	--	--	--	--	--	--	--
956	0	0	0	0	0	--	--
957	0	0	0	0	0	0	0
958	--	--	--	--	--	--	--
959	0	0	0	0	0	0	0
960	0	0	0	0	0	0	0
MEAN	0	0	0	0	0	0	0
SO	0.3	0.0	0.3	0.0	0.0	0.0	0.0
N	10	10	10	9	10	9	9

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

DRAFT

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Heinz Bodies

STUDY 10: 098  
ABBR: HB

SEX: FEMALE  
UNITS: %

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
821	--	--	--	--	--	--	--
822	--	--	--	--	--	--	--
823	0.0	0.0	0.0	0.0	0.0	0.0	0.0
824	0.0	0.0	0.0	--	0.0	0.0	0.0
825	--	--	--	--	--	--	--
826	--	--	--	--	--	--	--
827	0.0	0.0	0.0	0.0	0.0	0.0	0.0
828	--	--	--	--	--	--	--
829	--	--	--	--	--	--	--
830	0.0	0.0	0.0	0.0	0.0	0.0	0.0
831	0.0	0.0	0.3	0.0	0.0	0.0	0.0
832	--	--	--	--	--	--	--
833	--	--	--	--	--	--	--
834	0.0	0.5	0.4	0.0	0.0	0.0	0.0
835	0.0	0.0	0.0	0.0	0.0	0.0	0.0
836	0.0	0.0	0.5	0.0	0.0	0.0	0.0
837	0.0	0.0	0.2	0.0	0.0	0.0	0.0
838	--	--	--	--	--	--	--
839	--	--	--	--	--	--	--
840	0.0	0.0	0.0	0.0	0.0	0.0	0.0
MEAN	0.0	0.1	0.1	0.0	0.0	0.0	0.0
SD	0.00	0.16	0.20	0.00	0.00	0.00	0.00
N	10	10	10	9	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
861	0.0	0.0	0.0	0.0	0.0	0.0	0.0
862	--	--	--	--	--	--	--
863	--	--	--	--	--	--	--
864	0.0	0.0	0.1	0.0	0.0	0.0	0.0
865	--	--	--	--	--	--	--
866	--	--	--	--	--	--	--
867	0.2	0.0	0.3	0.0	0.0	0.0	0.0
868	0.0	0.0	0.0	0.1	--	0.0	0.0
869	--	--	--	--	--	--	--
870	--	--	--	--	--	--	--
871	0.0	0.1	0.0	0.0	0.0	0.0	0.0
872	--	--	--	--	--	--	--
873	0.0	0.4	0.0	0.0	0.0	0.0	0.2
874	0.0	0.9	0.0	0.0	0.0	0.0	0.0
875	--	--	--	--	--	--	--
876	--	--	--	--	--	--	--
877	0.0	0.3	0.2	0.0	0.0	0.0	0.0
878	--	--	--	--	--	--	--
879	0.0	0.0	0.4	0.0	0.0	0.0	0.0
880	0.0	0.4	0.0	0.1	0.0	0.0	0.0
MEAN	0.0	0.2	0.1	0.0	0.0	0.0	0.0
SD	0.06	0.30	0.15	0.04	0.00	0.00	0.06
N	10	10	10	10	9	10	10

(--)-Data Unavailable

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

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Heinz Bodies

STUDY 10: 098  
ABBR: HB

SEX: FEMALE  
UNITS: %

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
901	0.0	0.0	0.0	0.7	0.0	0.0	0.0
902	0.0	0.5	0.3	0.0	0.0	0.0	0.0
903	--	--	--	--	--	--	--
904	0.2	0.1	0.0	0.1	--	0.0	0.0
905	--	--	--	--	--	--	--
906	--	--	--	--	--	--	--
907	--	--	--	--	--	--	--
908	0.1	0.0	0.5	0.0	0.0	0.0	0.0
909	0.0	0.0	0.0	0.0	0.0	0.0	0.0
910	--	--	--	--	--	--	--
911	--	--	--	--	--	--	--
912	0.0	1.1	0.0	--	0.0	0.0	0.0
913	--	--	--	--	--	--	--
914	--	--	--	--	--	--	--
915	0.1	0.0	0.0	0.0	0.0	0.0	0.0
916	0.2	0.1	0.0	0.0	0.0	0.0	0.0
917	--	--	--	--	--	--	--
918	0.0	1.0	0.0	0.0	0.0	0.0	0.0
919	0.4	0.0	0.0	0.0	0.0	0.0	0.0
920	--	--	--	--	--	--	--
MEAN	0.1	0.3	0.1	0.1	0.0	0.0	0.0
SD	0.13	0.43	0.18	0.23	0.00	0.00	0.00
N	10	10	10	9	9	10	10

GROUP: 18.0:18.0 mg base/kg/day							
941	0.9	0.0	0.0	0.0	0.0	0.0	0.0
942	1.7	0.1	0.1	CL	0.0	0.0	0.0
943	--	--	--	--	--	--	--
944	0.8	1.3	0.2	0.1	0.0	0.0	0.0
945	--	--	--	--	--	--	--
946	--	--	--	--	--	--	--
947	--	--	--	--	--	--	--
948	--	--	--	--	--	--	--
949	1.4	0.2	0.2	0.7	0.0	0.0	0.0
950	--	--	--	--	--	--	--
951	--	--	--	--	--	--	--
952	--	--	--	--	--	--	--
953	1.9	0.4	0.0	0.4	0.0	0.0	0.0
954	1.0	0.7	0.3	1.9	0.0	0.0	0.0
955	--	--	--	--	--	--	--
956	2.8	0.5	1.3	1.1	0.0	--	--
957	1.9	0.3	0.1	1.0	0.0	0.0	0.0
958	--	--	--	--	--	--	--
959	0.8	0.0	0.0	1.1	0.0	0.0	0.0
960	3.7	0.3	0.0	0.1	0.0	0.0	0.0
MEAN	1.7	0.4	0.2	0.7	0.0	0.0	0.0
SD	0.95	0.39	0.39	0.63	0.00	0.00	0.00
N	10	10	10	9	10	9	9

(--)-Data Unavailable

CL-Clotted

DRAFT

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: % Methemoglobin

STUDY ID: 098  
ABBR: %METHGB

SEX: FEMALE  
UNITS: %

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
821	--	--	--	--	--	--	--
822	--	--	--	--	--	--	--
823	0.5	0.7	0.6	0.0	0.4	0.5	0.9
824	0.4	0.2	1.0	--	0.0	0.5	0.3
825	--	--	--	--	--	--	--
826	--	--	--	--	--	--	--
827	0.7	0.6	0.9	0.1	0.5	0.6	0.8
828	--	--	--	--	--	--	--
829	--	--	--	--	--	--	--
830	0.7	0.2	0.6	0.1	0.5	0.8	0.7
831	0.2	0.3	0.7	1.2	0.0	0.1	0.5
832	--	--	--	--	--	--	--
833	--	--	--	--	--	--	--
834	0.4	0.4	0.1	1.7	1.1	1.0	0.6
835	0.1	0.2	1.1	0.7	0.4	0.5	0.7
836	0.5	1.0	0.5	0.1	0.3	0.6	1.3
837	1.1	0.7	0.5	0.8	1.5	0.9	0.8
838	--	--	--	--	--	--	--
839	--	--	--	--	--	--	--
840	0.1	0.4	0.7	1.0	0.2	0.6	0.8
MEAN	0.5	0.5	0.7	0.6	0.5	0.6	0.7
SD	0.31	0.27	0.29	0.60	0.47	0.25	0.26
N	10	10	10	9	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
861	1.1	0.4	1.2	0.6	0.0	0.8	1.0
862	--	--	--	--	--	--	--
863	--	--	--	--	--	--	--
864	0.4	0.6	0.0	0.8	0.2	0.8	0.5
865	--	--	--	--	--	--	--
866	--	--	--	--	--	--	--
867	0.4	0.4	0.9	0.5	0.0	0.7	0.7
868	0.2	0.0	0.3	0.0	--	0.8	1.0
869	--	--	--	--	--	--	--
870	--	--	--	--	--	--	--
871	0.7	0.2	0.5	0.6	0.2	0.3	0.8
872	--	--	--	--	--	--	--
873	0.2	1.4	0.6	0.7	0.5	0.7	0.7
874	0.2	0.7	1.0	0.4	0.6	0.4	0.9
875	--	--	--	--	--	--	--
876	--	--	--	--	--	--	--
877	0.8	1.0	0.6	0.5	0.2	0.2	0.9
878	--	--	--	--	--	--	--
879	0.1	1.0	0.3	1.1	0.5	0.3	1.3
880	0.9	0.7	0.1	0.4	0.2	0.3	1.6
MEAN	0.5	0.6	0.6	0.6	0.3	0.5	0.9
SD	0.35	0.42	0.39	0.29	0.22	0.25	0.32
N	10	10	10	10	9	10	10

(--)-Data Unavailable

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: % Methemoglobin

STUDY ID: 098  
ABBR: %METHGB

SEX: FEMALE  
UNITS: %

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
901	0.5	2.1	4.2	4.7	0.1	1.4	0.6
902	0.7	2.9	5.0	6.4	0.3	0.3	1.1
903	--	--	--	--	--	--	--
904	1.3	3.7	6.1	6.5	--	0.5	0.4
905	--	--	--	--	--	--	--
906	--	--	--	--	--	--	--
907	--	--	--	--	--	--	--
908	0.8	3.5	4.7	5.5	0.0	0.2	0.4
909	0.4	3.1	3.3	3.6	0.0	0.1	0.9
910	--	--	--	--	--	--	--
911	--	--	--	--	--	--	--
912	0.7	2.0	2.8	--	0.5	0.9	1.2
913	--	--	--	--	--	--	--
914	--	--	--	--	--	--	--
915	0.7	1.4	3.0	3.1	0.9	0.4	1.2
916	1.8	1.9	3.5	2.3	0.0	0.9	0.8
917	--	--	--	--	--	--	--
918	0.6	2.1	4.4	5.3	1.7	0.8	0.6
919	1.1	2.6	4.9	5.0	0.0	1.0	0.6
920	--	--	--	--	--	--	--
MEAN	0.9	2.5	4.2	4.7	0.4	0.7	0.8
SD	0.42	0.75	1.04	1.45	0.58	0.41	0.31
N	10	10	10	9	9	10	10

GROUP: 18.0:18.0 mg base/kg/day							
941	10.1	5.8	6.1	7.8	0.1	1.0	0.6
942	15.9	6.1	6.6	13.4	1.6	0.8	0.1
943	--	--	--	--	--	--	--
944	11.2	7.5	6.8	9.8	0.0	0.2	0.2
945	--	--	--	--	--	--	--
946	--	--	--	--	--	--	--
947	--	--	--	--	--	--	--
948	--	--	--	--	--	--	--
949	13.9	8.4	9.0	11.3	1.0	0.6	1.2
950	--	--	--	--	--	--	--
951	--	--	--	--	--	--	--
952	--	--	--	--	--	--	--
953	12.4	7.5	9.6	11.7	1.2	0.5	0.7
954	15.0	9.8	10.7	16.3	2.0	0.7	0.8
955	--	--	--	--	--	--	--
956	12.9	10.6	10.3	11.8	1.7	--	--
957	10.5	6.6	10.1	12.8	2.2	0.7	0.1
958	--	--	--	--	--	--	--
959	14.6	11.5	14.2	15.9	2.1	0.9	1.3
960	12.4	6.8	8.9	11.3	2.0	1.1	0.9
MEAN	12.9	8.1	9.2	12.2	1.4	0.7	0.7
SD	1.95	1.96	2.40	2.57	0.80	0.27	0.45
N	10	10	10	10	10	9	9

(--)-Data Unavailable

DRAFT

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Platelets

STUDY ID: 098  
ABBR: PLT

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
821	--	--	--	--	--	--	--
822	--	--	--	--	--	--	--
823	919	1099	1118	1069	990	964	1015
824	1287	1140	1064	--	913	919	963
825	--	--	--	--	--	--	--
826	--	--	--	--	--	--	--
827	1190	1022	682	979	1002	959	1092
828	--	--	--	--	--	--	--
829	--	--	--	--	--	--	--
830	1224	1240	818	1039	1145	998	1109
831	1440	1271	1187	1156	1075	1105	985
832	--	--	--	--	--	--	--
833	--	--	--	--	--	--	--
834	1280	1227	1127	867	1037	990	1034
835	1263	1188	1104	910	957	1020	979
836	1189	1143	1050	795	885	872	966
837	1117	1034	949	959	640	519	722
838	--	--	--	--	--	--	--
839	--	--	--	--	--	--	--
840	1262	1335	1199	1077	1030	1032	944
MEAN	1217	1170	1030	983	967	938	981
SD	134.6	101.6	166.7	114.0	137.7	160.3	106.3
N	10	10	10	9	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
861	1118	1071	990	844	912	918	813
862	--	--	--	--	--	--	--
863	--	--	--	--	--	--	--
864	1251	1184	1066	1032	1000	905	950
865	--	--	--	--	--	--	--
866	--	--	--	--	--	--	--
867	1345	1392	1112	992	993	1112	1022
868	1050	1127	905	833	--	400	955
869	--	--	--	--	--	--	--
870	--	--	--	--	--	--	--
871	1325	1221	1184	1301	1157	1216	1220
872	--	--	--	--	--	--	--
873	1280	1229	1151	1141	1056	1061	1070
874	1448	1375	1227	1027	1118	1045	1089
875	--	--	--	--	--	--	--
876	--	--	--	--	--	--	--
877	1171	787	1053	967	944	974	982
878	--	--	--	--	--	--	--
879	1433	1496	1250	1246	1340	1266	1165
880	1632	1438	1222	1310	769	1142	1007
MEAN	1305	1232	1116	1069	1032	1004	1027
SD	172.3	209.7	112.7	174.5	162.9	243.2	116.1
N	10	10	10	10	9	10	10

(--)-Data Unavailable

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Platelets

STUDY ID: 098  
ABBR: PLT

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
901	1176	1128	1029	889	1062	1071	1113
902	1176	1208	1037	1040	1004	954	983
903	--	--	--	--	--	--	--
904	1457	1393	1264	1271	--	1218	1165
905	--	--	--	--	--	--	--
906	--	--	--	--	--	--	--
907	--	--	--	--	--	--	--
908	1628	1294	1082	1303	1057	1048	1075
909	1205	1119	1004	840	1003	1011	997
910	--	--	--	--	--	--	--
911	--	--	--	--	--	--	--
912	1058	1258	990	--	928	736	1000
913	--	--	--	--	--	--	--
914	--	--	--	--	--	--	--
915	1172	1201	1047	1153	1120	1092	940
916	1370	1245	1206	1170	815	1098	1046
917	--	--	--	--	--	--	--
918	1304	1250	1025	1035	727	998	982
919	997	1113	1039	997	1059	942	970
920	--	--	--	--	--	--	--
MEAN	1254	1221	1072	1078	975	1017	1027
SD	189.4	87.5	90.2	159.8	129.1	127.1	71.1
N	10	10	10	9	9	10	10

GROUP: 18.0:18.0 mg base/kg/day							
941	1199	1228	950	920	887	1064	935
942	828	823	868	246	833	969	895
943	--	--	--	--	--	--	--
944	1535	1329	1253	1280	1208	1163	1123
945	--	--	--	--	--	--	--
946	--	--	--	--	--	--	--
947	--	--	--	--	--	--	--
948	--	--	--	--	--	--	--
949	1279	1209	1013	854	984	877	834
950	--	--	--	--	--	--	--
951	--	--	--	--	--	--	--
952	--	--	--	--	--	--	--
953	1482	1382	1140	805	1017	1012	909
954	1115	1063	735	722	859	819	795
955	--	--	--	--	--	--	--
956	1315	1230	1093	804	1049	--	--
957	1815	1243	1202	1070	1098	1010	1013
958	--	--	--	--	--	--	--
959	1279	1335	1225	1169	1210	1086	1051
960	954	921	981	848	810	742	830
MEAN	1280	1176	1046	872	996	971	932
SD	286.3	184.0	167.7	283.0	147.7	135.2	110.6
N	10	10	10	10	10	9	9

(--)-Data Unavailable

DRAFT

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

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

STUDY ID: 098  
ABBR: APTT

SEX: FEMALE  
UNITS: sec

ANIMAL ID	Week 14	Week 27
GROUP: 0:0 mg base/kg/day		
821	14.5	--
822	14.7	--
823	--	15.6
824	--	11.8
825	15.2	--
826	17.3	--
827	--	12.8
828	16.5	--
829	11.7	--
830	--	10.0
831	--	12.8
832	15.7	--
833	13.5	--
834	--	13.8
835	--	15.5
836	--	14.2
837	--	11.1
838	17.1	--
839	18.9	--
840	--	10.0
MEAN	15.5	12.8
SD	2.07	2.05
N	10	10

ANIMAL ID	Week 14	Week 27
GROUP: 0.5:0.5 mg base/kg/day		
861	--	15.3
862	16.3	--
863	16.0	--
864	--	16.4
865	17.5	--
866	14.2	--
867	--	15.0
868	--	13.1
869	15.2	--
870	11.2	--
871	--	10.4
872	11.7	--
873	--	12.8
874	--	8.2
875	15.4	--
876	14.2	--
877	--	15.1
878	14.1	--
879	--	12.3
880	--	16.1
MEAN	14.6	13.5
SD	1.97	2.65
N	10	10

(--)-Data Unavailable

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

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

STUDY ID: 098  
ABBR: APTT

SEX: FEMALE  
UNITS: sec

ANIMAL ID	Week 14	Week 27
GROUP: 6.0:6.0 mg base/kg/day		
901	--	18.0
902	--	11.9
903	13.5	--
904	--	12.5
905	16.2	--
906	13.0	--
907	9.0	--
908	--	13.9
909	--	14.1
910	12.4	--
911	10.7	--
912	--	8.5
913	15.7	--
914	15.1	--
915	--	13.1
916	--	16.9
917	15.7	--
918	--	14.9
919	--	13.2
920	14.7	--
MEAN	13.6	13.7
SD	2.37	2.64
N	10	10

GROUP: 18.0:18.0 mg base/kg/day		
941	--	15.2
942	--	15.3
943	13.1	--
944	--	15.8
945	12.4	--
946	11.3	--
947	15.7	--
948	8.5	--
949	--	18.3
950	7.2	--
951	10.4	--
952	13.2	--
953	--	14.6
954	--	16.2
955	18.4	--
956	--	--
957	--	16.6
958	12.5	--
959	--	11.6
960	--	14.2
MEAN	12.3	15.3
SD	3.25	1.84
N	10	9

(--)-Data Unavailable

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

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Leukocytes

STUDY ID: 098  
ABBR: WBC

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
821	--	--	--	--	--	--	--
822	--	--	--	--	--	--	--
823	12.6	7.0	8.5	9.8	6.1	7.4	7.7
824	12.9	10.4	6.5	--	5.7	5.5	8.1
825	--	--	--	--	--	--	--
826	--	--	--	--	--	--	--
827	17.5	14.2	9.4	10.0	9.0	11.9	10.9
828	--	--	--	--	--	--	--
829	--	--	--	--	--	--	--
830	17.9	11.2	8.8	10.0	7.9	8.9	8.2
831	21.6	16.3	15.4	14.2	15.9	13.6	10.7
832	--	--	--	--	--	--	--
833	--	--	--	--	--	--	--
834	13.1	15.1	13.4	12.5	9.0	10.2	8.3
835	11.1	9.0	8.4	8.6	7.8	9.8	7.8
836	17.8	9.5	11.7	10.1	9.9	8.8	9.4
837	16.7	10.4	10.7	8.4	8.4	7.5	9.6
838	--	--	--	--	--	--	--
839	--	--	--	--	--	--	--
840	15.4	12.6	11.4	12.3	10.1	9.5	10.8
MEAN	15.7	11.6	10.4	10.7	9.0	9.3	9.2
SD	3.23	2.93	2.65	1.93	2.83	2.31	1.30
N	10	10	10	9	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
861	13.1	11.1	14.5	9.6	10.0	11.2	6.9
862	--	--	--	--	--	--	--
863	--	--	--	--	--	--	--
864	18.9	21.4	20.0	12.8	11.0	11.6	11.7
865	--	--	--	--	--	--	--
866	--	--	--	--	--	--	--
867	19.4	14.1	10.3	10.2	10.5	9.1	9.5
868	16.6	18.5	14.8	9.4	--	6.9	8.9
869	--	--	--	--	--	--	--
870	--	--	--	--	--	--	--
871	19.7	11.4	14.7	12.1	12.0	10.8	12.6
872	--	--	--	--	--	--	--
873	11.2	11.9	12.6	10.2	10.2	11.0	10.3
874	14.0	17.0	12.9	12.0	9.3	8.9	6.8
875	--	--	--	--	--	--	--
876	--	--	--	--	--	--	--
877	16.5	13.9	10.2	9.6	10.1	10.2	8.6
878	--	--	--	--	--	--	--
879	17.6	18.8	12.6	12.0	11.8	9.2	9.6
880	29.0	16.4	13.2	14.0	12.4	12.1	10.9
MEAN	17.6	15.5	13.6	11.2	10.8	10.1	9.6
SD	4.90	3.52	2.78	1.59	1.05	1.57	1.89
N	10	10	10	10	9	10	10

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

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

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Leukocytes

STUDY ID: 098  
ABBR: WBC

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
901	17.4	14.2	25.0	17.2	10.3	11.0	11.7
902	14.1	11.1	11.8	16.3	5.8	6.0	8.1
903	--	--	--	--	--	--	--
904	18.9	19.4	17.5	14.1	--	10.0	7.3
905	--	--	--	--	--	--	--
906	--	--	--	--	--	--	--
907	--	--	--	--	--	--	--
908	13.9	12.5	10.9	10.7	7.5	7.3	8.6
909	12.5	12.7	10.0	8.7	7.3	9.8	8.5
910	--	--	--	--	--	--	--
911	--	--	--	--	--	--	--
912	18.8	29.9	21.8	--	14.4	9.5	11.4
913	--	--	--	--	--	--	--
914	--	--	--	--	--	--	--
915	22.7	16.6	17.8	14.4	10.8	10.0	11.0
916	16.9	12.3	12.7	11.1	9.6	11.2	9.8
917	--	--	--	--	--	--	--
918	21.2	23.6	18.9	20.6	8.8	12.6	13.9
919	17.4	19.9	15.4	12.6	8.7	8.1	9.8
920	--	--	--	--	--	--	--
MEAN	17.4	17.2	16.2	14.0	9.2	9.6	10.0
SD	3.23	6.03	4.93	3.68	2.49	1.95	2.01
N	10	10	10	9	9	10	10

GROUP: 18.0:18.0 mg base/kg/day							
941	28.3	17.1	23.0	14.1	10.9	9.6	9.6
942	20.8	19.1	14.6	19.8	9.0	11.4	7.5
943	--	--	--	--	--	--	--
944	23.3	15.3	17.9	20.2	14.4	11.6	10.3
945	--	--	--	--	--	--	--
946	--	--	--	--	--	--	--
947	--	--	--	--	--	--	--
948	--	--	--	--	--	--	--
949	32.4	31.1	30.2	31.1	19.4	11.1	13.1
950	--	--	--	--	--	--	--
951	--	--	--	--	--	--	--
952	--	--	--	--	--	--	--
953	32.5	24.0	25.3	18.5	13.0	13.8	7.4
954	24.9	20.9	20.9	23.0	10.3	8.8	9.5
955	--	--	--	--	--	--	--
956	17.9	17.6	24.5	29.4	10.1	--	--
957	23.5	25.7	18.9	22.3	14.7	10.7	9.1
958	--	--	--	--	--	--	--
959	19.1	17.4	21.3	24.3	13.9	10.2	8.5
960	34.9	27.2	27.0	27.7	13.4	9.6	7.5
MEAN	25.8	21.5	22.4	23.0	12.9	10.8	9.2
SD	5.98	5.21	4.62	5.25	3.03	1.47	1.81
N	10	10	10	10	10	9	9

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

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

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: M. Neutrophils

STUDY ID: 098  
ABBR: M. Neutrop

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
821	--	--	--	--	--	--	--
822	--	--	--	--	--	--	--
823	0.9	1.6	1.1	1.8	1.2	1.5	1.6
824	1.2	1.0	0.9	--	1.1	0.9	2.0
825	--	--	--	--	--	--	--
826	--	--	--	--	--	--	--
827	2.8	1.6	1.0	1.1	1.6	2.4	4.7
828	--	--	--	--	--	--	--
829	--	--	--	--	--	--	--
830	2.7	1.0	1.6	2.0	1.2	2.1	1.3
831	2.4	1.6	2.3	3.7	3.0	1.5	1.2
832	--	--	--	--	--	--	--
833	--	--	--	--	--	--	--
834	1.3	0.6	1.1	2.6	0.7	1.3	0.4
835	1.4	0.9	0.3	1.9	0.8	1.0	0.8
836	3.7	1.6	3.2	1.8	1.6	1.3	1.3
837	2.3	0.9	1.3	1.2	0.8	1.0	0.0
838	--	--	--	--	--	--	--
839	--	--	--	--	--	--	--
840	2.5	2.0	1.0	1.0	0.7	0.8	2.2
MEAN	2.1	1.3	1.4	1.9	1.3	1.4	1.6
SD	0.89	0.45	0.82	0.84	0.69	0.52	1.29
N	10	10	10	9	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
861	2.2	1.3	1.7	1.2	3.7	1.8	0.7
862	--	--	--	--	--	--	--
863	--	--	--	--	--	--	--
864	3.8	2.8	1.2	0.9	2.2	1.6	4.0
865	--	--	--	--	--	--	--
866	--	--	--	--	--	--	--
867	1.6	1.0	1.9	0.6	0.7	1.0	0.6
868	0.7	1.3	2.2	0.7	--	0.6	1.1
869	--	--	--	--	--	--	--
870	--	--	--	--	--	--	--
871	3.2	0.7	1.6	1.5	2.5	1.0	2.4
872	--	--	--	--	--	--	--
873	1.3	1.9	1.3	0.1	0.7	1.9	1.6
874	0.7	0.9	0.5	1.2	1.7	1.1	1.5
875	--	--	--	--	--	--	--
876	--	--	--	--	--	--	--
877	2.0	2.8	1.0	1.2	1.4	2.8	2.3
878	--	--	--	--	--	--	--
879	1.1	2.3	0.3	1.8	2.0	0.9	1.6
880	3.8	0.5	2.4	1.1	1.7	0.6	2.0
MEAN	2.0	1.6	1.4	1.0	1.8	1.3	1.8
SD	1.19	0.85	0.69	0.48	0.93	0.69	0.99
N	10	10	10	10	9	10	10

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

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

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: M. Neutrophils

STUDY ID: 098  
ABBR: M. Neutrop

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
901	1.0	1.4	5.5	1.7	1.9	0.9	1.3
902	3.4	1.3	2.1	2.8	0.6	1.1	2.6
903	--	--	--	--	--	--	--
904	2.5	3.9	1.8	2.5	--	0.9	2.0
905	--	--	--	--	--	--	--
906	--	--	--	--	--	--	--
907	--	--	--	--	--	--	--
908	2.1	2.4	2.8	3.3	1.8	1.8	2.8
909	1.5	3.2	4.7	4.3	1.3	1.4	1.3
910	--	--	--	--	--	--	--
911	--	--	--	--	--	--	--
912	0.4	7.8	5.2	--	3.7	1.3	1.5
913	--	--	--	--	--	--	--
914	--	--	--	--	--	--	--
915	4.8	2.5	5.2	3.3	2.6	2.3	2.3
916	1.9	2.2	1.1	2.8	1.8	0.2	1.5
917	--	--	--	--	--	--	--
918	2.3	3.3	3.6	2.5	3.0	0.9	1.1
919	2.8	3.0	2.8	3.0	0.9	1.1	1.3
920	--	--	--	--	--	--	--
MEAN	2.3	3.1	3.5	2.9	2.0	1.2	1.8
SD	1.24	1.84	1.59	0.71	1.00	0.57	0.61
N	10	10	10	9	9	10	10

GROUP: 18.0:18.0 mg base/kg/day							
941	3.7	1.4	4.6	1.8	2.2	2.8	2.9
942	3.3	5.2	1.8	--	2.5	3.6	2.1
943	--	--	--	--	--	--	--
944	4.9	2.1	2.1	2.6	3.5	1.7	0.9
945	--	--	--	--	--	--	--
946	--	--	--	--	--	--	--
947	--	--	--	--	--	--	--
948	--	--	--	--	--	--	--
949	6.5	4.0	2.7	4.7	4.1	1.2	1.7
950	--	--	--	--	--	--	--
951	--	--	--	--	--	--	--
952	--	--	--	--	--	--	--
953	5.2	2.9	2.0	3.1	2.0	1.4	0.9
954	4.5	5.2	1.7	4.8	1.6	1.6	0.5
955	--	--	--	--	--	--	--
956	3.4	3.0	2.7	2.9	1.4	--	--
957	6.1	4.1	1.7	3.8	2.6	1.3	1.8
958	--	--	--	--	--	--	--
959	4.6	2.8	3.0	4.9	2.6	2.0	2.0
960	5.2	1.6	2.2	1.9	2.5	1.9	1.0
MEAN	4.7	3.2	2.5	3.4	2.5	1.9	1.5
SD	1.08	1.36	0.88	1.22	0.81	0.78	0.76
N	10	10	10	9	10	9	9

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

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

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: I. Neutrophils

STUDY ID: 098  
ABBR: I. Neutrop

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
821	--	--	--	--	--	--	--
822	--	--	--	--	--	--	--
823	0.0	0.0	0.0	0.0	0.0	0.0	0.0
824	0.0	0.0	0.0	--	0.0	0.0	0.0
825	--	--	--	--	--	--	--
826	--	--	--	--	--	--	--
827	14.2	0.0	0.0	0.0	0.0	0.0	0.0
828	--	--	--	--	--	--	--
829	--	--	--	--	--	--	--
830	0.0	0.0	0.0	0.0	0.0	0.0	0.0
831	0.0	0.0	0.0	0.0	0.0	0.0	0.0
832	--	--	--	--	--	--	--
833	--	--	--	--	--	--	--
834	0.0	0.0	0.0	0.0	0.0	0.0	0.0
835	0.0	0.0	0.0	0.0	0.0	0.0	0.0
836	0.0	0.0	0.0	0.0	0.0	0.0	0.0
837	0.0	0.0	0.0	0.0	0.0	0.0	2.2
838	--	--	--	--	--	--	--
839	--	--	--	--	--	--	--
840	0.0	0.0	0.0	0.0	0.0	0.0	0.0
MEAN	1.4	0.0	0.0	0.0	0.0	0.0	0.2
SD	4.49	0.00	0.00	0.00	0.00	0.00	0.70
N	10	10	10	9	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
861	0.0	0.0	0.0	0.0	0.0	0.0	0.0
862	--	--	--	--	--	--	--
863	--	--	--	--	--	--	--
864	0.0	0.0	0.0	0.0	0.0	0.0	0.0
865	--	--	--	--	--	--	--
866	--	--	--	--	--	--	--
867	0.0	0.0	0.0	0.0	0.0	0.0	0.0
868	0.0	0.0	0.0	0.0	--	0.0	0.0
869	--	--	--	--	--	--	--
870	--	--	--	--	--	--	--
871	0.0	0.1	0.0	0.0	0.0	0.0	0.0
872	--	--	--	--	--	--	--
873	0.0	0.0	0.0	0.0	0.0	0.0	0.0
874	0.0	0.0	0.0	0.0	0.0	0.0	0.0
875	--	--	--	--	--	--	--
876	--	--	--	--	--	--	--
877	0.0	0.0	0.0	0.0	0.0	0.0	0.0
878	--	--	--	--	--	--	--
879	0.0	0.0	0.0	0.0	0.0	0.0	0.0
880	0.0	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
SD	0.00	0.03	0.00	0.00	0.00	0.00	0.00
N	10	10	10	10	9	10	10

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

DRAFT

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: I. Neutrophils

STUDY ID: 098  
ABBR: I. Neutrop

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
901	0.0	0.0	0.0	0.0	0.0	0.0	0.0
902	0.0	0.0	0.0	0.0	0.0	0.0	0.0
903	--	--	--	--	--	--	--
904	0.0	0.0	0.0	0.0	--	0.0	0.0
905	--	--	--	--	--	--	--
906	--	--	--	--	--	--	--
907	--	--	--	--	--	--	--
908	0.0	0.0	0.0	0.0	0.0	0.0	0.0
909	0.0	0.0	0.0	0.0	0.0	0.0	0.0
910	--	--	--	--	--	--	--
911	--	--	--	--	--	--	--
912	0.0	0.0	0.0	--	0.0	0.0	0.0
913	--	--	--	--	--	--	--
914	--	--	--	--	--	--	--
915	0.0	0.0	0.0	0.0	0.0	0.0	0.0
916	0.0	0.0	0.0	0.0	0.0	0.0	0.0
917	--	--	--	--	--	--	--
918	18.2	0.0	0.0	0.0	0.0	0.0	0.0
919	0.0	0.0	0.0	0.0	0.0	0.0	0.0
920	--	--	--	--	--	--	--
MEAN	1.8	0.0	0.0	0.0	0.0	0.0	0.0
SD	5.76	0.00	0.00	0.00	0.00	0.00	0.00
N	10	10	10	9	9	10	10

GROUP: 18.0:18.0 mg base/kg/day							
941	0.0	0.0	0.0	0.0	0.0	0.0	0.0
942	0.0	0.0	0.0	--	0.0	0.0	0.0
943	--	--	--	--	--	--	--
944	0.0	0.0	0.0	0.0	0.0	0.0	0.0
945	--	--	--	--	--	--	--
946	--	--	--	--	--	--	--
947	--	--	--	--	--	--	--
948	--	--	--	--	--	--	--
949	0.0	0.0	0.0	0.0	0.0	0.0	0.0
950	--	--	--	--	--	--	--
951	--	--	--	--	--	--	--
952	--	--	--	--	--	--	--
953	0.0	0.0	0.0	0.0	0.0	0.0	0.0
954	0.0	0.0	0.0	0.0	0.0	0.0	0.0
955	--	--	--	--	--	--	--
956	0.0	0.0	0.0	0.0	0.0	--	--
957	0.0	0.0	0.0	0.0	0.0	0.0	0.0
958	--	--	--	--	--	--	--
959	0.0	0.0	0.0	0.0	0.0	0.0	0.0
960	0.0	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
SD	0.00	0.00	0.00	0.00	0.00	0.00	0.00
N	10	10	10	9	10	9	9

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

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

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Lymphocytes

STUDY ID: 098  
ABBR: Lymphocyte

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
821	--	--	--	--	--	--	--
822	--	--	--	--	--	--	--
823	11.3	5.2	6.3	7.6	4.8	5.6	5.2
824	9.8	8.5	5.1	--	4.3	4.3	5.9
825	--	--	--	--	--	--	--
826	--	--	--	--	--	--	--
827	0.4	12.5	7.7	8.6	7.2	8.6	5.8
828	--	--	--	--	--	--	--
829	--	--	--	--	--	--	--
830	15.2	9.7	6.5	7.8	6.3	6.1	6.2
831	18.1	14.2	12.3	9.9	12.4	11.6	8.9
832	--	--	--	--	--	--	--
833	--	--	--	--	--	--	--
834	11.8	12.7	11.9	9.8	7.5	8.6	7.9
835	9.3	7.5	7.3	6.6	6.6	8.5	6.5
836	13.4	7.2	8.1	7.9	8.1	7.0	7.5
837	14.0	9.4	9.2	7.2	7.1	6.2	0.0
838	--	--	--	--	--	--	--
839	--	--	--	--	--	--	--
840	12.9	10.0	9.6	10.5	9.0	8.5	8.5
MEAN	11.6	9.7	8.4	8.4	7.3	7.5	6.2
SD	4.71	2.79	2.36	1.35	2.27	2.08	2.51
N	10	10	10	9	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
861	10.6	9.3	11.9	8.1	6.0	8.7	5.9
862	--	--	--	--	--	--	--
863	--	--	--	--	--	--	--
864	14.6	17.1	17.8	11.8	7.9	9.4	6.9
865	--	--	--	--	--	--	--
866	--	--	--	--	--	--	--
867	17.7	12.7	7.9	9.3	9.3	7.2	8.6
868	15.4	16.3	12.1	8.3	--	6.1	7.6
869	--	--	--	--	--	--	--
870	--	--	--	--	--	--	--
871	16.5	10.6	11.9	9.7	8.8	9.4	9.8
872	--	--	--	--	--	--	--
873	9.6	9.6	10.7	9.9	9.1	8.5	8.0
874	13.2	15.5	11.6	10.6	6.7	7.7	5.1
875	--	--	--	--	--	--	--
876	--	--	--	--	--	--	--
877	13.9	10.6	8.8	8.3	8.6	7.3	5.8
878	--	--	--	--	--	--	--
879	16.5	15.8	11.6	9.2	9.4	8.0	7.3
880	25.2	15.3	10.7	12.6	10.3	11.3	8.4
MEAN	15.3	13.3	11.5	9.8	8.5	8.4	7.3
SD	4.32	3.04	2.62	1.51	1.37	1.46	1.45
N	10	10	10	10	9	10	10

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Lymphocytes

STUDY ID: 098  
ABBR: Lymphocyte

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
901	15.3	12.4	18.8	14.3	8.0	9.5	9.8
902	10.6	9.1	9.3	12.4	4.8	4.6	5.3
903	--	--	--	--	--	--	--
904	15.7	15.5	15.8	11.6	--	8.9	4.9
905	--	--	--	--	--	--	--
906	--	--	--	--	--	--	--
907	--	--	--	--	--	--	--
908	11.5	9.9	7.3	6.5	5.3	5.4	5.4
909	10.0	8.9	4.6	4.4	5.6	7.9	7.1
910	--	--	--	--	--	--	--
911	--	--	--	--	--	--	--
912	18.0	20.6	16.1	--	9.6	7.7	8.4
913	--	--	--	--	--	--	--
914	--	--	--	--	--	--	--
915	17.7	13.3	11.9	10.1	7.6	6.9	8.1
916	14.4	9.8	10.3	7.8	7.5	10.3	7.5
917	--	--	--	--	--	--	--
918	0.6	19.4	14.6	17.5	5.8	11.6	12.5
919	14.4	16.5	11.4	9.2	7.2	6.9	8.3
920	--	--	--	--	--	--	--
MEAN	12.8	13.5	12.0	10.4	6.8	8.0	7.7
SD	5.10	4.30	4.37	4.04	1.55	2.16	2.30
N	10	10	10	9	9	10	10

GROUP: 18.0:18.0 mg base/kg/day							
941	23.2	13.5	16.1	11.6	8.1	6.3	6.1
942	15.0	11.3	11.0	--	6.1	7.0	4.7
943	--	--	--	--	--	--	--
944	16.3	12.4	14.0	14.5	10.7	9.5	8.7
945	--	--	--	--	--	--	--
946	--	--	--	--	--	--	--
947	--	--	--	--	--	--	--
948	--	--	--	--	--	--	--
949	24.6	24.6	26.6	21.8	13.8	9.0	10.7
950	--	--	--	--	--	--	--
951	--	--	--	--	--	--	--
952	--	--	--	--	--	--	--
953	25.7	18.7	15.2	13.0	10.7	11.7	6.1
954	18.4	13.4	16.9	14.5	8.5	7.0	8.5
955	--	--	--	--	--	--	--
956	13.1	12.3	18.4	22.9	8.4	--	--
957	15.5	16.7	14.9	17.6	11.3	9.3	6.9
958	--	--	--	--	--	--	--
959	13.6	12.9	15.5	15.8	11.0	7.7	5.9
960	26.2	22.6	21.9	22.7	10.2	7.0	6.5
MEAN	19.2	15.8	17.1	17.2	9.9	8.3	7.1
SD	5.22	4.67	4.39	4.32	2.15	1.73	1.84
N	10	10	10	9	10	9	9

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

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

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Monocytes

STUDY ID: 098  
ABBR: Monocytes

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
821	--	--	--	--	--	--	--
822	--	--	--	--	--	--	--
823	0.4	0.1	1.0	0.3	0.2	0.4	0.8
824	1.8	0.7	0.5	--	0.2	0.1	0.2
825	--	--	--	--	--	--	--
826	--	--	--	--	--	--	--
827	0.2	0.1	0.7	0.2	0.2	0.7	0.3
828	--	--	--	--	--	--	--
829	--	--	--	--	--	--	--
830	0.0	0.3	0.6	0.1	0.2	0.5	0.6
831	0.6	0.5	0.6	0.6	0.5	0.4	0.5
832	--	--	--	--	--	--	--
833	--	--	--	--	--	--	--
834	0.0	1.5	0.3	0.1	0.8	0.3	0.0
835	0.2	0.5	0.8	0.1	0.4	0.2	0.5
836	0.5	0.5	0.2	0.3	0.2	0.4	0.5
837	0.0	0.0	0.2	0.0	0.4	0.2	7.1
838	--	--	--	--	--	--	--
839	--	--	--	--	--	--	--
840	0.0	0.5	0.6	0.6	0.0	0.2	0.1
MEAN	0.4	0.5	0.6	0.3	0.3	0.3	1.1
SD	0.55	0.43	0.26	0.22	0.22	0.18	2.14
N	10	10	10	9	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
861	0.3	0.4	0.6	0.3	0.2	0.4	0.2
862	--	--	--	--	--	--	--
863	--	--	--	--	--	--	--
864	0.4	1.5	1.0	0.1	0.8	0.5	0.6
865	--	--	--	--	--	--	--
866	--	--	--	--	--	--	--
867	0.0	0.4	0.5	0.1	0.2	0.5	0.4
868	0.5	0.6	0.4	0.5	--	0.2	0.0
869	--	--	--	--	--	--	--
870	--	--	--	--	--	--	--
871	0.0	0.0	0.7	1.0	0.5	0.4	0.4
872	--	--	--	--	--	--	--
873	0.2	0.4	0.6	0.2	0.2	0.6	0.6
874	0.1	0.7	0.6	0.0	0.7	0.2	0.1
875	--	--	--	--	--	--	--
876	--	--	--	--	--	--	--
877	0.3	0.6	0.1	0.1	0.0	0.1	0.4
878	--	--	--	--	--	--	--
879	0.0	0.2	0.3	0.5	0.2	0.1	0.6
880	0.0	0.2	0.1	0.1	0.2	0.2	0.4
MEAN	0.2	0.5	0.5	0.3	0.3	0.3	0.4
SD	0.19	0.41	0.28	0.30	0.27	0.18	0.21
N	10	10	10	10	9	10	10

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Monocytes

STUDY ID: 098  
ABBR: Monocytes

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
901	0.7	0.1	0.5	0.9	0.4	0.6	0.5
902	0.1	0.6	0.1	0.8	0.2	0.2	0.0
903	--	--	--	--	--	--	--
904	0.4	0.0	0.0	0.0	--	0.1	0.2
905	--	--	--	--	--	--	--
906	--	--	--	--	--	--	--
907	--	--	--	--	--	--	--
908	0.3	0.1	0.7	0.5	0.4	0.1	0.4
909	0.9	0.5	0.5	0.0	0.2	0.3	0.2
910	--	--	--	--	--	--	--
911	--	--	--	--	--	--	--
912	0.2	1.5	0.2	--	0.9	0.2	1.1
913	--	--	--	--	--	--	--
914	--	--	--	--	--	--	--
915	0.0	0.7	0.7	0.6	0.5	0.7	0.3
916	0.5	0.1	1.3	0.4	0.2	0.7	0.6
917	--	--	--	--	--	--	--
918	0.0	0.5	0.6	0.6	0.0	0.1	0.3
919	0.0	0.2	1.1	0.4	0.6	0.1	0.2
920	--	--	--	--	--	--	--
MEAN	0.3	0.4	0.6	0.5	0.4	0.3	0.4
SD	0.31	0.45	0.41	0.31	0.27	0.26	0.30
N	10	10	10	9	9	10	10

GROUP: 18.0:18.0 mg base/kg/day							
941	1.4	2.1	2.3	0.6	0.3	0.4	0.4
942	2.5	2.7	1.8	--	0.4	0.2	0.7
943	--	--	--	--	--	--	--
944	1.9	0.8	1.6	3.0	0.0	0.1	0.5
945	--	--	--	--	--	--	--
946	--	--	--	--	--	--	--
947	--	--	--	--	--	--	--
948	--	--	--	--	--	--	--
949	1.0	2.5	0.9	4.7	1.2	0.6	0.7
950	--	--	--	--	--	--	--
951	--	--	--	--	--	--	--
952	--	--	--	--	--	--	--
953	1.6	2.4	8.1	2.4	0.3	0.7	0.4
954	2.0	2.1	2.1	3.7	0.1	0.1	0.3
955	--	--	--	--	--	--	--
956	1.1	2.1	3.2	3.5	0.3	--	--
957	1.9	4.1	2.3	0.9	0.7	0.0	0.4
958	--	--	--	--	--	--	--
959	1.0	1.6	2.8	3.4	0.3	0.4	0.4
960	3.1	3.0	3.0	3.0	0.7	0.5	0.1
MEAN	1.8	2.3	2.8	2.8	0.4	0.3	0.4
SD	0.68	0.87	1.98	1.32	0.35	0.24	0.19
N	10	10	10	9	10	9	9

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

DRAFT

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Eosinophils

STUDY ID: 098  
ABBR: Eosinophil

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
821	--	--	--	--	--	--	--
822	--	--	--	--	--	--	--
823	0.0	0.1	0.1	0.1	0.0	0.0	0.1
824	0.1	0.1	0.0	--	0.1	0.2	0.0
825	--	--	--	--	--	--	--
826	--	--	--	--	--	--	--
827	0.0	0.0	0.0	0.1	0.0	0.2	0.1
828	--	--	--	--	--	--	--
829	--	--	--	--	--	--	--
830	0.0	0.1	0.1	0.1	0.2	0.2	0.1
831	0.4	0.0	0.2	0.0	0.0	0.1	0.1
832	--	--	--	--	--	--	--
833	--	--	--	--	--	--	--
834	0.0	0.3	0.1	0.0	0.0	0.0	0.0
835	0.1	0.1	0.0	0.0	0.1	0.1	0.0
836	0.2	0.2	0.2	0.1	0.0	0.0	0.1
837	0.3	0.1	0.0	0.0	0.1	0.2	0.1
838	--	--	--	--	--	--	--
839	--	--	--	--	--	--	--
840	0.0	0.1	0.2	0.2	0.4	0.1	0.0
MEAN	0.1	0.1	0.1	0.1	0.1	0.1	0.1
SO	0.14	0.09	0.09	0.07	0.13	0.09	0.05
N	10	10	10	9	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
861	0.0	0.0	0.3	0.0	0.1	0.2	0.1
862	--	--	--	--	--	--	--
863	--	--	--	--	--	--	--
864	0.2	0.0	0.0	0.0	0.1	0.1	0.2
865	--	--	--	--	--	--	--
866	--	--	--	--	--	--	--
867	0.2	0.0	0.0	0.2	0.2	0.5	0.0
868	0.0	0.4	0.0	0.0	--	0.0	0.3
869	--	--	--	--	--	--	--
870	--	--	--	--	--	--	--
871	0.0	0.0	0.4	0.0	0.2	0.0	0.0
872	--	--	--	--	--	--	--
873	0.0	0.0	0.0	0.0	0.2	0.1	0.0
874	0.0	0.0	0.1	0.2	0.2	0.0	0.1
875	--	--	--	--	--	--	--
876	--	--	--	--	--	--	--
877	0.3	0.0	0.3	0.1	0.1	0.0	0.0
878	--	--	--	--	--	--	--
879	0.0	0.6	0.5	0.5	0.1	0.2	0.1
880	0.0	0.5	0.0	0.1	0.1	0.0	0.1
MEAN	0.1	0.2	0.2	0.1	0.1	0.1	0.1
SO	0.12	0.25	0.20	0.16	0.05	0.16	0.10
N	10	10	10	10	9	10	10

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Eosinophils

STUDY ID: 098  
ABBR: Eosinophil

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
901	0.3	0.3	0.3	0.3	0.0	0.1	0.1
902	0.0	0.1	0.2	0.3	0.2	0.1	0.2
903	--	--	--	--	--	--	--
904	0.4	0.0	0.0	0.0	--	0.1	0.1
905	--	--	--	--	--	--	--
906	--	--	--	--	--	--	--
907	--	--	--	--	--	--	--
908	0.0	0.1	0.1	0.3	0.0	0.0	0.0
909	0.1	0.1	0.2	0.1	0.1	0.2	0.0
910	--	--	--	--	--	--	--
911	--	--	--	--	--	--	--
912	0.2	0.0	0.2	--	0.1	0.3	0.3
913	--	--	--	--	--	--	--
914	--	--	--	--	--	--	--
915	0.2	0.2	0.0	0.4	0.1	0.1	0.2
916	0.2	0.1	0.0	0.1	0.1	0.0	0.2
917	--	--	--	--	--	--	--
918	0.0	0.5	0.2	0.0	0.0	0.0	0.0
919	0.2	0.2	0.2	0.0	0.0	0.0	0.0
920	--	--	--	--	--	--	--
MEAN	0.2	0.2	0.1	0.2	0.1	0.1	0.1
SD	0.13	0.15	0.11	0.16	0.07	0.10	0.11
N	10	10	10	9	9	10	10

GROUP: 18.0:18.0 mg base/kg/day							
941	0.0	0.2	0.0	0.1	0.3	0.1	0.2
942	0.0	0.0	0.1	--	0.0	0.6	0.0
943	--	--	--	--	--	--	--
944	0.2	0.0	0.2	0.0	0.3	0.2	0.2
945	--	--	--	--	--	--	--
946	--	--	--	--	--	--	--
947	--	--	--	--	--	--	--
948	--	--	--	--	--	--	--
949	0.3	0.0	0.0	0.0	0.4	0.3	0.0
950	--	--	--	--	--	--	--
951	--	--	--	--	--	--	--
952	--	--	--	--	--	--	--
953	0.0	0.0	0.0	0.0	0.1	0.0	0.0
954	0.0	0.2	0.2	0.0	0.0	0.2	0.3
955	--	--	--	--	--	--	--
956	0.4	0.2	0.2	0.0	0.0	--	--
957	0.0	0.8	0.0	0.0	0.0	0.1	0.0
958	--	--	--	--	--	--	--
959	0.0	0.2	0.0	0.2	0.0	0.1	0.3
960	0.3	0.0	0.0	0.0	0.0	0.2	0.0
MEAN	0.1	0.2	0.1	0.0	0.1	0.2	0.1
SD	0.16	0.25	0.09	0.07	0.16	0.17	0.14
N	10	10	10	9	10	9	9

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Basophils

STUDY ID: 098  
ABBR: Basophils

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 0:0 mg base/kg/day							
821	--	--	--	--	--	--	--
822	--	--	--	--	--	--	--
823	0.0	0.0	0.0	0.0	0.0	0.0	0.0
824	0.0	0.0	0.0	--	0.0	0.0	0.0
825	--	--	--	--	--	--	--
826	--	--	--	--	--	--	--
827	0.0	0.0	0.0	0.0	0.0	0.0	0.0
828	--	--	--	--	--	--	--
829	--	--	--	--	--	--	--
830	0.0	0.0	0.0	0.0	0.0	0.0	0.0
831	0.0	0.0	0.0	0.0	0.0	0.0	0.0
832	--	--	--	--	--	--	--
833	--	--	--	--	--	--	--
834	0.0	0.0	0.0	0.0	0.0	0.0	0.0
835	0.0	0.0	0.0	0.0	0.0	0.0	0.0
836	0.0	0.0	0.0	0.0	0.0	0.0	0.0
837	0.0	0.0	0.0	0.0	0.0	0.0	0.2
838	--	--	--	--	--	--	--
839	--	--	--	--	--	--	--
840	0.0	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
SD	0.00	0.00	0.00	0.00	0.00	0.00	0.06
N	10	10	10	9	10	10	10

GROUP: 0.5:0.5 mg base/kg/day							
861	0.0	0.0	0.0	0.0	0.0	0.0	0.0
862	--	--	--	--	--	--	--
863	--	--	--	--	--	--	--
864	0.0	0.0	0.0	0.0	0.0	0.0	0.0
865	--	--	--	--	--	--	--
866	--	--	--	--	--	--	--
867	0.0	0.0	0.0	0.0	0.0	0.0	0.0
868	0.0	0.0	0.0	0.0	--	0.0	0.0
869	--	--	--	--	--	--	--
870	--	--	--	--	--	--	--
871	0.0	0.0	0.0	0.0	0.0	0.0	0.0
872	--	--	--	--	--	--	--
873	0.0	0.0	0.0	0.0	0.0	0.0	0.0
874	0.0	0.0	0.0	0.0	0.0	0.0	0.0
875	--	--	--	--	--	--	--
876	--	--	--	--	--	--	--
877	0.0	0.0	0.0	0.0	0.0	0.0	0.0
878	--	--	--	--	--	--	--
879	0.0	0.0	0.0	0.0	0.0	0.0	0.0
880	0.0	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
SD	0.00	0.00	0.00	0.00	0.00	0.00	0.00
N	10	10	10	10	9	10	10

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

DRAFT

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

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Basophils

STUDY ID: 098  
ABBR: Basophils

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

ANIMAL ID	Week 2	Week 4	Week 8	Week 13	Week 16	Week 21	Week 27
GROUP: 6.0:6.0 mg base/kg/day							
901	0.0	0.0	0.0	0.0	0.0	0.0	0.0
902	0.0	0.0	0.0	0.0	0.0	0.0	0.0
903	--	--	--	--	--	--	--
904	0.0	0.0	0.0	0.0	--	0.0	0.0
905	--	--	--	--	--	--	--
906	--	--	--	--	--	--	--
907	--	--	--	--	--	--	--
908	0.0	0.0	0.0	0.0	0.0	0.0	0.0
909	0.0	0.0	0.0	0.0	0.0	0.0	0.0
910	--	--	--	--	--	--	--
911	--	--	--	--	--	--	--
912	0.0	0.0	0.0	--	0.0	0.0	0.0
913	--	--	--	--	--	--	--
914	--	--	--	--	--	--	--
915	0.0	0.0	0.0	0.0	0.0	0.0	0.0
916	0.0	0.0	0.0	0.0	0.0	0.0	0.0
917	--	--	--	--	--	--	--
918	0.0	0.0	0.0	0.0	0.0	0.0	0.0
919	0.0	0.0	0.0	0.0	0.0	0.0	0.0
920	--	--	--	--	--	--	--
MEAN	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
N	10	10	10	9	9	10	10

GROUP: 18.0:18.0 mg base/kg/day							
941	0.0	0.0	0.0	0.0	0.0	0.0	0.0
942	0.0	0.0	0.0	--	0.0	0.0	0.0
943	--	--	--	--	--	--	--
944	0.0	0.0	0.0	0.0	0.0	0.0	0.0
945	--	--	--	--	--	--	--
946	--	--	--	--	--	--	--
947	--	--	--	--	--	--	--
948	--	--	--	--	--	--	--
949	0.0	0.0	0.0	0.0	0.0	0.0	0.0
950	--	--	--	--	--	--	--
951	--	--	--	--	--	--	--
952	--	--	--	--	--	--	--
953	0.0	0.0	0.0	0.0	0.0	0.0	0.0
954	0.0	0.0	0.0	0.0	0.0	0.0	0.0
955	--	--	--	--	--	--	--
956	0.0	0.0	0.0	0.0	0.0	--	--
957	0.0	0.0	0.0	0.0	0.0	0.0	0.0
958	--	--	--	--	--	--	--
959	0.0	0.0	0.0	0.0	0.0	0.0	0.0
960	0.0	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
SD	0.00	0.00	0.00	0.00	0.00	0.00	0.00
N	10	10	10	9	10	9	9

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

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

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 0 : 0 mg base/kg/day

SEX: MALE

ANIMAL ID	Week 2	Week 4	Week 8	Week 13
801	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Poikilocytes,Slight; Anisocytosis,Slight
802	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
803	--	--	--	--
804	--	--	--	--
805	--	--	--	--
806	Polychromasia,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
807	Polychromasia,Slight Macrocytes,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight
808	--	--	--	--
809	Polychromasia,Slight Macrocytes,Moderate	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
810	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Target Cells, Moderate	Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate
811	Polychromasia,Slight Macrocytes,Slight	Polychromasia,Slight Anisocytosis,Slight	Target Cells,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
812	--	--	--	Polychromasia,Slight Anisocytosis,Slight
813	--	--	--	--
814	Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
815	Polychromasia, Moderate; Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate

(--)-Data Unavailable

DRAFT

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

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 0 : 0 mg base/kg/day

SEX: MALE

ANIMAL ID	Week 2	Week 4	Week 8	Week 13
816	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Target Cells,Slight	Polychromasia,Slight Target Cells, Moderate; Anisocytosis,Slight
817	--	--	--	--
818	--	--	--	--
819	--	--	--	--
820	--	--	--	--

(--)-Data Unavailable

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

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 0 : 0 mg base/kg/day

SEX: MALE

ANIMAL ID	Week 16	Week 21	Week 27
801	Anisocytosis,Slight; Polychromasia,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Poikilocytes,Slight; Target Cells,Slight; Anisocytosis,Slight
802	Anisocytosis,Slight; Polychromasia,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
803	--	--	--
804	--	--	--
805	--	--	--
806	Anisocytosis,Slight; Polychromasia,Slight	Polychromasia,Slight Anisocytosis,Slight	Target Cells,Slight; Anisocytosis,Slight
807	Anisocytosis,Slight; Polychromasia,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
808	--	--	--
809	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight	Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
810	Anisocytosis,Slight; Target Cells,Slight	Polychromasia,Slight Poikilocytes,Slight; Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
811	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight	Polychromasia,Slight Anisocytosis,Slight; Howell-Jolly Bodies, Slight
812	--	--	--
813	--	--	--
814	Anisocytosis,Slight; Polychromasia,Slight	Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Anisocytosis,Slight

(--)-Data Unavailable

DRAFT

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

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 0 : 0 mg base/kg/day

SEX: MALE

ANIMAL ID	Week 16	Week 21	Week 27
815	Anisocytosis,Slight; Polychromasia,Slight Poikilocytes,Slight; Target Cells,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
816	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
817	--	--	--
818	--	--	--
819	--	--	--
820	--	--	--

(--)-Data Unavailable

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

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

SEX: MALE

GROUP: 0.5 : 0.5 mg base/kg/day

ANIMAL ID	Week 2	Week 4	Week 8	Week 13
841	--	--	--	--
842	--	--	--	--
843	--	--	--	--
844	Macrocytes, Moderate; Polychromasia, Moderate	Polychromasia, Slight Anisocytosis, Slight	Anisocytosis, Slight	Polychromasia, Slight Target Cells, Slight
845	--	--	--	--
846	Polychromasia, Slight	Polychromasia, Slight Anisocytosis, Slight	Polychromasia, Slight Poikilocytes, Slight; Anisocytosis, Slight	Polychromasia, Slight
847	--	--	--	--
848	Normal Red Blood Cells	Polychromasia, Slight Anisocytosis, Slight	Polychromasia, Slight Anisocytosis, Slight	Polychromasia, Slight Anisocytosis, Slight
849	--	--	--	--
850	Polychromasia, Slight Macrocytes, Slight	Polychromasia, Slight Anisocytosis, Slight	Polychromasia, Slight Anisocytosis, Slight	Polychromasia, Slight Target Cells, Slight; Anisocytosis, Slight
851	Polychromasia, Slight Anisocytosis, Slight	Polychromasia, Slight Target Cells, Slight; Anisocytosis, Slight	Polychromasia, Slight Anisocytosis, Slight	Polychromasia, Slight Anisocytosis, Slight
852	Polychromasia, Moderate; Macrocytes, Slight	Polychromasia, Slight Anisocytosis, Slight; Howell-Jolly Bodies, Slight	Polychromasia, Slight Anisocytosis, Slight	Polychromasia, Slight Target Cells, Slight; Anisocytosis, Slight
853	Polychromasia, Slight	Anisocytosis, Slight	Target Cells, Slight	Poikilocytes, Slight; Anisocytosis, Slight
854	--	--	--	--
855	--	--	--	--
856	--	--	--	--
857	--	--	--	--
858	Polychromasia, Slight Anisocytosis, Slight	Polychromasia, Slight Anisocytosis, Slight	Anisocytosis, Slight	Polychromasia, Slight Anisocytosis, Slight

(--)-Data Unavailable

DRAFT

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

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 0.5 : 0.5 mg base/kg/day

SEX: MALE

ANIMAL ID	Week 2	Week 4	Week 8	Week 13
859	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
860	Polychromasia, Moderate;Macrocytes, Moderate	Polychromasia,Slight Target Cells,Slight; Rouleaux Formation, Slight	Target Cells,Slight; Anisocytosis,Slight	Polychromasia, Moderate;Target Cells,Slight; Anisocytosis,Slight

(--)-Data Unavailable

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

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

SEX: MALE

GROUP: 0.5 : 0.5 mg base/kg/day

ANIMAL ID	Week 16	Week 21	Week 27
841	--	--	--
842	--	--	--
843	--	--	--
844	Anisocytosis,Slight; Polychromasia,Slight	Normal Red Blood Cells	Polychromasia,Slight Poikilocytes,Slight; Anisocytosis,Slight
845	--	--	--
846	Anisocytosis,Slight; Target Cells,Slight	Polychromasia,Slight	Polychromasia,Slight Anisocytosis,Slight
847	--	--	--
848	Anisocytosis,Slight; Polychromasia,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight; Howell-Jolly Bodies, Slight
849	--	--	--
850	Anisocytosis, Moderate; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
851	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Poikilocytes,Slight; Target Cells,Slight; Anisocytosis,Slight
852	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight
853	Anisocytosis,Slight; Polychromasia,Slight	Polychromasia,Slight Anisocytosis,Slight; Howell-Jolly Bodies, Slight	Polychromasia,Slight Poikilocytes,Slight; Target Cells,Slight; Anisocytosis,Slight
854	--	--	--
855	--	--	--
856	--	--	--

(--)-Data Unavailable

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

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

SEX: MALE

GROUP: 0.5 : 0.5 mg base/kg/day

ANIMAL ID	Week 16	Week 21	Week 27
857	--	--	--
858	Anisocytosis,Slight; Polychromasia,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
859	Anisocytosis,Slight; Polychromasia,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight; Howell-Jolly Bodies, Slight
860	Anisocytosis,Slight; Polychromasia,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells, Moderate; Anisocytosis,Slight

(--)-Data Unavailable

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

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 6.0 : 6.0 mg base/kg/day

SEX: MALE

ANIMAL ID	Week 2	Week 4	Week 8	Week 13
881	--	--	--	--
882	--	--	--	--
883	--	--	--	--
884	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight; Howell-Jolly Bodies, Slight	Polychromasia,Slight Anisocytosis,Slight	Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight
885	--	--	--	--
886	--	--	--	--
887	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate	--
888	--	--	--	--
889	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
890	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight	Polychromasia,Slight Anisocytosis,Slight
891	--	--	--	--
892	--	--	--	--
893	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells, Moderate; Anisocytosis,Slight; Howell-Jolly Bodies, Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight	Polychromasia, Moderate;Target Cells,Moderate; Anisocytosis, Moderate; Howell-Jolly Bodies, Slight
894	--	--	--	--
895	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight

(--)-Data Unavailable

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

DRAFT

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 6.0 : 6.0 mg base/kg/day

SEX: MALE

ANIMAL ID	Week 2	Week 4	Week 8	Week 13
896	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight
897	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Target Cells, Moderate; Anisocytosis, Moderate
898	--	--	--	--
899	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight; Howell-Jolly Bodies, Moderate	Polychromasia,Slight Target Cells, Moderate; Anisocytosis,Slight; Howell-Jolly Bodies, Moderate	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
900	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight

(--)-Data Unavailable

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

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 6.0 : 6.0 mg base/kg/day

SEX: MALE

ANIMAL ID	Week 16	Week 21	Week 27
881	--	--	--
882	--	--	--
883	--	--	--
884	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
885	--	--	--
886	--	--	--
887	Anisocytosis,Slight; Polychromasia,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
888	--	--	--
889	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
890	Anisocytosis, Moderate; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
891	--	--	--
892	--	--	--
893	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
894	--	--	--
895	Anisocytosis,Slight; Target Cells,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
896	Anisocytosis,Slight; Polychromasia,Slight	Polychromasia,Slight Anisocytosis,Slight	Normal Red Blood Cells

(--)-Data Unavailable

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

## MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 6.0 : 6.0 mg base/kg/day

SEX: MALE

ANIMAL ID	Week 16	Week 21	Week 27
897	Anisocytosis,Slight; Target Cells,Slight	Polychromasia,Slight Target Cells, Moderate; Anisocytosis,Slight; Howell-Jolly Bodies, Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
898	--	--	--
899	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
900	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight

(--)-Data Unavailable

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

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 18.0 : 18.0 mg base/kg/day

SEX: MALE

ANIMAL ID	Week 2	Week 4	Week 8	Week 13
921	--	--	--	--
922	--	--	--	Polychromasia,Slight Anisocytosis,Slight
923	Polychromasia, Moderate;Target Cells,Slight; Macrocytes,Moderate	Polychromasia, Moderate; Poikilocytes,Slight; Target Cells, Moderate; Anisocytosis, Moderate	Polychromasia, Moderate; Poikilocytes,Slight; Target Cells,Slight; Anisocytosis, Moderate; Howell-Jolly Bodies, Slight	Polychromasia, Moderate;Target Cells,Slight; Anisocytosis,Slight
924	--	--	--	--
925	--	--	--	--
926	--	--	--	--
927	Polychromasia,Slight Macrocytes,Moderate	Polychromasia,Slight Anisocytosis,Slight; Howell-Jolly Bodies, Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight
928	--	--	--	--
929	Polychromasia,Slight Poikilocytes,Slight; Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight	Polychromasia,Slight Poikilocytes,Slight; Anisocytosis,Slight	Polychromasia, Moderate;Target Cells,Moderate; Anisocytosis,Slight; Howell-Jolly Bodies, Moderate	Polychromasia,Slight Anisocytosis,Slight
930	Polychromasia, Moderate; Anisocytosis,Slight	Polychromasia, Moderate;Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Moderate
931	--	--	--	--
932	--	Polychromasia, Moderate; Anisocytosis, Moderate; Howell-Jolly Bodies, Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia, Moderate;Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight

(--)-Data Unavailable

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

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 18.0 : 18.0 mg base/kg/day

SEX: MALE

ANIMAL ID	Week 2	Week 4	Week 8	Week 13
933	Polychromasia,Slight Anisocytosis,Slight; Large Platelets; Howell-Jolly Bodies, Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia, Moderate;Target Cells,Slight; Anisocytosis, Moderate	Target Cells, Moderate; Anisocytosis,Slight
934	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	--
935	Polychromasia, Moderate;Target Cells,Slight; Macrocytes,Moderate; Howell-Jolly Bodies, Moderate	Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Moderate	Polychromasia, Moderate;Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Moderate
936	--	--	--	--
937	Polychromasia,Slight Target Cells,Slight; Macrocytes,Slight	--	--	--
938	--	--	--	--
939	Polychromasia,Slight Target Cells,Slight; Macrocytes,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate; Howell-Jolly Bodies, Slight	Polychromasia, Moderate;Target Cells,Moderate; Anisocytosis, Moderate; Howell-Jolly Bodies, Slight
940	Polychromasia,Slight Anisocytosis,Slight	Polychromasia, Moderate; Poikilocytes,Slight; Target Cells,Slight; Anisocytosis, Moderate	Polychromasia, Moderate; Poikilocytes,Slight; Target Cells, Moderate; Anisocytosis,Slight; Howell-Jolly Bodies, Moderate	Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate; Howell-Jolly Bodies, Moderate

(--)-Data Unavailable

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

DRAFT

MORPHOLOGY OBSERVATIONS

STUDY ID: 093

GROUP: 18.0 : 18.0 mg base/kg/day

SEX: MALE

ANIMAL ID	Week 16	Week 21	Week 27
921	--	--	--
922	Anisocytosis, Moderate; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Anisocytosis,Slight	Anisocytosis,Slight
923	Anisocytosis, Moderate; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
924	--	--	--
925	--	--	--
926	--	--	--
927	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
928	--	--	--
929	Anisocytosis, Moderate; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
930	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
931	--	--	--
932	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
933	Anisocytosis, Moderate; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
934	--	--	--
935	Anisocytosis,Slight; Target Cells,Slight; Howell-Jolly Bodies, Slight	Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Anisocytosis,Slight

(--)-Data Unavailable

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

DRAFT

MORPHOLOGY OBSERVATIONS

STUDY ID: 093

GROUP: 18.0 : 18.0 mg base/kg/day

SEX: MALE

ANIMAL ID	Week 16	Week 21	Week 27
936	--	--	--
937	--	--	--
938	--	--	--
939	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight; Howell-Jolly Bodies, Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Poikilocytes,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight
940	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight	Polychromasia;Slight	Target Cells,Slight; Anisocytosis,Slight

(--)-Data Unavailable

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

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 0 : 0 mg base/kg/day

SEX: FEMALE

ANIMAL ID	Week 2	Week 4	Week 8	Week 13
821	--	--	--	--
822	--	--	--	--
823	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Anisocytosis,Slight	Target Cells,Slight; Anisocytosis,Slight
824	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	--
825	--	--	--	--
826	--	--	--	--
827	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight	Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
828	--	--	--	--
829	--	--	--	--
830	Polychromasia,Slight Macrocytes,Moderate	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
831	Polychromasia,Slight Macrocytes,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Target Cells,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
832	--	--	--	--
833	--	--	--	--
834	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
835	Polychromasia,Slight Macrocytes,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate
836	Polychromasia,Slight Macrocytes,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight

(--)-Data Unavailable

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

DRAFT

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 0 : 0 mg base/kg/day

SEX: FEMALE

ANIMAL ID	Week 2	Week 4	Week 8	Week 13
837	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
838	--	--	--	--
839	--	--	--	--
840	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight

(--)-Data Unavailable

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

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 0 : 0 mg base/kg/day

SEX: FEMALE

ANIMAL ID	Week 16	Week 21	Week 27
821	--	--	--
822	--	--	--
823	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Anisocytosis,Slight
824	Anisocytosis, Moderate; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate
825	--	--	--
826	--	--	--
827	Anisocytosis,Slight; Polychromasia,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Poikilocytes,Slight; Target Cells,Slight; Anisocytosis, Moderate;Crenation, Slight
828	--	--	--
829	--	--	--
830	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
831	Anisocytosis,Slight; Polychromasia,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
832	--	--	--
833	--	--	--
834	Anisocytosis,Slight; Polychromasia,Slight	Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
835	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight

(--)-Data Unavailable

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

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 0 : 0 mg base/kg/day

SEX: FEMALE

ANIMAL ID	Week 16	Week 21	Week 27
836	Anisocytosis,Slight; Polychromasia,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
837	Anisocytosis,Slight; Polychromasia,Slight	Polychromasia,Slight Anisocytosis,Slight; Howell-Jolly Bodies, Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight
838	--	--	--
839	--	--	--
840	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight

(--)-Data Unavailable

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

DRAFT

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 0.5 : 0.5 mg base/kg/day

SEX: FEMALE

ANIMAL ID	Week 2	Week 4	Week 8	Week 13
861	Polychromasia,Slight Macrocytes,Moderate	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
862	--	--	--	--
863	--	--	--	--
864	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
865	--	--	--	--
866	--	--	--	--
867	Target Cells,Slight; Macrocytes,Moderate; Polychromasia,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
868	Polychromasia,Slight Macrocytes,Slight	Polychromasia,Slight Anisocytosis,Slight; Howell-Jolly Bodies, Slight	Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
869	--	--	--	--
870	--	--	--	--
871	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
872	--	--	--	--
873	Polychromasia,Slight Poikilocytes,Slight; Macrocytes,Moderate	Polychromasia,Slight Anisocytosis,Slight	Anisocytosis,Slight	Target Cells,Slight
874	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Anisocytosis,Slight; Howell-Jolly Bodies, Slight	Polychromasia,Slight Target Cells,Slight
875	--	--	--	--
876	--	--	--	--

(--)-Data Unavailable

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

DRAFT

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 0.5 : 0.5 mg base/kg/day

SEX: FEMALE

ANIMAL ID	Week 2	Week 4	Week 8	Week 13
877	Polychromasia, Moderate;Macrocytes, Moderate	Polychromasia,Slight Anisocytosis,Slight	Target Cells,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight
878	--	--	--	--
879	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
880	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia, Moderate;Target Cells,Slight; Anisocytosis,Slight

(--)-Data Unavailable

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

DRAFT

MORPHOLOGY OBSERVATIONS

STUDY ID: 093

GROUP: 0.5 : 0.5 mg base/kg/day

SEX: FEMALE

ANIMAL ID	Week 16	Week 21	Week 27
861	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Anisocytosis,Slight	Anisocytosis,Slight
862	--	--	--
863	--	--	--
864	Anisocytosis,Slight; Target Cells,Slight	Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Anisocytosis,Slight
865	--	--	--
866	--	--	--
867	Anisocytosis,Slight; Polychromasia,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
868	--	Polychromasia,Slight	Anisocytosis,Slight
869	--	--	--
870	--	--	--
871	Anisocytosis, Moderate; Polychromasia,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
872	--	--	--
873	Anisocytosis,Slight; Polychromasia,Slight	Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
874	Anisocytosis,Slight; Polychromasia,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
875	--	--	--
876	--	--	--
877	Anisocytosis,Slight; Target Cells,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
878	--	--	--
879	Anisocytosis,Slight; Polychromasia,Slight	Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight

(--)-Data Unavailable

DRAFT

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

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 0.5 : 0.5 mg base/kg/day

SEX: FEMALE

ANIMAL ID	Week 16	Week 21	Week 27
880	Anisocytosis,Slight; Polychromasia,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight

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

DRAFT

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 6.0 : 6.0 mg base/kg/day

SEX: FEMALE

ANIMAL ID	Week 2	Week 4	Week 8	Week 13
901	Polychromasia,Slight Macrocytes,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight
902	Polychromasia,Slight Macrocytes,Slight	Polychromasia,Slight Anisocytosis, Moderate	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
903	--	--	--	--
904	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight
905	--	--	--	--
906	--	--	--	--
907	--	--	--	--
908	Polychromasia,Slight Macrocytes,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia, Moderate;Target Cells,Moderate; Anisocytosis, Moderate
909	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
910	--	--	--	--
911	--	--	--	--
912	Polychromasia,Slight Target Cells,Slight; Macrocytes,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate	--
913	--	--	--	--
914	--	--	--	--
915	Polychromasia,Slight Anisocytosis	Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate	Polychromasia,Slight Anisocytosis, Moderate	Polychromasia,Slight Anisocytosis,Slight

(--)-Data Unavailable

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

DRAFT

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 6.0 : 6.0 mg base/kg/day

SEX: FEMALE

ANIMAL ID	Week 2	Week 4	Week 8	Week 13
916	Polychromasia, Moderate;Macrocytes, Slight	Polychromasia, Moderate;Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Target Cells,Slight; Anisocytosis,Slight
917	--	--	--	--
918	Polychromasia,Slight Macrocytes,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Poikilocytes,Slight; Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate; Howell-Jolly Bodies, Slight
919	Polychromasia,Slight	Polychromasia,Slight Anisocytosis,Slight	Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
920	--	--	--	--

(--)-Data Unavailable

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

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

SEX: FEMALE

GROUP: 6.0 : 6.0 mg base/kg/day

ANIMAL ID	Week 16	Week 21	Week 27
901	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Anisocytosis,Slight
902	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
903	--	--	--
904	--	Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
905	--	--	--
906	--	--	--
907	--	--	--
908	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
909	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
910	--	--	--
911	--	--	--
912	Anisocytosis,Slight; Polychromasia,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
913	--	--	--
914	--	--	--
915	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight; Howell-Jolly Bodies, Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight
916	Anisocytosis,Slight; Polychromasia,Slight	Polychromasia,Slight	Polychromasia,Slight Anisocytosis,Slight
917	--	--	--

(--)-Data Unavailable

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

DRAFT

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 6.0 : 6.0 mg base/kg/day

SEX: FEMALE

ANIMAL ID	Week 16	Week 21	Week 27
918	Anisocytosis,Slight; Target Cells,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
919	Anisocytosis,Slight; Polychromasia,Slight	Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
920	--	--	--

(--)-Data Unavailable

DRAFT

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

MORPHOLOGY OBSERVATIONS

STUDY ID: 093

GROUP: 18.0 : 18.0 mg base/kg/day

SEX: FEMALE

ANIMAL ID	Week 2	Week 4	Week 8	Week 13
941	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Poikilocytes,Slight; Anisocytosis, Moderate	Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate	Polychromasia, Moderate;Target Cells,Slight; Anisocytosis, Moderate
942	Polychromasia, Moderate;Macrocytes, Moderate	Polychromasia, Moderate;Target Cells,Moderate; Anisocytosis, Moderate	Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate	Clotted Sample
943	--	--	--	--
944	Anisocytosis, Moderate; Polychromasia,Slight Poikilocytes,Slight; Target Cells,Slight; Howell-Jolly Bodies, Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate; Howell-Jolly Bodies, Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
945	--	--	--	--
946	--	--	--	--
947	--	--	--	--
948	--	--	--	--
949	Polychromasia,Slight Poikilocytes,Slight; Anisocytosis,Slight	Polychromasia,Slight Poikilocytes,Slight; Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate
950	--	--	--	--
951	--	--	--	--
952	--	--	--	--
953	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Moderate	Polychromasia, Moderate;Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate; Howell-Jolly Bodies, Slight

(--)-Data Unavailable

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

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

SEX: FEMALE

GROUP: 18.0 : 18.0 mg base/kg/day

ANIMAL ID	Week 2	Week 4	Week 8	Week 13
954	Polychromasia, Moderate; Target Cells, Slight; Macrocytes, Moderate; Howell-Jolly Bodies, Slight	Polychromasia, Slight Target Cells, Slight; Anisocytosis, Moderate; Howell-Jolly Bodies, Slight	Polychromasia, Slight Target Cells, Slight; Anisocytosis, Slight; Howell-Jolly Bodies, Slight	Polychromasia, Moderate; Target Cells, Moderate; Anisocytosis, Moderate; Howell-Jolly Bodies, Slight
955	--	--	--	--
956	Polychromasia, Moderate; Macrocytes, Moderate	Polychromasia, Slight Anisocytosis, Moderate; Howell-Jolly Bodies, Slight	Polychromasia, Moderate; Target Cells, Moderate; Anisocytosis, Moderate; Howell-Jolly Bodies, Slight	Polychromasia, Slight Target Cells, Slight; Anisocytosis, Slight
957	Polychromasia, Slight Poikilocytes, Moderate; Target Cells, Slight; Anisocytosis, Slight	Polychromasia, Mod. to Marked; Target Cells, Slight; Anisocytosis, Slight	Polychromasia, Slight Target Cells, Slight; Anisocytosis, Slight	Polychromasia, Moderate; Target Cells, Slight; Anisocytosis, Slight; Howell-Jolly Bodies, Slight
958	--	--	--	--
959	Polychromasia, Moderate; Macrocytes, Moderate	Polychromasia, Slight Target Cells, Slight; Anisocytosis, Moderate; Howell-Jolly Bodies, Slight	Polychromasia, Moderate; Target Cells, Slight; Anisocytosis, Moderate	Polychromasia, Moderate; Target Cells, Moderate; Anisocytosis, Moderate
960	Polychromasia, Slight Poikilocytes, Slight; Target Cells, Slight; Anisocytosis, Slight	Polychromasia, Moderate; Target Cells, Slight; Anisocytosis, Slight; Howell-Jolly Bodies, Moderate	Polychromasia, Slight Target Cells, Slight; Anisocytosis, Slight	Polychromasia, Moderate; Target Cells, Slight; Anisocytosis, Mod. to Marked

(--)-Data Unavailable

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

DRAFT

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 18.0 : 18.0 mg base/kg/day

SEX: FEMALE

ANIMAL ID	Week 16	Week 21	Week 27
941	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells, Moderate; Anisocytosis,Slight
942	Anisocytosis,Slight; Polychromasia,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
943	--	--	--
944	Anisocytosis,Slight; Polychromasia,Slight Howell-Jolly Bodies, Slight	Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
945	--	--	--
946	--	--	--
947	--	--	--
948	--	--	--
949	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
950	--	--	--
951	--	--	--
952	--	--	--
953	Anisocytosis,Slight; Polychromasia, Moderate;Target Cells,Slight; Howell-Jolly Bodies, Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
954	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Anisocytosis,Slight	Target Cells,Slight; Anisocytosis,Slight
955	--	--	--
956	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight	--	--

(--)-Data Unavailable

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

D R A F T

MORPHOLOGY OBSERVATIONS

STUDY ID: 078

GROUP: 18.0 : 18.0 mg base/kg/day

SEX: FEMALE

ANIMAL ID	Week 16	Week 21	Week 27
957	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight; Howell-Jolly Bodies, Slight
958	--	--	--
959	Anisocytosis, Moderate; Polychromasia,Slight Target Cells,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight
960	Anisocytosis,Slight; Polychromasia,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight

(--)-Data Unavailable

DRAFT

APPENDIX 8  
Ophthalmology Report

# ANIMAL EYE ASSOCIATES

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# DRAFT

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GRETCHEN M. SCHMIDT, DVM  
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## OPHTHALMIC REPORT

UIC/TRL Study No. 098


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

On December 9, 1992, (Week -1), a sufficient number of Sprague Dawley rats were given ophthalmic examinations by indirect ophthalmoscopy to result in eighty males and eighty females suitable for the study.

On March 10, 1993 (Week 12), I re-examined the remaining 155 rats. One mid dose male was diagnosed with corneal neovascularization and a cataract, and one low dose female demonstrated a cataract. In both cases, the fundus was not visible. Both lesions were of traumatic origin and were not treatment-related. In addition, ocular lesions were not seen in high dose animals. All other rats appeared similar (no lesions) to the previous pretest examinations done on December 9, 1992.

On June 9, 1993 (Week 26), I re-examined the remaining 79 rats. All observed lesions were considered incidental as they were not seen in Week 12 and a dose-related pattern was not apparent. At this time, one low dose male was diagnosed with corneal keratitis and corneal neovascularization; a second low dose male demonstrated a cortical opacity of the lens. Retinal degeneration and optic nerve degeneration were diagnosed in one mid dose male and a cataract (fundus not visible) was seen in a mid dose male and a mid dose female. In two low dose females, corneal neovascularization and lens endophthalmitis were seen, with one of these two diagnosed rats also displaying a cataract. The fundus was not visible in either rat. One high dose female was diagnosed with retinal degeneration, optic nerve degeneration and a mild cataract. In all cases, lesions were of traumatic origin and were not treatment-related. All remaining rats appeared similar (no lesions) to previous examinations.

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

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

DRAFT

Ophthalmic Examinations  
Males

Dose (mg/kg/day)	Animal Number	Week -1		Week 12		Week 26		
		R.E.	L.E.	R.E.	L.E.	R.E.	L.E.	
0	801	WNL	WNL	WNL	WNL	WNL	WNL	
	802	WNL	WNL	WNL	WNL	WNL	WNL	
	803	WNL	WNL	WNL	WNL	-	-	
	804	WNL	WNL	WNL	WNL	-	-	
	805	WNL	WNL	WNL	WNL	-	-	
	806	WNL	WNL	WNL	WNL	WNL	WNL	
	807	WNL	WNL	WNL	WNL	WNL	WNL	
	808	WNL	WNL	WNL	WNL	-	-	
	809	WNL	WNL	WNL	WNL	WNL	WNL	
	810	WNL	WNL	WNL	WNL	WNL	WNL	
	811	WNL	WNL	WNL	WNL	WNL	WNL	
	812	WNL	WNL	WNL	WNL	-	-	
	813	WNL	WNL	WNL	WNL	-	-	
	814	WNL	WNL	WNL	WNL	WNL	WNL	
	815	WNL	WNL	WNL	WNL	WNL	WNL	
	816	WNL	WNL	WNL	WNL	WNL	WNL	
	817	WNL	WNL	WNL	WNL	WNL	-	-
	818	WNL	WNL	WNL	WNL	WNL	-	-
	819	WNL	WNL	WNL	WNL	WNL	-	-
	820	WNL	WNL	WNL	WNL	WNL	-	-
0.5	841	WNL	WNL	WNL	WNL	-	-	
	842	WNL	WNL	WNL	WNL	-	-	
	843	WNL	WNL	WNL	WNL	-	-	
	844	WNL	WNL	WNL	WNL	WNL	WNL	
	845	WNL	WNL	WNL	WNL	-	-	
	846	WNL	WNL	WNL	WNL	CKT/CN	WNL	
	847	WNL	WNL	WNL	WNL	-	-	
	848	WNL	WNL	WNL	WNL	WNL	WNL	
	849	WNL	WNL	WNL	WNL	-	-	
	850	WNL	WNL	WNL	WNL	WNL	WNL	
	851	WNL	WNL	WNL	WNL	WNL	COL	
	852	WNL	WNL	WNL	WNL	WNL	WNL	
	853	WNL	WNL	WNL	WNL	WNL	WNL	
	854	WNL	WNL	WNL	WNL	-	-	
	855	WNL	WNL	WNL	WNL	-	-	
	856	WNL	WNL	WNL	WNL	-	-	
	857	WNL	WNL	WNL	WNL	-	-	
	858	WNL	WNL	WNL	WNL	WNL	WNL	
	859	WNL	WNL	WNL	WNL	WNL	WNL	
	860	WNL	WNL	WNL	WNL	WNL	WNL	

Dose = mg base/kg/day  
R.E. = Right Eye  
L.E. = Left Eye  
\* = Animal Previously Died  
- = Animal Previously Sacrificed  
WNL = Within Normal Limits  
CKT = Corneal Keratitis  
CN = Corneal Neovascularization  
LC = Lens Cataract  
LE = Lens Endophthalmitis  
FNV = Fundus Not Visible  
MC = Mild Cataract  
COL = Cortical Opacity of Lens  
RD = Retinal Degeneration  
OND = Optic Nerve Degeneration (Gliosis)

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238609  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

Ophthalmic Examinations  
Males

Dose (mg/kg/day)	Animal Number	Week -1		Week 12		Week 26		
		R.E.	L.E.	R.E.	L.E.	R.E.	L.E.	
6	881	WNL	WNL	WNL	WNL	-	-	
	882	WNL	WNL	WNL	WNL	-	-	
	883	WNL	WNL	WNL	WNL	-	-	
	884	WNL	WNL	WNL	WNL	WNL	WNL	
	885	WNL	WNL	WNL	WNL	-	-	
	886	WNL	WNL	WNL	WNL	-	-	
	887	WNL	WNL	WNL	WNL	WNL	WNL	
	888	WNL	WNL	WNL	WNL	*	*	
	889	WNL	WNL	WNL	WNL	WNL	WNL	
	890	WNL	WNL	WNL	WNL	WNL	WNL	
	891	WNL	WNL	WNL	WNL	-	-	
	892	WNL	WNL	WNL	WNL	-	-	
	893	WNL	WNL	WNL	WNL	RD/OND	WNL	
	894	WNL	WNL	WNL	WNL	-	-	
	895	WNL	WNL	WNL	WNL	WNL	WNL	
	896	WNL	WNL	WNL	WNL	WNL	WNL	
	897	WNL	WNL	WNL	WNL	WNL	WNL	
	898	WNL	WNL	WNL	WNL	WNL	-	
	899	WNL	WNL	WNL	LC/CN/FNV	WNL	LC/FNV	WNL
	900	WNL	WNL	WNL	WNL	WNL	WNL	WNL
18	921	WNL	WNL	*	*	*	*	
	922	WNL	WNL	WNL	WNL	WNL	WNL	
	923	WNL	WNL	WNL	WNL	WNL	WNL	
	924	WNL	WNL	WNL	WNL	-	-	
	925	WNL	WNL	WNL	WNL	-	-	
	926	WNL	WNL	*	*	*	*	
	927	WNL	WNL	WNL	WNL	WNL	WNL	
	928	WNL	WNL	WNL	WNL	-	-	
	929	WNL	WNL	WNL	WNL	WNL	WNL	
	930	WNL	WNL	WNL	WNL	WNL	WNL	
	931	WNL	WNL	WNL	WNL	-	-	
	932	WNL	WNL	WNL	WNL	WNL	WNL	
	933	WNL	WNL	WNL	WNL	WNL	WNL	
	934	WNL	WNL	*	*	*	*	
	935	WNL	WNL	WNL	WNL	WNL	WNL	
	936	WNL	WNL	*	*	*	*	
	937	WNL	WNL	*	*	*	*	
	938	WNL	WNL	WNL	WNL	-	-	
	939	WNL	WNL	WNL	WNL	WNL	WNL	
	940	WNL	WNL	WNL	WNL	WNL	WNL	

Dose = mg base/kg/day  
 R.E. = Right Eye  
 L.E. = Left Eye  
 \* = Animal Previously Died  
 - = Animal Previously Sacrificed  
 WNL = Within Normal Limits  
 CKT = Corneal Keratitis  
 CN = Corneal Neovascularization  
 LC = Lens Cataract  
 LE = Lens Endophthalmitis  
 FNV = Fundus Not Visible  
 MC = Mild Cataract  
 COL = Cortical Opacity of Lens  
 RD = Retinal Degeneration  
 OND = Optic Nerve Degeneration (Gliosis)

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

DRAFT

Ophthalmic Examinations  
Females

Dose (mg/kg/day)	Animal Number	Week -1		Week 12		Week 26	
		R.E.	L.E.	R.E.	L.E.	R.E.	L.E.
0	821	WNL	WNL	WNL	WNL	-	-
	822	WNL	WNL	WNL	WNL	-	-
	823	WNL	WNL	WNL	WNL	WNL	WNL
	824	WNL	WNL	WNL	WNL	WNL	WNL
	825	WNL	WNL	WNL	WNL	-	-
	826	WNL	WNL	WNL	WNL	-	-
	827	WNL	WNL	WNL	WNL	WNL	WNL
	828	WNL	WNL	WNL	WNL	-	-
	829	WNL	WNL	WNL	WNL	-	-
	830	WNL	WNL	WNL	WNL	WNL	WNL
	831	WNL	WNL	WNL	WNL	WNL	WNL
	832	WNL	WNL	WNL	WNL	-	-
	833	WNL	WNL	WNL	WNL	-	-
	834	WNL	WNL	WNL	WNL	WNL	WNL
	835	WNL	WNL	WNL	WNL	WNL	WNL
	836	WNL	WNL	WNL	WNL	WNL	WNL
	837	WNL	WNL	WNL	WNL	WNL	WNL
838	WNL	WNL	WNL	WNL	WNL	-	-
839	WNL	WNL	WNL	WNL	WNL	-	-
840	WNL	WNL	WNL	WNL	WNL	WNL	WNL
0.5	861	WNL	WNL	WNL	WNL	WNL	WNL
	862	WNL	WNL	WNL	WNL	-	-
	863	WNL	WNL	WNL	WNL	-	-
	864	WNL	WNL	WNL	WNL	WNL	WNL
	865	WNL	WNL	WNL	WNL	-	-
	866	WNL	WNL	WNL	WNL	-	-
	867	WNL	WNL	WNL	WNL	WNL	WNL
	868	WNL	WNL	WNL	WNL	LC/CN/LE/FNV	WNL
	869	WNL	WNL	WNL	WNL	-	-
	870	WNL	WNL	WNL	WNL	-	-
	871	WNL	WNL	WNL	WNL	WNL	WNL
	872	WNL	WNL	WNL	WNL	-	-
	873	WNL	WNL	WNL	WNL	WNL	WNL
	874	WNL	WNL	WNL	WNL	WNL	WNL
	875	WNL	WNL	WNL	WNL	-	-
	876	WNL	WNL	WNL	WNL	-	-
	877	WNL	WNL	WNL	WNL	WNL	WNL
878	WNL	WNL	WNL	WNL	-	-	
879	WNL	WNL	WNL	WNL	WNL	WNL	
880	WNL	WNL	LC/FNV	WNL	CN/LE/FNV	WNL	

Dose = mg base/kg/day  
 R.E. = Right Eye  
 L.E. = Left Eye  
 \* = Animal Previously Died  
 - = Animal Previously Sacrificed  
 WNL = Within Normal Limits  
 CKT = Corneal Keratitis  
 CN = Corneal Neovascularization  
 LC = Lens Cataract  
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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

Ophthalmic Examinations  
Females

Dose (mg/kg/day)	Animal Number	Week -1		Week 12		Week 26	
		R.E.	L.E.	R.E.	L.E.	R.E.	L.E.
6	901	WNL	WNL	WNL	WNL	WNL	WNL
	902	WNL	WNL	WNL	WNL	WNL	WNL
	903	WNL	WNL	WNL	WNL	-	-
	904	WNL	WNL	WNL	WNL	WNL	WNL
	905	WNL	WNL	WNL	WNL	-	-
	906	WNL	WNL	WNL	WNL	-	-
	907	WNL	WNL	WNL	WNL	-	-
	908	WNL	WNL	WNL	WNL	WNL	WNL
	909	WNL	WNL	WNL	WNL	WNL	WNL
	910	WNL	WNL	WNL	WNL	-	-
	911	WNL	WNL	WNL	WNL	-	-
	912	WNL	WNL	WNL	WNL	WNL	WNL
	913	WNL	WNL	WNL	WNL	-	-
	914	WNL	WNL	WNL	WNL	-	-
	915	WNL	WNL	WNL	WNL	WNL	WNL
	916	WNL	WNL	WNL	WNL	WNL	WNL
	917	WNL	WNL	WNL	WNL	-	-
	918	WNL	WNL	WNL	WNL	LC/FNV	WNL
	919	WNL	WNL	WNL	WNL	WNL	WNL
920	WNL	WNL	WNL	WNL	WNL	-	
18	941	WNL	WNL	WNL	WNL	WNL	WNL
	942	WNL	WNL	WNL	WNL	RD/OND/MC	WNL
	943	WNL	WNL	WNL	WNL	-	-
	944	WNL	WNL	WNL	WNL	WNL	WNL
	945	WNL	WNL	WNL	WNL	-	-
	946	WNL	WNL	WNL	WNL	-	-
	947	WNL	WNL	WNL	WNL	-	-
	948	WNL	WNL	WNL	WNL	-	-
	949	WNL	WNL	WNL	WNL	WNL	WNL
	950	WNL	WNL	WNL	WNL	-	-
	951	WNL	WNL	WNL	WNL	-	-
	952	WNL	WNL	WNL	WNL	-	-
	953	WNL	WNL	WNL	WNL	WNL	WNL
	954	WNL	WNL	WNL	WNL	WNL	WNL
	955	WNL	WNL	WNL	WNL	-	-
	956	WNL	WNL	WNL	WNL	*	*
	957	WNL	WNL	WNL	WNL	WNL	WNL
	958	WNL	WNL	WNL	WNL	-	-
	959	WNL	WNL	WNL	WNL	WNL	WNL
960	WNL	WNL	WNL	WNL	WNL	WNL	

Dose = mg base/kg/day  
R.E. = Right Eye  
L.E. = Left Eye  
\* = Animal Previously Died  
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CKT = Corneal Keratitis  
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LC = Lens Cataract  
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FNV = Fundus Not Visible  
MC = Mild Cataract  
COL = Cortical Opacity of Lens  
RD = Retinal Degeneration  
OND = Optic Nerve Degeneration (Gliosis)

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APPENDIX 9

Individual Organ Weights

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

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098  
SEX: MALE

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

ANIMAL ID: BALANCE NO.:	801	802	803	804	805	806	807	808	809
BODY WEIGHT (G)	627.6	561.7	497.7	497.6	560.5	555.8	502.4	564.8	622.4
Adrenals (pr) (G)	0.050	0.050	0.083	0.061	0.079	0.080	0.070	0.075	0.090
% BODY WEIGHT	0.008	0.009	0.017	0.012	0.014	0.014	0.014	0.013	0.014
Brain (G)	2.190	2.120	2.147	2.152	2.111	2.160	2.190	2.329	2.180
% BODY WEIGHT	0.349	0.377	0.431	0.432	0.377	0.389	0.436	0.412	0.350
Heart (G)	1.880	1.630	1.625	1.494	1.583	1.710	1.410	1.760	2.040
% BODY WEIGHT	0.300	0.290	0.327	0.300	0.282	0.308	0.281	0.312	0.328
Kidneys (pr) (G)	4.400	4.270	3.723	3.670	3.731	4.550	3.470	4.085	4.420
% BODY WEIGHT	0.701	0.760	0.748	0.738	0.666	0.819	0.691	0.723	0.710
Liver (G)	19.880	19.940	17.653	15.586	17.219	18.520	14.800	15.689	18.760
% BODY WEIGHT	3.168	3.550	3.547	3.132	3.072	3.332	2.946	2.778	3.014
Spleen (G)	0.750	0.730	0.632	0.737	0.771	0.780	0.680	0.793	0.940
% BODY WEIGHT	0.120	0.130	0.127	0.148	0.138	0.140	0.135	0.140	0.151
Testes w/Epidid. (pr) (G)	5.700	5.370	5.282	5.045	5.463	5.110	5.260	5.505	6.110
% BODY WEIGHT	0.908	0.956	1.061	1.014	0.975	0.919	1.047	0.975	0.982

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

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098  
SEX: MALE

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

ANIMAL ID: BALANCE NO.:	810	811	812	813	814	815	816	817	818
BODY WEIGHT (G)	546.4	609.8	473.6	436.0	602.0	709.8	707.9	501.2	525.8
Adrenals (pr) (G)	0.070	0.090	0.059	0.055	0.080	0.090	0.090	0.059	0.055
% BODY WEIGHT	0.013	0.015	0.012	0.013	0.013	0.013	0.013	0.012	0.010
Brain (G)	2.110	2.010	2.206	2.091	2.200	2.250	2.310	2.132	2.153
% BODY WEIGHT	0.386	0.330	0.466	0.480	0.365	0.317	0.326	0.425	0.409
Heart (G)	1.580	1.710	1.536	1.464	1.790	2.200	2.210	1.449	1.626
% BODY WEIGHT	0.289	0.280	0.324	0.336	0.297	0.310	0.312	0.289	0.309
Kidneys (pr) (G)	3.780	4.780	4.221	3.443	4.020	4.880	4.980	4.002	3.916
% BODY WEIGHT	0.692	0.784	0.891	0.790	0.668	0.688	0.703	0.798	0.745
Liver (G)	16.980	18.720	14.103	13.903	18.120	24.760	26.660	14.234	16.077
% BODY WEIGHT	3.108	3.070	2.978	3.189	3.010	3.488	3.766	2.840	3.058
Spleen (G)	0.800	0.970	0.784	0.667	0.740	1.020	1.070	0.788	0.921
% BODY WEIGHT	0.146	0.159	0.166	0.153	0.123	0.144	0.151	0.157	0.175
Testes w/Epidid. (pr) (G)	5.800	4.940	5.718	4.408	5.290	4.970	5.790	5.143	5.129
% BODY WEIGHT	1.061	0.810	1.207	1.011	0.879	0.700	0.818	1.026	0.975

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

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098  
SEX: MALE

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

ANIMAL ID: BALANCE NO.:	819	820
BODY WEIGHT (G)	505.0	565.9
Adrenals (pr) (G)	0.071	0.061
% BODY WEIGHT	0.014	0.011
Brain (G)	1.974	1.990
% BODY WEIGHT	0.391	0.352
Heart (G)	1.606	1.568
% BODY WEIGHT	0.318	0.277
Kidneys (pr) (G)	3.939	4.057
% BODY WEIGHT	0.780	0.717
Liver (G)	15.583	20.395
% BODY WEIGHT	3.086	3.604
Spleen (G)	0.939	0.819
% BODY WEIGHT	0.186	0.145
Testes w/Epidid. (pr) (G)	5.624	5.248
% BODY WEIGHT	1.114	0.927

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

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098  
SEX: MALE

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

ANIMAL ID: BALANCE NO.:	841	842	843	844	845	846	847	848	849
BODY WEIGHT (G)	462.8	486.3	495.1	518.4	562.1	511.5	508.3	591.2	550.7
Adrenals (pr) (G)	0.052	0.059	0.054	0.060	0.067	0.090	0.071	0.070	0.062
% BODY WEIGHT	0.011	0.012	0.011	0.012	0.012	0.018	0.014	0.012	0.011
Brain (G)	2.137	2.161	2.066	2.180	2.136	2.110	2.195	1.980	2.277
% BODY WEIGHT	0.462	0.444	0.417	0.421	0.380	0.413	0.432	0.335	0.413
Heart (G)	1.534	1.816	1.944	1.510	1.691	1.440	1.763	1.980	1.669
% BODY WEIGHT	0.331	0.373	0.393	0.291	0.301	0.282	0.347	0.335	0.303
Kidneys (pr) (G)	3.900	3.878	4.266	3.610	4.059	3.450	4.002	3.920	3.911
% BODY WEIGHT	0.843	0.797	0.862	0.696	0.722	0.674	0.787	0.663	0.710
Liver (G)	16.079	17.733	18.379	13.150	20.133	12.930	16.575	15.620	16.714
% BODY WEIGHT	3.474	3.647	3.712	2.537	3.582	2.528	3.261	2.642	3.035
Spleen (G)	0.934	0.891	0.699	0.880	0.836	0.700	0.822	0.740	1.032
% BODY WEIGHT	0.202	0.183	0.141	0.170	0.149	0.137	0.162	0.125	0.187
Testes w/Epidid. (pr) (G)	4.945	4.996	5.311	5.400	5.583	5.220	4.888	5.260	4.609
% BODY WEIGHT	1.068	1.027	1.073	1.042	0.993	1.021	0.962	0.890	0.837

DRAFT

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

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098 SEX: MALE	GROUP: 2M - 0.5 mg base/kg/day								
	ALL FATES	ALL DAYS	ALL BALANCES						
ANIMAL ID: BALANCE NO.:	850	851	852	853	854	855	856	857	858
BODY WEIGHT (G)	549.0	572.9	617.4	614.0	523.9	585.5	553.0	422.2	623.5
Adrenals (pr) (G)	0.040	0.080	0.070	0.050	0.058	0.070	0.044	0.054	0.080
% BODY WEIGHT	0.007	0.014	0.011	0.008	0.011	0.012	0.008	0.013	0.013
Brain (G)	2.160	2.260	2.290	2.060	2.072	2.216	2.222	1.999	2.040
% BODY WEIGHT	0.393	0.394	0.371	0.336	0.395	0.378	0.402	0.473	0.327
Heart (G)	1.530	1.770	1.920	1.730	1.757	1.687	1.778	1.365	1.870
% BODY WEIGHT	0.279	0.309	0.311	0.282	0.335	0.288	0.322	0.323	0.300
Kidneys (pr) (G)	4.020	4.850	4.300	3.800	4.142	4.216	4.429	3.896	4.560
% BODY WEIGHT	0.732	0.847	0.696	0.619	0.791	0.720	0.801	0.923	0.731
Liver (G)	15.780	19.710	20.610	17.490	17.281	18.802	19.823	12.017	20.100
% BODY WEIGHT	2.874	3.440	3.338	2.849	3.299	3.211	3.585	2.846	3.224
Spleen (G)	0.730	0.850	0.950	0.810	0.994	1.050	0.923	0.634	0.950
% BODY WEIGHT	0.133	0.148	0.154	0.132	0.190	0.179	0.167	0.150	0.152
Testes w/Epidid. (pr) (G)	5.020	5.560	6.010	6.030	4.894	5.630	5.985	4.501	5.640
% BODY WEIGHT	0.914	0.971	0.973	0.982	0.934	0.962	1.082	1.066	0.905

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

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098  
SEX: MALE

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

ANIMAL ID: BALANCE NO.:	859	860
BODY WEIGHT (G)	653.2	649.0
Adrenals (pr) (G)	0.070	0.050
% BODY WEIGHT	0.011	0.008
Brain (G)	2.170	2.260
% BODY WEIGHT	0.332	0.348
Heart (G)	1.820	1.740
% BODY WEIGHT	0.279	0.268
Kidneys (pr) (G)	4.630	5.250
% BODY WEIGHT	0.709	0.809
Liver (G)	19.210	22.530
% BODY WEIGHT	2.941	3.471
Spleen (G)	0.780	1.060
% BODY WEIGHT	0.119	0.163
Testes w/Epidid. (pr) (G)	5.970	5.730
% BODY WEIGHT	0.914	0.883

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

DRAFT

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098  
 SEX: MALE

GROUP: 3M - 6.0 mg base/kg/day  
 ALL FATES ALL DAYS ALL BALANCES

ANIMAL ID: BALANCE NO.:	881	882	883	884	885	886	887	888	889
BODY WEIGHT (G)	403.7	476.6	392.9	515.8	418.0	371.7	565.5	472.8	678.0
Adrenals (pr) (G)	0.041	0.097	0.084	0.100	0.052	0.048	0.050	0.059	0.080
% BODY WEIGHT	0.010	0.020	0.021	0.019	0.012	0.013	0.009	0.012	0.012
Brain (G)	2.189	2.268	2.029	1.950	2.060	2.039	1.990	2.067	2.220
% BODY WEIGHT	0.542	0.476	0.516	0.378	0.493	0.549	0.352	0.437	0.327
Heart (G)	1.211	1.960	1.542	1.540	1.785	1.373	1.620	1.707	1.940
% BODY WEIGHT	0.300	0.411	0.392	0.299	0.427	0.369	0.286	0.361	0.286
Kidneys (pr) (G)	3.689	4.433	4.126	4.270	3.590	3.821	3.780	4.859	4.220
% BODY WEIGHT	0.914	0.930	1.050	0.828	0.859	1.028	0.668	1.028	0.622
Liver (G)	12.294	17.454	15.026	16.000	17.269	13.869	16.430	21.403	20.390
% BODY WEIGHT	3.045	3.662	3.824	3.102	4.131	3.731	2.905	4.527	3.007
Spleen (G)	1.076	1.281	1.062	0.820	1.563	1.247	0.780	1.747	0.960
% BODY WEIGHT	0.267	0.269	0.270	0.159	0.374	0.335	0.138	0.370	0.142
Testes w/Epidid. (pr) (G)	5.340	5.178	5.056	5.710	4.955	5.155	4.880	4.912	6.280
% BODY WEIGHT	1.323	1.086	1.287	1.107	1.185	1.387	0.863	1.039	0.926

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

DRAFT

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098 SEX: MALE	GROUP: 3M - 6.0 mg base/kg/day								
	ALL FATES	ALL DAYS	ALL BALANCES						
ANIMAL ID: BALANCE NO.:	890	891	892	893	894	895	896	897	898
BODY WEIGHT (G)	579.4	404.7	431.8	674.9	465.9	672.3	540.0	622.2	420.8
Adrenals (pr) (G)	0.040	0.072	0.059	0.050	0.048	0.080	0.070	0.080	0.063
% BODY WEIGHT	0.007	0.018	0.014	0.007	0.010	0.012	0.013	0.013	0.015
Brain (G)	2.220	1.993	2.141	1.870	2.213	2.220	2.290	1.980	2.105
% BODY WEIGHT	0.383	0.492	0.496	0.277	0.475	0.330	0.424	0.318	0.500
Heart (G)	1.780	1.316	1.474	1.720	1.464	1.760	1.650	1.740	1.829
% BODY WEIGHT	0.307	0.325	0.341	0.255	0.314	0.262	0.306	0.280	0.435
Kidneys (pr) (G)	4.750	3.394	3.507	4.100	4.693	4.670	3.940	4.650	4.049
% BODY WEIGHT	0.820	0.839	0.812	0.607	1.007	0.695	0.730	0.747	0.962
Liver (G)	21.600	13.535	16.183	18.200	18.796	26.760	16.160	22.640	16.780
% BODY WEIGHT	3.728	3.344	3.748	2.697	4.034	3.980	2.993	3.639	3.988
Spleen (G)	1.110	1.341	1.284	0.980	1.104	1.000	0.660	0.990	1.672
% BODY WEIGHT	0.192	0.331	0.297	0.145	0.237	0.149	0.122	0.159	0.397
Testes w/Epidid. (pr) (G)	5.670	2.616	5.136	5.070	4.921	4.930	4.550	5.780	4.689
% BODY WEIGHT	0.979	0.646	1.189	0.751	1.056	0.733	0.843	0.929	1.114

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605 **DRAFT**  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098  
 SEX: MALE

GROUP: 3M - 6.0 mg base/kg/day  
 ALL FATES ALL DAYS ALL BALANCES

ANIMAL ID:	899	900
BALANCE NO.:		
BODY WEIGHT (G)	500.7	596.6
Adrenals (pr) (G)	0.090	0.090
% BODY WEIGHT	0.018	0.015
Brain (G)	1.990	2.110
% BODY WEIGHT	0.397	0.354
Heart (G)	1.550	1.670
% BODY WEIGHT	0.310	0.280
Kidneys (pr) (G)	4.400	4.450
% BODY WEIGHT	0.879	0.746
Liver (G)	16.510	21.050
% BODY WEIGHT	3.297	3.528
Spleen (G)	0.680	0.700
% BODY WEIGHT	0.136	0.117
Testes w/Epidid. (pr) (G)	4.970	4.890
% BODY WEIGHT	0.993	0.820

DRAFT

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

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098  
SEX: MALE

GROUP: 4M - 18.0 mg base/kg/day  
ALL FATES      ALL DAYS      ALL BALANCES

ANIMAL ID: BALANCE NO.:	922	923	924	925	927	928	929	930	931
BODY WEIGHT (G)	479.0	564.5	381.8	368.3	580.3	447.3	569.2	618.0	347.5
Adrenals (pr) (G)	0.080	0.050	0.057	0.053	0.070	0.085	0.090	0.080	0.031
% BODY WEIGHT	0.017	0.009	0.015	0.014	0.012	0.019	0.016	0.013	0.009
Brain (G)	2.110	2.070	2.061	2.102	2.310	2.154	2.180	2.020	1.826
% BODY WEIGHT	0.441	0.367	0.540	0.571	0.398	0.482	0.383	0.327	0.525
Heart (G)	1.920	1.610	1.521	1.652	1.890	1.875	1.850	1.950	1.415
% BODY WEIGHT	0.401	0.285	0.398	0.449	0.326	0.419	0.325	0.316	0.407
Kidneys (pr) (G)	4.290	3.850	4.814	3.957	4.440	4.046	4.880	4.020	4.020
% BODY WEIGHT	0.896	0.682	1.261	1.074	0.765	0.905	0.857	0.650	1.157
Liver (G)	17.780	15.420	18.141	17.124	17.010	18.354	21.800	20.950	14.496
% BODY WEIGHT	3.712	2.732	4.751	4.649	2.931	4.103	3.830	3.390	4.172
Spleen (G)	1.230	1.370	1.686	2.532	0.990	2.812	1.270	1.290	1.950
% BODY WEIGHT	0.257	0.243	0.442	0.687	0.171	0.629	0.223	0.209	0.561
Testes w/Epidid. (pr) (G)	5.680	5.320	5.127	4.819	5.160	6.167	5.930	4.890	4.904
% BODY WEIGHT	1.186	0.942	1.343	1.308	0.889	1.379	1.042	0.791	1.411

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

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098  
SEX: MALE

GROUP: 4M - 18.0 mg base/kg/day  
ALL FATES ALL DAYS ALL BALANCES

ANIMAL ID: BALANCE NO.:	932	933	935	938	939	940
BODY WEIGHT (G)	521.2	565.8	512.8	376.7	523.0	589.4
Adrenals (pr) (G)	0.040	0.080	0.050	0.071	0.070	0.070
% BODY WEIGHT	0.008	0.014	0.010	0.019	0.013	0.012
Brain (G)	2.130	2.200	2.160	2.193	1.970	2.000
% BODY WEIGHT	0.409	0.389	0.421	0.582	0.377	0.339
Heart (G)	1.710	1.730	1.490	1.947	1.520	1.850
% BODY WEIGHT	0.328	0.306	0.291	0.517	0.291	0.314
Kidneys (pr) (G)	4.080	3.880	3.500	3.204	4.050	5.690
% BODY WEIGHT	0.783	0.686	0.683	0.851	0.774	0.965
Liver (G)	20.590	17.220	12.540	14.626	15.880	19.120
% BODY WEIGHT	3.950	3.043	2.445	3.883	3.036	3.244
Spleen (G)	1.300	1.530	0.880	2.309	1.310	1.300
% BODY WEIGHT	0.249	0.270	0.172	0.613	0.250	0.221
Testes w/Epidid. (pr) (G)	5.580	5.560	5.340	5.340	5.030	5.650
% BODY WEIGHT	1.071	0.983	1.041	1.418	0.962	0.959

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

DRAFT

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098  
 SEX: FEMALE

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

ANIMAL ID: BALANCE NO.:	821	822	823	824	825	826	827	828	829
BODY WEIGHT (G)	269.3	258.0	315.5	293.1	258.6	294.4	278.0	293.1	240.9
Adrenals (pr) (G)	0.072	0.070	0.090	0.070	0.088	0.096	0.110	0.072	0.053
% BODY WEIGHT	0.027	0.027	0.029	0.024	0.034	0.033	0.040	0.025	0.022
Brain (G)	2.030	1.947	2.170	2.050	2.038	2.048	2.110	1.907	1.969
% BODY WEIGHT	0.754	0.755	0.688	0.699	0.788	0.696	0.759	0.651	0.817
Heart (G)	0.864	0.855	1.130	0.960	0.919	0.964	1.010	0.949	0.917
% BODY WEIGHT	0.321	0.331	0.358	0.328	0.355	0.327	0.363	0.324	0.381
Kidneys (pr) (G)	2.158	1.933	2.080	2.230	2.237	2.316	2.220	2.190	2.187
% BODY WEIGHT	0.801	0.749	0.659	0.761	0.865	0.787	0.799	0.747	0.908
Liver (G)	9.884	7.411	9.470	7.720	8.736	9.769	8.860	8.885	7.549
% BODY WEIGHT	3.670	2.872	3.002	2.634	3.378	3.318	3.187	3.031	3.134
Ovaries (G)	0.111	0.126	0.090	0.080	0.121	0.170	0.120	0.143	0.104
% BODY WEIGHT	0.041	0.049	0.029	0.027	0.047	0.058	0.043	0.049	0.043
Spleen (G)	0.582	0.394	0.480	0.450	0.729	0.525	0.590	0.543	0.459
% BODY WEIGHT	0.216	0.153	0.152	0.154	0.282	0.178	0.212	0.185	0.191

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

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INDIVIDUAL ORGAN WEIGHTS

STUDY: 098  
 SEX: FEMALE

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

ANIMAL ID: BALANCE NO.:	830	831	832	833	834	835	836	837	838
BODY WEIGHT (G)	324.5	284.9	250.9	289.4	328.5	366.0	337.3	328.8	278.1
Adrenals (pr) (G)	0.110	0.050	0.067	0.070	0.080	0.070	0.070	0.070	0.076
% BODY WEIGHT	0.034	0.018	0.027	0.024	0.024	0.019	0.021	0.021	0.027
Brain (G)	1.990	1.860	2.010	1.916	1.960	2.000	2.110	1.860	2.139
% BODY WEIGHT	0.613	0.653	0.801	0.662	0.597	0.546	0.626	0.566	0.769
Heart (G)	1.370	1.070	1.132	0.960	1.120	1.090	1.120	1.060	1.060
% BODY WEIGHT	0.422	0.376	0.451	0.332	0.341	0.298	0.332	0.322	0.381
Kidneys (pr) (G)	2.220	2.110	1.896	1.920	2.190	2.170	2.280	2.570	2.233
% BODY WEIGHT	0.684	0.741	0.756	0.663	0.667	0.593	0.676	0.782	0.803
Liver (G)	9.880	8.240	8.267	7.607	8.710	10.000	9.840	9.190	10.232
% BODY WEIGHT	3.045	2.892	3.295	2.629	2.651	2.732	2.917	2.795	3.679
Ovaries (G)	0.110	0.090	0.120	0.117	0.100	0.130	0.130	0.130	0.112
% BODY WEIGHT	0.034	0.032	0.048	0.040	0.030	0.036	0.039	0.040	0.040
Spleen (G)	0.500	0.450	0.491	0.467	0.450	0.570	0.620	0.530	0.500
% BODY WEIGHT	0.154	0.158	0.196	0.161	0.137	0.156	0.184	0.161	0.180

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

DRAFT

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098  
 SEX: FEMALE

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

ANIMAL ID: BALANCE NO.:	839	840
BODY WEIGHT (G)	304.3	281.7
Adrenals (pr) (G)	0.052	0.100
% BODY WEIGHT	0.017	0.035
Brain (G)	1.991	2.010
% BODY WEIGHT	0.654	0.714
Heart (G)	1.049	1.190
% BODY WEIGHT	0.345	0.422
Kidneys (pr) (G)	2.249	2.340
% BODY WEIGHT	0.739	0.831
Liver (G)	9.243	8.760
% BODY WEIGHT	3.037	3.110
Ovaries (G)	0.088	0.110
% BODY WEIGHT	0.029	0.039
Spleen (G)	0.590	0.460
% BODY WEIGHT	0.194	0.163

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

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098  
SEX: FEMALE

GROUP: 2F - 0.5 mg base/kg/day  
ALL FATES ALL DAYS ALL BALANCES

ANIMAL ID: BALANCE NO.:	861	862	863	864	865	866	867	868	869
BODY WEIGHT (G)	348.6	258.8	248.3	287.8	246.6	272.6	343.6	281.6	298.4
Adrenals (pr) (G)	0.090	0.061	0.089	0.110	0.060	0.062	0.090	0.080	0.064
% BODY WEIGHT	0.026	0.024	0.036	0.038	0.024	0.023	0.026	0.028	0.021
Brain (G)	2.200	1.739	2.079	1.970	2.105	1.861	1.810	1.910	2.020
% BODY WEIGHT	0.631	0.672	0.837	0.685	0.854	0.683	0.527	0.678	0.677
Heart (G)	1.210	0.897	0.789	1.170	1.012	0.972	1.110	1.150	0.919
% BODY WEIGHT	0.347	0.347	0.318	0.407	0.410	0.357	0.323	0.408	0.308
Kidneys (pr) (G)	2.800	1.963	1.976	2.200	2.157	2.174	2.530	2.190	2.328
% BODY WEIGHT	0.803	0.759	0.796	0.764	0.875	0.798	0.736	0.778	0.780
Liver (G)	10.740	7.425	8.043	10.130	8.102	9.193	9.290	8.090	9.377
% BODY WEIGHT	3.081	2.869	3.239	3.520	3.285	3.372	2.704	2.873	3.142
Ovaries (G)	0.090	0.128	0.128	0.110	0.187	0.129	0.120	0.070	0.157
% BODY WEIGHT	0.026	0.049	0.052	0.038	0.076	0.047	0.035	0.025	0.053
Spleen (G)	0.440	0.589	0.449	0.520	0.477	0.556	0.620	0.390	0.865
% BODY WEIGHT	0.126	0.228	0.181	0.181	0.193	0.204	0.180	0.138	0.290

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

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INDIVIDUAL ORGAN WEIGHTS

ANIMAL ID: BALANCE NO.:	GROUP: 2F - 0.5 mg base/kg/day								
	870	871	872	873	874	875	876	877	878
STUDY: 098	ALL FATES								
SEX: FEMALE	ALL DAYS								
	ALL BALANCES								
BODY WEIGHT (G)	255.3	254.8	287.9	297.2	326.3	273.0	271.0	319.8	296.9
Adrenals (pr) (G)	0.072	0.090	0.086	0.060	0.100	0.097	0.101	0.080	0.049
% BODY WEIGHT	0.028	0.035	0.030	0.020	0.031	0.036	0.037	0.025	0.017
Brain (G)	2.103	1.950	1.934	2.060	1.890	1.992	2.040	1.960	1.913
% BODY WEIGHT	0.824	0.765	0.672	0.693	0.579	0.730	0.753	0.613	0.644
Heart (G)	0.831	0.850	0.890	1.040	1.120	1.074	0.952	1.160	0.993
% BODY WEIGHT	0.326	0.334	0.309	0.350	0.343	0.393	0.351	0.363	0.334
Kidneys (pr) (G)	2.078	1.840	1.873	2.050	2.180	2.252	2.373	2.080	1.941
% BODY WEIGHT	0.814	0.722	0.651	0.690	0.668	0.825	0.876	0.650	0.654
Liver (G)	8.108	7.770	7.919	7.660	8.650	9.211	9.427	9.310	8.221
% BODY WEIGHT	3.176	3.049	2.751	2.577	2.651	3.374	3.479	2.911	2.769
Ovaries (G)	0.102	0.090	0.153	0.100	0.170	0.120	0.128	0.090	0.090
% BODY WEIGHT	0.040	0.035	0.053	0.034	0.052	0.044	0.047	0.028	0.030
Spleen (G)	0.456	0.580	0.513	0.460	0.520	0.443	0.576	0.450	0.594
% BODY WEIGHT	0.179	0.228	0.178	0.155	0.159	0.162	0.213	0.141	0.200

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

DRAFT

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098  
 SEX: FEMALE

GROUP: 2F - 0.5 mg base/kg/day  
 ALL FATES ALL DAYS ALL BALANCES

ANIMAL ID: BALANCE NO.:	879	880
BODY WEIGHT (G)	266.9	368.2
Adrenals (pr) (G)	0.050	0.070
% BODY WEIGHT	0.019	0.019
Brain (G)	1.950	2.030
% BODY WEIGHT	0.731	0.551
Heart (G)	0.980	1.140
% BODY WEIGHT	0.367	0.310
Kidneys (pr) (G)	1.990	2.510
% BODY WEIGHT	0.746	0.682
Liver (G)	6.980	10.710
% BODY WEIGHT	2.615	2.909
Ovaries (G)	0.090	0.110
% BODY WEIGHT	0.034	0.030
Spleen (G)	0.540	0.610
% BODY WEIGHT	0.202	0.166

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

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098  
SEX: FEMALE

GROUP: 3F - 6.0 mg base/kg/day  
ALL FATES ALL DAYS ALL BALANCES

ANIMAL ID: BALANCE NO.:	901	902	903	904	905	906	907	908	909
BODY WEIGHT (G)	295.1	273.8	255.7	327.0	255.7	223.8	246.7	297.0	317.4
Adrenals (pr) (G)	0.090	0.070	0.084	0.090	0.119	0.079	0.084	0.100	0.070
% BODY WEIGHT	0.030	0.026	0.033	0.028	0.047	0.035	0.034	0.034	0.022
Brain (G)	2.010	2.010	1.986	2.090	1.969	1.865	1.940	2.130	2.030
% BODY WEIGHT	0.681	0.734	0.777	0.639	0.770	0.833	0.786	0.717	0.640
Heart (G)	1.010	0.970	1.062	1.110	0.874	0.810	0.942	1.180	1.040
% BODY WEIGHT	0.342	0.354	0.415	0.339	0.342	0.362	0.382	0.397	0.328
Kidneys (pr) (G)	2.450	2.010	2.451	2.330	2.250	2.140	2.316	2.660	2.360
% BODY WEIGHT	0.830	0.734	0.959	0.713	0.880	0.956	0.939	0.896	0.744
Liver (G)	8.590	7.990	9.119	9.840	9.594	7.899	8.467	11.000	10.120
% BODY WEIGHT	2.911	2.918	3.566	3.009	3.752	3.529	3.432	3.704	3.188
Ovaries (G)	0.090	0.140	0.198	0.120	0.173	0.132	0.142	0.090	0.140
% BODY WEIGHT	0.030	0.051	0.077	0.037	0.068	0.059	0.058	0.030	0.044
Spleen (G)	0.640	0.560	0.884	0.570	0.844	0.589	1.106	0.530	0.500
% BODY WEIGHT	0.217	0.205	0.346	0.174	0.330	0.263	0.448	0.178	0.158

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

DRAFT

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098  
 SEX: FEMALE

GROUP: 3F - 6.0 mg base/kg/day  
 ALL FATES ALL DAYS ALL BALANCES

ANIMAL ID: BALANCE NO.:	910	911	912	913	914	915	916	917	918
BODY WEIGHT (G)	255.5	256.4	320.9	268.4	243.2	276.4	305.5	237.6	283.8
Adrenals (pr) (G)	0.097	0.087	0.110	0.072	0.095	0.080	0.100	0.054	0.070
% BODY WEIGHT	0.038	0.034	0.034	0.027	0.039	0.029	0.033	0.023	0.025
Brain (G)	1.919	1.987	1.900	1.950	1.998	1.970	2.060	1.920	1.980
% BODY WEIGHT	0.751	0.775	0.592	0.727	0.822	0.713	0.674	0.808	0.698
Heart (G)	0.922	0.981	0.990	0.962	0.829	0.980	1.180	0.842	0.980
% BODY WEIGHT	0.361	0.383	0.309	0.358	0.341	0.355	0.386	0.354	0.345
Kidneys (pr) (G)	2.617	2.208	2.650	2.359	2.173	1.930	2.130	2.261	2.010
% BODY WEIGHT	1.024	0.861	0.826	0.879	0.894	0.698	0.697	0.952	0.708
Liver (G)	8.905	9.326	11.940	9.917	9.155	8.090	9.420	8.373	8.200
% BODY WEIGHT	3.485	3.637	3.721	3.695	3.764	2.927	3.083	3.524	2.889
Ovaries (G)	0.139	0.176	0.120	0.158	0.140	0.080	0.120	0.107	0.060
% BODY WEIGHT	0.054	0.069	0.037	0.059	0.058	0.029	0.039	0.045	0.021
Spleen (G)	0.721	0.942	0.550	0.889	0.647	0.540	0.550	0.752	0.520
% BODY WEIGHT	0.282	0.367	0.171	0.331	0.266	0.195	0.180	0.316	0.183

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

DRAFT

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098  
 SEX: FEMALE

GROUP: 3F - 6.0 mg base/kg/day  
 ALL FATES ALL DAYS ALL BALANCES

ANIMAL ID: BALANCE NO.:	919	920
BODY WEIGHT (G)	308.8	254.5
Adrenals (pr) (G)	0.060	0.071
% BODY WEIGHT	0.019	0.028
Brain (G)	2.150	1.937
% BODY WEIGHT	0.696	0.761
Heart (G)	1.030	1.019
% BODY WEIGHT	0.334	0.400
Kidneys (pr) (G)	2.370	2.234
% BODY WEIGHT	0.767	0.878
Liver (G)	9.070	9.178
% BODY WEIGHT	2.937	3.606
Ovaries (G)	0.150	0.108
% BODY WEIGHT	0.049	0.042
Spleen (G)	0.560	0.669
% BODY WEIGHT	0.181	0.263

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

DRAFT

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098  
 SEX: FEMALE

GROUP: 4F - 18.0 mg base/kg/day  
 ALL FATES      ALL DAYS      ALL BALANCES

ANIMAL ID: BALANCE NO.:	941	942	943	944	945	946	947	948	949
BODY WEIGHT (G)	278.3	272.1	247.3	305.3	227.7	262.8	227.5	242.9	268.8
Adrenals (pr) (G)	0.080	0.050	0.106	0.070	0.088	0.087	0.107	0.079	0.040
% BODY WEIGHT	0.029	0.018	0.043	0.023	0.039	0.033	0.047	0.033	0.015
Brain (G)	1.830	1.920	2.009	2.170	1.811	2.076	1.934	1.943	1.910
% BODY WEIGHT	0.658	0.706	0.812	0.711	0.795	0.790	0.850	0.800	0.711
Heart (G)	1.050	1.090	0.836	1.090	0.926	1.062	0.931	1.289	0.950
% BODY WEIGHT	0.377	0.401	0.338	0.357	0.407	0.404	0.409	0.531	0.353
Kidneys (pr) (G)	2.480	2.180	2.021	2.660	2.165	2.505	2.061	2.198	1.920
% BODY WEIGHT	0.891	0.801	0.817	0.871	0.951	0.953	0.906	0.905	0.714
Liver (G)	9.500	7.690	9.116	10.210	8.668	10.296	9.318	10.550	8.030
% BODY WEIGHT	3.414	2.826	3.686	3.344	3.807	3.918	4.096	4.343	2.987
Ovaries (G)	0.040	0.110	0.207	0.110	0.118	0.209	0.163	0.113	0.090
% BODY WEIGHT	0.014	0.040	0.084	0.036	0.052	0.080	0.072	0.047	0.033
Spleen (G)	0.940	0.700	1.089	0.930	1.332	1.645	1.339	1.946	0.880
% BODY WEIGHT	0.338	0.257	0.440	0.305	0.585	0.626	0.589	0.801	0.327

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

U N A T

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098  
 SEX: FEMALE

GROUP: 4F - 18.0 mg base/kg/day  
 ALL FATES      ALL DAYS      ALL BALANCES

ANIMAL ID: BALANCE NO.:	950	951	952	953	954	955	957	958	959
BODY WEIGHT (G)	242.8	225.1	222.1	306.3	297.1	247.0	305.1	217.8	310.0
Adrenals (pr) (G)	0.086	0.087	0.082	0.100	0.090	0.098	0.080	0.064	0.090
% BODY WEIGHT	0.035	0.039	0.037	0.033	0.030	0.040	0.026	0.029	0.029
Brain (G)	1.895	1.908	1.810	2.020	2.060	1.903	2.020	1.943	1.990
% BODY WEIGHT	0.780	0.848	0.815	0.659	0.693	0.770	0.662	0.892	0.642
Heart (G)	0.952	0.930	0.871	1.060	1.100	1.061	1.240	0.784	1.070
% BODY WEIGHT	0.392	0.413	0.392	0.346	0.370	0.430	0.406	0.360	0.345
Kidneys (pr) (G)	2.324	2.751	2.074	2.500	2.800	2.707	2.700	1.954	2.980
% BODY WEIGHT	0.957	1.222	0.934	0.816	0.942	1.096	0.885	0.897	0.961
Liver (G)	10.524	10.060	9.099	9.340	9.330	10.414	8.240	7.894	10.770
% BODY WEIGHT	4.334	4.469	4.097	3.049	3.140	4.216	2.701	3.624	3.474
Ovaries (G)	0.131	0.169	0.177	0.150	0.110	0.162	0.130	0.104	0.100
% BODY WEIGHT	0.054	0.075	0.080	0.049	0.037	0.066	0.043	0.048	0.032
Spleen (G)	1.406	1.228	1.333	0.700	0.910	1.545	0.720	1.160	0.700
% BODY WEIGHT	0.579	0.546	0.600	0.229	0.306	0.626	0.236	0.533	0.226

DRAFT

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

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098  
SEX: FEMALE

GROUP: 4F - 18.0 mg base/kg/day  
ALL FATES ALL DAYS ALL BALANCES

ANIMAL ID: 960  
BALANCE NO.:

BODY WEIGHT (G)	256.8
Adrenals (pr) (G)	0.110
% BODY WEIGHT	0.043
Brain (G)	1.970
% BODY WEIGHT	0.767
Heart (G)	1.200
% BODY WEIGHT	0.467
Kidneys (pr) (G)	2.310
% BODY WEIGHT	0.900
Liver (G)	7.670
% BODY WEIGHT	2.987
Ovaries (G)	0.080
% BODY WEIGHT	0.031
Spleen (G)	0.610
% BODY WEIGHT	0.238

DRAFT

APPENDIX 10  
Pathology Report

DRAFT PATHOLOGY REPORT FOR  
TRL STUDY NUMBER 098  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

PREPARED  
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SEPTEMBER 28, 1993

TABLE OF CONTENTS

SECTION	TITLE	PAGE
I	Pathology Narrative .....	3
	Summary of Experimental Design (Table I) .....	10
	Protocol-Required Tissues (Table II) .....	10
	Tissue Accountability Record (Table III) .....	11
	Report Codes Table .....	12
	Abbreviation List .....	13
II	Project Summary Table .....	14
	Males .....	15
	Females .....	19
III	Severity Summary Table .....	24
	Males .....	25
	Females .....	29
IV	Tabulated Animal Data .....	33
	Males .....	34
	Females .....	49
V	Correlation of Gross and Microscopic (Micro) Findings .....	68
	Males .....	69
	Females .....	95
VI	Quality Assurance Statement .....	122
VII	Appendix 1: Bone Marrow Report .....	124

SECTION I  
PATHOLOGY NARRATIVE

## DRAFT PATHOLOGY REPORT

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

#### INTRODUCTION

This pathology report, submitted by Pathology Associates, Inc. (PAI) to Toxicology Research Laboratory (TRL), represents the pathology findings for the study designated as "Thirteen Week Oral Toxicity Study of WR238605 with a Thirteen Week Recovery Period in Rats," TRL Study Number 098.

#### EXPERIMENTAL DESIGN AND METHODS

Three groups, each composed of male and female CD® (Virus Antibody Free) rats, were given the test article (WR238605) once daily by gavage for at least 13 weeks, starting with Day 0. Dose levels administered are shown in the Summary of Experimental Design (Table I). A control group of male and female rats was included, and received test article vehicle (aqueous 1% methylcellulose/0.4% Tween 80) by gavage for at least 13 weeks, starting with Day 0. Animals designated for sacrifice at the end of the 13 week dosing period were dosed up to and including the day prior to their scheduled sacrifice and necropsy on Days 91 and 92 (study week 14). Designated recovery animals were dosed for 91 days and then held for a 13 week recovery period before being sacrificed and necropsied at the beginning of study week 27. Scheduled necropsies were performed according to TRL Standard Operating Procedures under the supervision of Ralph M. Bunte, DVM.

Tissues required by the protocol, except as noted in the Tissue Accountability Record (Table III), were processed in accordance with PAI Standard Operating Procedures. Protocol-required tissues from control and high dose animals sacrificed at the end of dosing were evaluated by light microscopy. Results of this evaluation were summarized, and pituitary gland, thyroid gland, liver, spleen, lung, kidney, and bone marrow were identified as potential target organs. These tissues from low and middle dose groups sacrificed at the end of dosing, and from control and high dose recovery groups, were then processed. The potential target organs from these animals were evaluated/ re-evaluated by light microscopy. When necessary, in order to resolve discrepancies in evaluation, slides were randomized and examined without knowledge of treatment group or sex. Following these evaluations, lung, kidney, bone marrow, and spleen were identified as target organs. Lungs from low and middle dose recovery groups were then processed and examined microscopically in order to evaluate test article-related effects seen in the lungs of high dose recovery group animals.

Most tissues that were not accounted for were from animals that died during the study. No test article-related changes occurred in mammary gland, parathyroid gland, pituitary gland, diaphragm, or costochondral junction. For this reason, the unaccountability of the few tissues missing from terminal sacrifice animals is believed not to have affected the outcome of the study.

Microscopic findings for terminal sacrifice animals from all groups are summarized in the Project Summary Tables (Section II). The mean group severity scores for these animals 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 four parts: Unscheduled Deaths, Gross Lesions, 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.

### Unscheduled Deaths

Five high dose group males died prior to the end of dosing, during weeks 2 (#0921, #0926, #0936, and #0937) and 8 (#0934). The cause of death for each of the four animals that died during week 2 could not be determined. Each of these animals had inflammation in the structures of the thoracic cavity or multifocal inflammation consistent with septicemia when tissues from these animals were evaluated microscopically. However, no injuries, such as esophageal lacerations, that would explain the inflammation were found during review of tissues from these animals. Also, microscopic changes that were found to be test article-related in animals sacrificed at the end of dosing were not present in these animals. Microscopic evaluation of tissues from animal #0934 revealed alveolar proteinosis in the lung, hemoglobin nephrosis, and renal hemosiderosis. These were found to be test article-related changes in animals sacrificed at the end of dosing. For these reasons, the death of animal #0934 was attributed to the test article. One high dose group female (#0956) died following CO<sub>2</sub> anesthesia for blood collection (per Study Director) during the recovery period (week 16).

### Gross Lesions

Potentially treatment-related gross lesions were identified in the lungs of middle and high dose rats sacrificed at the end of dosing and after the recovery period. The lesions were morphologically consistent in all animals in which they occurred. They were described as multiple, irregular, white lesions on the pleura, which varied from focal to linear.

### Diagnostic Terms

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

#### Lung

Alveolar proteinosis consisted of two distinct components. First, there was pale, eosinophilic, amorphous to fibrillar material within alveoli. The second feature was discrete, large, round to oval cells which had abundant vacuolated cytoplasm. These cells were free in the lumina of alveoli and terminal bronchioles but did not appear to line alveolar septa. Occasionally, a few neutrophils were also present.

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

In recovery animals, there were clusters of macrophages filling randomly scattered alveoli. These cells contained variable cytoplasmic granules that were positive for iron by Perl's stain and were non-acid-fast. These granules were identified as hemosiderin. Hemosiderin can be distinguished

from lipofuscin by iron and acid-fast stains. Hemosiderin is iron (Perl's stain) positive and acid-fast negative, while lipofuscin is iron negative and acid-fast positive.

#### Kidney

Hemoglobin nephrosis was characterized by proteinic droplets in the lumen of renal tubules and by degenerative changes in the tubular epithelium. The degenerative changes in tubular epithelium consisted of irregularly scalloped luminal cell borders, proteinic cytoplasmic droplets, cytoplasmic vacuolation, and necrosis.

Hemosiderin was deposited as variably-sized golden-brown granules in the cytoplasm of tubular epithelial cells.

#### Spleen

Hyperplasia of the spleen consisted of an increase in normal cellular components in the spleen. This resulted in sections of spleen that appeared histologically normal except for an increased cross-sectional size.

#### Bone Marrow

Hemosiderin deposition in the bone marrow consisted of golden-brown granules in macrophages in the histologic sections of bone marrow.

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

### Histopathology Findings

#### Lung

Among animals sacrificed at the end of dosing, alveolar proteinosis was diagnosed in 0 out of 10, 0 out of 10, 10 out of 10, and 5 out of 5 males, and in 0 out of 10, 0 out of 10, 10 out of 10, and 10 out of 10 females in the control, low, middle, and high dose groups, respectively. Mean group severity scores for this change were 0.00, 0.00, 1.70, and 2.80 in males, and 0.00, 0.00, 1.60, and 2.20 in females in the control, low, middle, and high dose groups, respectively. Alveolar proteinosis did not occur in males or in females sacrificed after the recovery period. 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 of this change in animals sacrificed after the recovery period, indicates alveolar proteinosis to be a test article-related change. This lesion corresponded to the gross lesions described in the lungs of middle and high dose animals sacrificed at the end of dosing.

Chronic inflammation in the lung was observed only in animals sacrificed after the recovery period. In recovery males, this change occurred in 0 out of 10, 0 out of 10, 5 out of 10, and 1 out of 10 animals in the control, low, middle, and high dose groups, with mean group severity scores of 0.00, 0.00, 0.50, and 0.20, respectively. In recovery females, this change occurred in 0 out of 10, 0 out of 10, 7 out of 10, and 5 out of 9 animals in the control, low, middle, and high dose groups, with mean group severity scores of 0.00, 0.00, 1.10, and 0.67, respectively. Chronic inflammation was focal or multifocal, randomly distributed, usually subpleural, and not always associated with gross lesions (see Gross Lesions). For these reasons, the observation of chronic inflammation in a single 5-6 micron thick section of lung was fortuitous. These observations account for the lack of a dose-related incidence and the low mean group severity scores for this change. A possible relationship between chronic inflammation and alveolar proteinosis in the lung is speculative, as these changes occurred at different points in time. Such a relationship seems likely, however, as alveolar proteinosis had resolved by the end of the recovery period, and no other change that would have resulted in chronic inflammation of the lung was noted in animals

sacrificed at the end of dosing. For these reasons, chronic inflammation in the lungs of recovery animals was interpreted as part of the resolution of alveolar proteinosis and was, thus, secondary to a direct test article-related effect.

Deposition of hemosiderin pigment occurred in 1 out of 10 control males sacrificed at the end of dosing, with a mean group severity score of 0.20. This hemosiderin was associated with an area of previous hemorrhage in alveoli. Among animals sacrificed after the recovery period, hemosiderin deposition in the lung occurred in 1 out of 10, 7 out of 10, and 8 out of 10 males, and in 0 out of 10, 8 out of 10, and 9 out of 9 females in the low, middle, and high dose groups, respectively. Mean group severity scores for this change in these animals were 0.10, 0.80, and 0.80 in males, and 0.00, 1.20, and 1.11 in females in the low, middle, and high dose groups, respectively. This change did not occur in the lungs of control males or females sacrificed after the recovery period. The hemosiderin in the lung of the low dose male sacrificed after the recovery period was in the interstitium rather than the alveoli. For this reason, the hemosiderin in this animal was considered unrelated to the hemosiderin which occurred in alveoli of middle and high dose group recovery animals. The hemosiderin in alveoli of the lungs of middle and high dose group recovery animals was initially thought to be lipofuscin. Staining selected lungs with Perl's stain and an acid-fast stain confirmed the pigment to be hemosiderin rather than lipofuscin. In view of changes in the kidneys (discussed below), this hemosiderin most likely resulted from the presence of hemoglobin in the proteinic material seen in alveolar proteinosis. Alveolar macrophages, as part of the resolution of alveolar proteinosis, phagocytized this hemoglobin and processed it to hemosiderin. These clusters of hemosiderin-laden macrophages had not yet been able to clear out of the lung at the time of the recovery sacrifice. For these reasons, hemosiderin in alveolar macrophages was also interpreted as secondary to a direct test article-related effect.

The changes described as alveolar proteinosis in the lungs of these rats are similar to those described as alveolar proteinosis in the Fischer 344 rat. The causes for alveolar proteinosis in the rat are not known, but altered vascular permeability and abnormal surfactant production and degradation have been suggested.<sup>1</sup> These changes are also similar to changes related to chronic pulmonary edema in domestic animals.<sup>2</sup> Altered vascular permeability as the mechanism for alveolar proteinosis is also suggested by hemosiderin in alveolar macrophages in recovery rats. Fragments of cell membrane from lysed erythrocytes could also have passed into alveoli and contributed to the cholesterol clefts in the chronic inflammation. This would further support increased vascular permeability as the cause of 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, chronic inflammation, and hemosiderin in alveolar macrophages were considered pathophysiologically-related processes. Alveolar proteinosis was interpreted as a direct test article-related effect, while chronic inflammation and hemosiderin deposits were secondary test article-related effects representing resolution of the alveolar proteinosis.

#### Kidney

Hemoglobin nephrosis occurred in middle and high dose animals sacrificed at the end of dosing. This change did not occur in control or low dose animals sacrificed at the end of dosing or in control and high dose recovery animals. Among animals sacrificed at the end of dosing, hemoglobin nephrosis occurred in 5 out of 10 and 5 out of 5 males, and in 4 out of 10 and 10 out of 10 females in the middle and high dose groups, respectively. Mean group severity scores for

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<sup>1</sup> G.A. Boorman and S.L. Eustis, "Lung," Pathology of the Fischer Rat, Reference and 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> D.L. Dungworth, "Respiratory System," Pathology of Domestic Animals, eds. K.V.F. Jubb, P.C. Kennedy, and N. Palmer, (San Diego: Academic Press, Inc., 1985), pp. 407-448.

this change were 0.50 and 2.20 in males, and 0.40 and 1.50 in females in the middle and high dose groups, respectively.

Hemosiderin deposition did not occur in the tubular epithelium of control and low dose males and females sacrificed at the end of dosing. This change did occur in 1 out of 10 and 5 out of 5 males, and in 2 out of 10 and 10 out of 10 females in the middle and high dose groups, respectively, sacrificed at this time. Mean group severity scores were 0.10 and 2.20 in males, and 0.20 and 2.20 in females in the middle and high dose groups, respectively. Among animals sacrificed at the end of the recovery period, this change occurred in 0 out of 10 and 2 out of 10 males, and in 0 out of 10 and 1 out of 9 females in the control and high dose groups, respectively. Mean group severity scores for this change were 0.00 and 0.20 in males, and 0.00 and 0.11 in females in the control and high dose groups, respectively.

Hemoglobin that is removed or released from erythrocytes is normally cleared from the blood by combining with heme-binding proteins which are then removed from the circulation. When heme-binding proteins are overloaded, such as in hemolytic anemia, some unbound hemoglobin will form dimers which can pass through the glomerular filtration system and appear as eosinophilic (i.e. proteinic) droplets in the proximal convoluted tubule. Tubular epithelial cells will resorb and metabolize the hemoglobin dimers, but can be damaged if stromal elements of lysed erythrocytes also pass into the glomerular filtrate.<sup>3</sup> The hemosiderin deposited in tubular epithelium is additional evidence of hemoglobin passing into the glomerular filtrate. Changes in the lungs suggested that pulmonary vascular permeability was increased. It is less clear whether these renal changes were associated with normal or increased vascular permeability in the glomerulus. For these reasons, and due to incidence and mean group severity scores at the end of dosing and after the recovery period, hemoglobin nephrosis and hemosiderin deposition in tubular epithelium were interpreted as secondary to increased erythrocyte destruction rather than as direct test article-related effects.

#### Bone Marrow

Evaluation of sections of bone marrow revealed deposition of hemosiderin in 2 out of 5 males and in 5 out of 10 females in the high dose group sacrificed at the end of dosing. Mean group severity scores for this change were 0.40 in high dose males and 0.50 in high dose females. This change did not occur in control, low, or middle dose animals sacrificed at the end of dosing, or in control and high dose animals sacrificed after the recovery period. Evaluation of femoral bone marrow smears of male and female treated animals sacrificed at the end of dosing revealed no treatment-related effect in the M:E ratio (Appendix 1). Hemosiderin deposition in the bone marrow and kidney suggests increased erythrocyte destruction. Increased erythrocyte destruction must have been mild, however, as evidenced by the absence of a decrease in the M:E ratio at the end of dosing. For these reasons, hemosiderin deposition in the bone marrow was interpreted as secondary to mildly increased erythrocyte destruction.

#### Spleen

Among animals sacrificed at the end of dosing, splenic hyperplasia was diagnosed in 0 out of 10, 4 out of 10, and 5 out of 5 males, and in 0 out of 10, 0 out of 10, and 8 out of 10 females in the low, middle, and high dose groups, respectively. Mean group severity scores for this finding in these animals were 0.00, 0.60, and 2.20 in males, and 0.00, 0.00, and 1.50 in females in the low, middle, and high dose groups, respectively. This change did not occur in control animal sacrificed at the end of dosing or in control and high dose animals sacrificed after the recovery period. The mechanism by which splenic hyperplasia occurred is not clear. Antigenic stimulation of splenic lymphocytes, generalized stimulation of sinusoidal phagocytes, or both seem most likely, as this change was not associated with increased hemosiderin deposits or extramedullary hematopoiesis.

<sup>3</sup> N.F. Cheville, Cell Pathology, (Ames: The Iowa State University Press, 1983), p. 578.

Based on dosed-related incidence and mean group severity scores in animals sacrificed at the end of dosing, and on resolution of this change in recovery animals, splenic hyperplasia was interpreted as a direct test article-related effect.

#### Other Lesions

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

In summary, the principal pathology findings in this study were those in the lungs, kidney, bone marrow and spleen. Alveolar proteinosis in the lung was a direct test article-related change in middle and high dose groups. While this change was morphologically distinct, the mechanism of its development was less clear. The two most likely mechanisms would be alteration of the vascular permeability, causing persistent alveolar edema, or alteration of surfactant production and degradation. Chronic inflammation and hemosiderin deposition in alveolar macrophages were considered secondary effects of the test article, representing resolution of alveolar proteinosis. Changes in the kidney and bone marrow were considered secondary to increased erythrocyte destruction. These changes had resolved or were resolving at the end of the recovery period. Splenic hyperplasia was associated with proportional increases in the size of lymphoid and sinusoidal elements rather than with extramedullary hematopoiesis or hemosiderin deposition. Based on incidence and mean group severity scores, splenic hyperplasia was interpreted as a direct test article-related effect in middle and high dose groups at the end of dosing, but the mechanism of its occurrence was not clear.

#### CONCLUSIONS

Under the conditions of this study, oral administration of WR238605 to rats for thirteen weeks was associated with changes in the lungs, kidneys, bone marrow, and spleen. Alveolar proteinosis was a direct test article-related change in the lungs of middle and high dose animals sacrificed at the end of dosing. Chronic inflammation and hemosiderin deposition in alveolar macrophages occurred in lungs of middle and high dose animals sacrificed after the recovery period. These changes were interpreted as part of the resolution of alveolar proteinosis and were, thus, considered to be secondarily related to the test article.

Hemoglobin nephrosis and hemosiderin deposition occurred in the kidneys of middle and high dose animals at the end of dosing, but were resolving or had resolved by the end of the recovery period. Hemosiderin deposition also occurred in the bone marrow of high dose animals sacrificed at the end of dosing, but had resolved after the recovery period. These changes in kidney and bone marrow were interpreted as secondary to mildly increased erythrocyte destruction, and were considered secondary test article-related effects. This was consistent with the results of bone marrow smear evaluations.

Splenic hyperplasia in the middle and high dose groups was interpreted as a direct test article-related effect, but no mechanism for its occurrence was identified.

The no-effect level was clearly the low dose level (0.5 mg base/kg/day) for direct and secondary test article-related effects. All of the changes observed at the higher doses had resolved or were resolving by the end of the recovery period.

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

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Date

TABLE I

SUMMARY OF EXPERIMENTAL DESIGN

Treatment Group	Dose Level (mg base/kg/day)	Number of Males	Number of Females
1	0	10+10*	10+10*
2	0.5	10+10*	10+10*
3	6.0	10+10*	10+10*
4	18.0	10+10*	10+10*

\*Recovery Animals

TABLE II

PROTOCOL-REQUIRED TISSUES

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

TABLE III  
 TISSUE ACCOUNTABILITY RECORD

TREATMENT GROUP	ANIMAL NUMBER	FATE	TISSUE	REASON TISSUE NOT PRESENT
1	0803	TS	Mammary gland	U
1	0817	TS	Parathyroid gland	U
1	0821	TS	Mammary gland	U
1-R	0835	TS	Pituitary gland	E
1	0839	TS	Parathyroid gland	U
2	0849	TS	Pituitary gland	E
4	0924	TS	Diaphragm	M
4	0925	TS	Costochondral junction	U
4	0926	ND	Duodenum	A
4	0926	ND	Eyes	A
4	0926	ND	Mammary gland	U
4	0934	ND	Salivary gland	M
4	0934	ND	Parathyroid gland	U
4	0934	ND	Mesenteric lymph node	M
4	0936	ND	Pituitary gland	M
4	0936	ND	Trachea	A
4	0936	ND	Thyroid gland	A
4	0936	ND	Colon	A
4	0936	ND	Ileum	A
4	0936	ND	Cecum	A
4	0936	ND	Mesenteric lymph node	M
4	0936	ND	Eyes	A
4	0937	ND	Thymus	U
4	0937	ND	Parathyroid gland	U
4	0938	TS	Parathyroid gland	U
4-R	0956	ND	Parathyroid gland	U
4-R	0956	ND	Mammary gland	U
4-R	0956	ND	Sciatic nerve	U

TS: Terminal Sacrifice  
 ND: Natural Death  
 U: Unavailable/Unsuitable for microscopic evaluation  
 M: Not present in wet tissue at trimming  
 E: Not present in cassette at embedding  
 A: Autolysis precludes evaluation

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

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Report Codes Table

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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

D R A F T

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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	Metastatic site (+)
-	No data entered

HISTOPATHOLOGY TABLES

ABBREVIATION LIST

Cytopl - Cytoplasm

Epith - Epithelium

Granulomat - Granulomatous

Hyperpl - Hyperplasia

Infiltr - Infiltrate

Inflam - Inflammation

Perivasc - Perivascular

R - Recovery

Regenerat - Regeneration

Seminif - Seminiferous

Tubulr - Tubular

Vacuo - Vacuolation

SECTION II  
PROJECT SUMMARY TABLE

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

**Project Summary Table**

SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: TRL098  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: MALE

D R A F T

PAGE 15

GROUP:	1	2	3	4	1 - R	2 - R	3 - R	4 - R
NUMBER OF ANIMALS:	10	10	10	5	10	10	10	10

	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%
BRAIN	# Ex	10		0	0		5		0		0		0		0	
PITUITARY GLAND	# Ex	10		9	10		5		10		0		0		10	
Pars distalis, cyst		1 (10)		0 (0)	0 (0)		0 (0)		0 (0)		0		0		0 (0)	
Pars distalis, hyperplasia		0 (0)		0 (0)	0 (0)		0 (0)		0 (0)		0		0		1 (10)	
Pars distalis, vacuo, cytopl		9 (90)		9 (100)	10 (100)		5 (100)		10 (100)		0		0		9 (90)	
Pars intermedia, cyst		0 (0)		0 (0)	0 (0)		0 (0)		1 (10)		0		0		0 (0)	
Rathke's cleft, tubulr hyperpl		0 (0)		0 (0)	0 (0)		0 (0)		0 (0)		0		0		1 (10)	
SPINAL CORD, THORACIC	# Ex	10		0	0		5		0		0		0		0	
THYMUS	# Ex	10		0	0		5		0		0		0		0	
Congestion		2 (20)		0	0		0 (0)		0		0		0		0	
SALIVARY GLAND	# Ex	10		0	0		5		0		0		0		0	
PANCREAS	# Ex	10		0	0		5		0		0		0		0	
Inflammation, chronic		1 (10)		0	0		0 (0)		0		0		0		0	
Lobule, degeneration		0 (0)		0	0		1 (20)		0		0		0		0	
ADRENAL GLAND	# Ex	10		0	0		5		0		0		0		0	
Cortex, vacuolation, cytoplasm		6 (60)		0	0		2 (40)		0		0		0		0	
TRACHEA	# Ex	10		0	0		5		0		0		0		0	
THYROID GLAND	# Ex	10		10	10		5		10		0		0		10	
PARATHYROID GLAND	# Ex	9		0	0		4		0		0		0		0	
ESOPHAGUS	# Ex	10		0	0		5		0		0		0		0	

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

**Project Summary Table**

SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: TRL098  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: MALE

DRAFT

PAGE 16

GROUP:		1	2	3	4	1 - R	2 - R	3 - R	4 - R
NUMBER OF ANIMALS:		10	10	10	5	10	10	10	10
HEART	# Ex	10	0	0	5	0	0	0	0
Cardiomyopathy		4 (40)	0	0	1 (20)	0	0	0	0
DUODENUM	# Ex	10	0	0	5	0	0	0	0
COLON	# Ex	10	0	0	5	0	0	0	0
STOMACH	# Ex	10	0	0	5	0	0	0	0
LIVER	# Ex	10	10	10	5	10	0	0	10
Hepatocyte, vacuo, cytoplasm		1 (10)	3 (30)	0 (0)	0 (0)	0 (0)	0	0	1 (10)
Inflammation, subacute		2 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0	0	0 (0)
Lobular hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0	0	0 (0)
Periportal, infiltr, cellular		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0	0	0 (0)
Pigment, hemosiderin		0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0	0	0 (0)
SPLEEN	# Ex	10	10	10	5	10	0	0	10
Hyperplasia		0 (0)	0 (0)	4 (40)	5 (100)	0 (0)	0	0	0 (0)
Pigment, hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0	0	1 (10)
JEJUNUM	# Ex	10	0	0	5	0	0	0	0
LUNG	# Ex	10	10	10	5	10	10	10	10
Alveolar epithelium, hyperpl		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)
Alveolar hystiocytosis		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (30)
Alveolar proteinosis		0 (0)	0 (0)	10 (100)	5 (100)	0 (0)	0 (0)	0 (0)	0 (0)
Hemorrhage		2 (20)	0 (0)	0 (0)	0 (0)	2 (20)	4 (40)	2 (20)	0 (0)
Inflammation, chronic		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	5 (50)	1 (10)
Inflammation, perivasc, acute		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Inflammation, subacute		4 (40)	0 (0)	3 (30)	0 (0)	2 (20)	3 (30)	3 (30)	2 (20)
Pigment, hemosiderin		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	7 (70)	8 (80)

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

**Project Summary Table**

SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: TRL098  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: MALE

D R A F T

PAGE 17

GROUP:	1	2	3	4	1 - R	2 - R	3 - R	4 - R
NUMBER OF ANIMALS:	10	10	10	5	10	10	10	10

		#	%	#	%	#	%	#	%	#	%	#	%	#	%		
KIDNEY	# Ex	10		10		10		5		10		0		0		10	
Cortex, cyst		0	(0)	0	(0)	0	(0)	0	(0)	1	(10)	0		0		0	(0)
Infiltrate, cellular		0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0		0		1	(10)
Nephropathy		4	(40)	0	(0)	0	(0)	0	(0)	2	(20)	0		0		1	(10)
Nephrosis, hemoglobin		0	(0)	0	(0)	5	(50)	5	(100)	0	(0)	0		0		0	(0)
Pigment, hemosiderin		0	(0)	0	(0)	1	(10)	5	(100)	0	(0)	0		0		2	(20)
Renal tubule, dilatation		1	(10)	0	(0)	0	(0)	0	(0)	0	(0)	0		0		0	(0)
Renal tubule, epith, regenerat		0	(0)	0	(0)	1	(10)	0	(0)	1	(10)	0		0		0	(0)
URINARY BLADDER	# Ex	10		0		0		5		0		0		0		0	
Calculus		3	(30)	0		0		1	(20)	0		0		0		0	
Epithelium, ulcer		1	(10)	0		0		0	(0)	0		0		0		0	
PROSTATE	# Ex	10		0		0		5		0		0		0		0	
Inflammation, subacute		1	(10)	0		0		0	(0)	0		0		0		0	
SKIN	# Ex	10		0		0		5		0		0		0		0	
MAMMARY GLAND	# Ex	9		0		0		5		0		0		0		0	
ILEUM	# Ex	10		0		0		5		0		0		0		0	
CECUM	# Ex	10		0		0		5		0		0		0		0	
LYMPH NODE, MESENTERIC	# Ex	10		0		0		5		0		0		0		0	
SKELETAL MUSCLE	# Ex	10		0		0		5		0		0		0		0	
SCIATIC NERVE	# Ex	10		0		0		5		0		0		0		0	

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

**Project Summary Table**

SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: TRL098  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: MALE

DRAFT

PAGE 18

GROUP:	1	2	3	4	1 - R	2 - R	3 - R	4 - R
NUMBER OF ANIMALS:	10	10	10	5	10	10	10	10

	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%	
TESTES	# Ex	10		0		0		5		0		0		0		0	
Seminif tubules, giant cells		0	(0)	0		0		1	(20)	0		0		0		0	
EPIDIDYMIS	# Ex	10		0		0		5		0		0		0		0	
TONGUE	# Ex	10		0		0		5		0		0		0		0	
DIAPHRAGM	# Ex	10		0		0		4		0		0		0		0	
RIB	# Ex	10		0		0		5		0		0		0		0	
COSTOCHONDRAL JUNCTION	# Ex	10		0		0		4		0		0		0		0	
STERNUM	# Ex	10		0		0		5		0		0		0		0	
BONE MARROW	# Ex	10		10		10		5		10		0		0		10	
Pigment, hemosiderin		0	(0)	0	(0)	0	(0)	2	(40)	0	(0)	0		0		0	(0)
EYE	# Ex	10		0		0		5		0		0		0		0	
HARDERIAN GLAND	# Ex	10		0		0		5		0		0		0		0	

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

**Project Summary Table**

SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: TRL098  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: FEMALE

D R A F T

PAGE 19

GROUP:	1	2	3	4	1 - R	2 - R	3 - R	4 - R
NUMBER OF ANIMALS:	10	10	10	10	10	10	10	9

	# Ex	1		2		3		4		1 - R		2 - R		3 - R		4 - R	
		#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%
BRAIN		10		0		0		10		0		0		0		0	
PITUITARY GLAND		10		10		10		10		9		0		0		9	
Pars distalis, adenoma		0	(0)	0	(0)	0	(0)	0	(0)	2	(22)	0		0		0	(0)
Pars distalis, cyst		1	(10)	0	(0)	0	(0)	1	(10)	0	(0)	0		0		0	(0)
Pars distalis, vacuo, cytopl		0	(0)	0	(0)	0	(0)	0	(0)	2	(22)	0		0		0	(0)
Pars intermedia, cyst		0	(0)	0	(0)	0	(0)	0	(0)	1	(11)	0		0		0	(0)
SPINAL CORD, THORACIC		10		0		0		10		0		0		0		0	
THYMUS		10		0		0		10		0		0		0		0	
SALIVARY GLAND		10		0		0		10		0		0		0		0	
PANCREAS		10		0		0		10		0		0		0		0	
ADRENAL GLAND		10		0		0		10		0		0		0		0	
Cortex, cystic degeneration		1	(10)	0		0		0	(0)	0		0		0		0	
Cortex, pigment, lipofuscin		0	(0)	0		0		2	(20)	0		0		0		0	
TRACHEA		10		0		0		10		0		0		0		0	
THYROID GLAND		10		10		10		10		10		0		0		9	
PARATHYROID GLAND		9		0		0		10		0		0		0		0	
Fibrosis		1	(11)	0		0		0	(0)	0		0		0		0	
ESOPHAGUS		10		0		0		10		0		0		0		0	

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

**Project Summary Table**

SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

DRAFT

PAGE 20

PROJECT ID. NO: TRL098  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: FEMALE

GROUP:	1	2	3	4	1 - R	2 - R	3 - R	4 - R
NUMBER OF ANIMALS:	10	10	10	10	10	10	10	9

		#	%	#	%	#	%	#	%	#	%	#	%	#	%
HEART	# Ex	10		0		0		10		0		0		0	
Cardiomyopathy		0	(0)	0		0		2	(20)	0		0		0	
Hemorrhage		1	(10)	0		0		0	(0)	0		0		0	
DUODENUM	# Ex	10		0		0		10		0		0		0	
COLON	# Ex	10		0		0		10		0		0		0	
STOMACH	# Ex	10		0		0		10		0		0		0	
Non-glandular, inflammation		1	(10)	0		0		0	(0)	0		0		0	
LIVER	# Ex	10		10		10		10		10		0		0	9
Basophilic focus		0	(0)	1	(10)	0	(0)	0	(0)	0	(0)	0	(0)	0	0 (0)
Bile duct, hyperplasia		0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	4 (44)
Hepatocyte, vacuo, cytoplasm		0	(0)	0	(0)	0	(0)	0	(0)	1	(10)	0	(0)	0	0 (0)
Infiltrate, cellular		0	(0)	0	(0)	3	(30)	0	(0)	0	(0)	0	(0)	0	0 (0)
Inflammation, subacute		3	(30)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	0 (0)
Periportal, infiltr, cellular		0	(0)	1	(10)	0	(0)	0	(0)	0	(0)	0	(0)	0	1 (11)
Pigment, hemosiderin		0	(0)	0	(0)	2	(20)	0	(0)	0	(0)	0	(0)	0	0 (0)
Portal, fibrosis		0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	1 (11)
SPLEEN	# Ex	10		10		10		10		10		0		0	9
Hyperplasia		0	(0)	0	(0)	0	(0)	8	(80)	0	(0)	0	(0)	0	0 (0)
Pigment, hemosiderin		0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	1 (11)
JEJUNUM	# Ex	10		0		0		10		0		0		0	0
LUNG	# Ex	10		10		10		10		10		10		10	9
Alveolar hystiocytosis		0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	3 (33)
Alveolar proteinosis		0	(0)	0	(0)	10	(100)	10	(100)	0	(0)	0	(0)	0	0 (0)
Hemorrhage		1	(10)	0	(0)	0	(0)	0	(0)	0	(0)	1	(10)	0	0 (0)
Inflammation, acute		0	(0)	0	(0)	0	(0)	2	(20)	0	(0)	0	(0)	0	0 (0)
Inflammation, chronic		0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	7	(70)
Inflammation, subacute		2	(20)	0	(0)	5	(50)	1	(10)	0	(0)	0	(0)	1	(10)

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
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 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

**Project Summary Table**

SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: TRL098  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: FEMALE

D R A F T

PAGE 21

GROUP:	1	2	3	4	1 - R	2 - R	3 - R	4 - R
NUMBER OF ANIMALS:	10	10	10	10	10	10	10	9

	# Ex	1		2		3		4		1 - R		2 - R		3 - R		4 - R	
		#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%
LUNG		10		10		10		10		10		10		10		9	
Pigment, hemosiderin		0 (0)		0 (0)		0 (0)		0 (0)		0 (0)		0 (0)		8 (80)		9 (100)	
KIDNEY		10		10		10		10		10		0		0		9	
Cortex, cyst		0 (0)		0 (0)		0 (0)		0 (0)		0 (0)		0		0		1 (11)	
Nephrocalcinosis		7 (70)		6 (60)		5 (50)		4 (40)		6 (60)		0		0		7 (78)	
Nephropathy		0 (0)		0 (0)		0 (0)		0 (0)		0 (0)		0		0		1 (11)	
Nephrosis, hemoglobin		0 (0)		0 (0)		4 (40)		10 (100)		0 (0)		0		0		0 (0)	
Pigment, hemosiderin		0 (0)		0 (0)		2 (20)		10 (100)		0 (0)		0		0		1 (11)	
Renal tubule, casts, proteinic		0 (0)		0 (0)		0 (0)		0 (0)		1 (10)		0		0		0 (0)	
URINARY BLADDER		10		0		0		10		0		0		0		0	
SKIN		10		0		0		10		0		0		0		0	
MAMMARY GLAND		9		0		0		10		0		0		0		0	
ILEUM		10		0		0		10		0		0		0		0	
CECUM		10		0		0		10		0		0		0		0	
LYMPH NODE, MESENTERIC		10		0		0		10		0		0		0		0	
SKELETAL MUSCLE		10		0		0		10		0		0		0		0	
SCIATIC NERVE		10		0		0		10		0		0		0		0	
OVARY		10		0		0		10		0		0		0		0	

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

**Project Summary Table**

SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: TRL098  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: FEMALE

D R A F T

PAGE 22

GROUP:	1	2	3	4	1 - R	2 - R	3 - R	4 - R
NUMBER OF ANIMALS:	10	10	10	10	10	10	10	9

		#	%		#	%		#	%		#	%		#	%		#	%
ORGAN	# Ex																	
UTERUS	10	0		0			10	0		0			0				0	
Decidua	1	(10)		0			0	(0)		0			0				0	
Dilatation	3	(30)		0			3	(30)		0			0				0	
Hemorrhage	1	(10)		0			0	(0)		0			0				0	
Inflammation, acute	1	(10)		0			0	(0)		0			0				0	
TONGUE	10	0		0			10	0		0			0				0	
DIAPHRAGM	10	0		0			10	0		0			0				0	
RIB	10	0		0			10	0		0			0				0	
COSTOCHONDRAL JUNCTION	10	0		0			10	0		0			0				0	
STERNUM	10	0		0			10	0		0			0				0	
BONE MARROW	10			10			10			10			0				0	
Pigment, hemosiderin	0	(0)		0	(0)		5	(50)		0	(0)		0				0	(0)
EYE	10	0		0			10	0		0			0				0	
HARDERIAN GLAND	10	0		0			10	0		0			0				0	
Infiltrate, cellular	0	(0)		0			1	(10)		0			0				0	
Inflammation, subacute	1	(10)		0			0	(0)		0			0				0	

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
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**Project Summary Table**

SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: TRL098  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: FEMALE

D R A F T

PAGE 23

GROUP:	1	2	3	4	1 - R	2 - R	3 - R	4 - R
NUMBER OF ANIMALS:	10	10	10	10	10	10	10	9

OTHER TISSUES AND LESIONS:

	#	%	#	%	#	%	#	%	#	%	#	%	#	%
SKIN, EAR - Inflamm, granulomat	0	(0)	0	(0)	0	(0)	1	(10)	0	(0)	0	(0)	0	(0)
SKIN - Granuloma, foreign body	0	(0)	0	(0)	0	(0)	1	(10)	0	(0)	0	(0)	0	(0)
SKIN, HEAD - Inflamm, chronic	1	(10)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)

09-Sep-1993

SECTION III  
SEVERITY SUMMARY TABLE

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Severity Summary Table

PROJECT ID. NO: TRL098  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: MALE

D R A F T

PAGE 25

GROUP:	1	2	3	4	1 - R	2 - R	3 - R	4 - R
NUMBER OF ANIMALS:	10	10	10	5	10	10	10	10

	# Ex	# SEV	# SEV	# SEV	# SEV	# SEV	# SEV	# SEV	# SEV
BRAIN	10	0	0	0	5	0	0	0	0
PITUITARY GLAND	10	9	10	10	5	10	0	0	10
Pars distalis, hyperplasia	0	0	0	0	0	0	0	0	1 0.10
Pars distalis, vacuo, cytopl	9 0.90	9 1.11	10 1.50	10 1.50	5 1.40	10 1.30	0	0	9 1.00
Rathke's cleft, tubulr hyperpl	0	0	0	0	0	0	0	0	1 0.10
SPINAL CORD, THORACIC	10	0	0	0	5	0	0	0	0
THYMUS	10	0	0	0	5	0	0	0	0
Congestion	2 0.30	0	0	0	0	0	0	0	0
SALIVARY GLAND	10	0	0	0	5	0	0	0	0
PANCREAS	10	0	0	0	5	0	0	0	0
Inflammation, chronic	1 0.10	0	0	0	0	0	0	0	0
Lobule, degeneration	0	0	0	0	1 0.20	0	0	0	0
ADRENAL GLAND	10	0	0	0	5	0	0	0	0
Cortex, vacuolation, cytoplasm	6 0.70	0	0	0	2 0.40	0	0	0	0
TRACHEA	10	0	0	0	5	0	0	0	0
THYROID GLAND	10	10	10	10	5	10	0	0	10
PARATHYROID GLAND	9	0	0	0	4	0	0	0	0
ESOPHAGUS	10	0	0	0	5	0	0	0	0

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Severity Summary Table

DRAFT

PAGE 26

PROJECT ID. NO: TRL098  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: MALE

GROUP:		1	2	3	4	1 - R	2 - R	3 - R	4 - R
NUMBER OF ANIMALS:		10	10	10	5	10	10	10	10
HEART	# Ex	10	0	0	5	0	0	0	0
Cardiomyopathy		4 0.40	0	0	1 0.20	0	0	0	0
DUODENUM	# Ex	10	0	0	5	0	0	0	0
COLON	# Ex	10	0	0	5	0	0	0	0
STOMACH	# Ex	10	0	0	5	0	0	0	0
LIVER	# Ex	10	10	10	5	10	0	0	10
Hepatocyte, vacuo, cytoplasm		1 0.10	3 0.40	0	0	0	0	0	1 0.10
Inflammation, subacute		2 0.20	0	0	0	0	0	0	0
Lobular hyperplasia		0	0	0	0	1 0.20	0	0	0
Periportal, infiltr, cellular		0	0	0	0	1 0.10	0	0	0
Pigment, hemosiderin		0	0	0	1 0.20	0	0	0	0
SPLEEN	# Ex	10	10	10	5	10	0	0	10
Hyperplasia		0	0	4 0.60	5 2.20	0	0	0	0
Pigment, hemosiderin		0	0	0	0	0	0	0	1 0.10
JEJUNUM	# Ex	10	0	0	5	0	0	0	0
LUNG	# Ex	10	10	10	5	10	10	10	10
Alveolar epithelium, hyperpl		0	0	0	0	0	0	0	1 0.10
Alveolar hystiocytosis		1 0.10	0	0	0	0	0	0	3 0.30
Alveolar proteinosis		0	0	10 1.70	5 2.80	0	0	0	0
Hemorrhage		2 0.30	0	0	0	2 0.20	4 0.40	2 0.20	0
Inflammation, chronic		0	0	0	0	0	0	5 0.50	1 0.20
Inflammation, perivasc, acute		1 0.10	0	0	0	0	0	0	0
Inflammation, subacute		4 0.60	0	3 0.30	0	2 0.20	3 0.30	3 0.30	2 0.20
Pigment, hemosiderin		1 0.20	0	0	0	0	1 0.10	7 0.80	8 0.80

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Severity Summary Table

D R A F T

PAGE 27

PROJECT ID. NO: TRL098  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: MALE

GROUP:	1		2		3		4		1 - R		2 - R		3 - R		4 - R		
NUMBER OF ANIMALS:	10		10		10		5		10		10		10		10		
	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV	
KIDNEY	# Ex	10		10		10		5		10		0		0		10	
Infiltrate, cellular		0		0		0		0		0		0		0		1	0.10
Nephropathy		4	0.40	0		0		0		2	0.20	0		0		1	0.10
Nephrosis, hemoglobin		0		0		5	0.50	5	2.20	0		0		0		0	
Pigment, hemosiderin		0		0		1	0.10	5	2.20	0		0		0		2	0.20
Renal tubule, dilatation		1	0.10	0		0		0		0		0		0		0	
Renal tubule, epith, regenerat		0		0		1	0.10	0		1	0.10	0		0		0	
URINARY BLADDER	# Ex	10		0		0		5		0		0		0		0	
Epithelium, ulcer		1	0.10	0		0		0		0		0		0		0	
PROSTATE	# Ex	10		0		0		5		0		0		0		0	
Inflammation, subacute		1	0.10	0		0		0		0		0		0		0	
SKIN	# Ex	10		0		0		5		0		0		0		0	
MAMMARY GLAND	# Ex	9		0		0		5		0		0		0		0	
ILEUM	# Ex	10		0		0		5		0		0		0		0	
CECUM	# Ex	10		0		0		5		0		0		0		0	
LYMPH NODE, MESENTERIC	# Ex	10		0		0		5		0		0		0		0	
SKELETAL MUSCLE	# Ex	10		0		0		5		0		0		0		0	
SCIATIC NERVE	# Ex	10		0		0		5		0		0		0		0	
TESTES	# Ex	10		0		0		5		0		0		0		0	
Seminif tubules, giant cells		0		0		0		1	0.20	0		0		0		0	

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Severity Summary Table

PROJECT ID. NO: TRL098  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: MALE

D R A F T

PAGE 28

GROUP:	1	2	3	4	1 - R	2 - R	3 - R	4 - R
NUMBER OF ANIMALS:	10	10	10	5	10	10	10	10
EPIDIDYMIS	# Ex 10	# SEV 0	# SEV 0	# SEV 5	# SEV 0	# SEV 0	# SEV 0	# SEV 0
TONGUE	# Ex 10	# SEV 0	# SEV 0	# SEV 5	# SEV 0	# SEV 0	# SEV 0	# SEV 0
DIAPHRAGM	# Ex 10	# SEV 0	# SEV 0	# SEV 4	# SEV 0	# SEV 0	# SEV 0	# SEV 0
RIB	# Ex 10	# SEV 0	# SEV 0	# SEV 5	# SEV 0	# SEV 0	# SEV 0	# SEV 0
COSTOCHONDRAL JUNCTION	# Ex 10	# SEV 0	# SEV 0	# SEV 4	# SEV 0	# SEV 0	# SEV 0	# SEV 0
STERNUM	# Ex 10	# SEV 0	# SEV 0	# SEV 5	# SEV 0	# SEV 0	# SEV 0	# SEV 0
BONE MARROW	# Ex 10	# SEV 10	# SEV 10	# SEV 5	# SEV 10	# SEV 0	# SEV 0	# SEV 10
Pigment, hemosiderin	0	0	0	2 0.40	0	0	0	0
EYE	# Ex 10	# SEV 0	# SEV 0	# SEV 5	# SEV 0	# SEV 0	# SEV 0	# SEV 0
HARDERIAN GLAND	# Ex 10	# SEV 0	# SEV 0	# SEV 5	# SEV 0	# SEV 0	# SEV 0	# SEV 0

\* Severity calculated by the number of tissues examined.

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Severity Summary Table

PROJECT ID. NO: TRL098  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: FEMALE

DRAFT

PAGE 29

GROUP:	1		2		3		4		1 - R		2 - R		3 - R		4 - R	
NUMBER OF ANIMALS:	10		10		10		10		10		10		10		9	
	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV
BRAIN	# Ex	10	0	0	0	10	0	0	0	0	0	0	0	0	0	0
PITUITARY GLAND	# Ex	10	10	10	10	10	9	0	0	0	0	0	0	0	9	0
Pars distalis, vacuo, cytopl		0	0	0	0	0	2	0.22	0	0	0	0	0	0	0	0
SPINAL CORD, THORACIC	# Ex	10	0	0	0	10	0	0	0	0	0	0	0	0	0	0
THYMUS	# Ex	10	0	0	0	10	0	0	0	0	0	0	0	0	0	0
SALIVARY GLAND	# Ex	10	0	0	0	10	0	0	0	0	0	0	0	0	0	0
PANCREAS	# Ex	10	0	0	0	10	0	0	0	0	0	0	0	0	0	0
ADRENAL GLAND	# Ex	10	0	0	0	10	0	0	0	0	0	0	0	0	0	0
Cortex, cystic degeneration		1	0.10	0	0	0	0	0	0	0	0	0	0	0	0	0
Cortex, pigment, lipofuscin		0	0	0	0	2	0.20	0	0	0	0	0	0	0	0	0
TRACHEA	# Ex	10	0	0	0	10	0	0	0	0	0	0	0	0	0	0
THYROID GLAND	# Ex	10	10	10	10	10	10	0	0	0	0	0	0	0	9	0
PARATHYROID GLAND	# Ex	9	0	0	0	10	0	0	0	0	0	0	0	0	0	0
Fibrosis		1	0.22	0	0	0	0	0	0	0	0	0	0	0	0	0
ESOPHAGUS	# Ex	10	0	0	0	10	0	0	0	0	0	0	0	0	0	0
HEART	# Ex	10	0	0	0	10	0	0	0	0	0	0	0	0	0	0
Cardiomyopathy		0	0	0	0	2	0.20	0	0	0	0	0	0	0	0	0
Hemorrhage		1	0.10	0	0	0	0	0	0	0	0	0	0	0	0	0

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Severity Summary Table

PROJECT ID. NO: TRL098  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: FEMALE

D R A F T

PAGE 30

GROUP:	1	2	3	4	1 - R	2 - R	3 - R	4 - R
NUMBER OF ANIMALS:	10	10	10	10	10	10	10	9
	# SEV	# SEV	# SEV	# SEV	# SEV	# SEV	# SEV	# SEV
DUODENUM	# Ex 10	0	0	10	0	0	0	0
COLON	# Ex 10	0	0	10	0	0	0	0
STOMACH	# Ex 10	0	0	10	0	0	0	0
Non-glandular, inflammation	1 0.10	0	0	0	0	0	0	0
LIVER	# Ex 10	10	10	10	10	0	0	9
Basophilic focus	0	1 0.10	0	0	0	0	0	0
Bile duct, hyperplasia	0	0	0	0	0	0	0	4 0.67
Hepatocyte, vacuo, cytoplasm	0	0	0	0	1 0.10	0	0	0
Infiltrate, cellular	0	0	3 0.30	0	0	0	0	0
Inflammation, subacute	3 0.30	0	0	0	0	0	0	0
Periportal, infiltr, cellular	0	1 0.10	0	0	0	0	0	1 0.11
Pigment, hemosiderin	0	0	2 0.20	0	0	0	0	0
Portal, fibrosis	0	0	0	0	0	0	0	1 0.11
SPLEEN	# Ex 10	10	10	10	10	0	0	9
Hyperplasia	0	0	0	8 1.50	0	0	0	0
Pigment, hemosiderin	0	0	0	0	0	0	0	1 0.11
JEJUNUM	# Ex 10	0	0	10	0	0	0	0
LUNG	# Ex 10	10	10	10	10	10	10	9
Alveolar hystiocytosis	0	0	0	0	0	0	0	3 0.33
Alveolar proteinosis	0	0	10 1.60	10 2.20	0	0	0	0
Hemorrhage	1 0.10	0	0	0	0	1 0.10	0	0
Inflammation, acute	0	0	0	2 0.20	0	0	0	0
Inflammation, chronic	0	0	0	0	0	0	7 1.10	5 0.67
Inflammation, subacute	2 0.20	0	5 0.50	1 0.10	0	0	1 0.10	0
Pigment, hemosiderin	0	0	0	0	0	0	8 1.20	9 1.11

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Severity Summary Table

PROJECT ID. NO: TRL098  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: FEMALE

D R A F T

PAGE 31

GROUP:	1	2	3	4	1 - R	2 - R	3 - R	4 - R
NUMBER OF ANIMALS:	10	10	10	10	10	10	10	9
KIDNEY	# Ex 10	# SEV 10	# SEV 10	# SEV 10	# SEV 10	# SEV 0	# SEV 0	# SEV 9
Nephrocalcinosis	7 0.90	6 0.60	5 0.50	4 0.40	6 0.60	0	0	7 0.89
Nephropathy	0	0	0	0	0	0	0	1 0.11
Nephrosis, hemoglobin	0	0	4 0.40	10 1.50	0	0	0	0
Pigment, hemosiderin	0	0	2 0.20	10 2.20	0	0	0	1 0.11
Renal tubule, casts, proteinic	0	0	0	0	1 0.10	0	0	0
URINARY BLADDER	# Ex 10	0	0	10	0	0	0	0
SKIN	# Ex 10	0	0	10	0	0	0	0
MAMMARY GLAND	# Ex 9	0	0	10	0	0	0	0
ILEUM	# Ex 10	0	0	10	0	0	0	0
CECUM	# Ex 10	0	0	10	0	0	0	0
LYMPH NODE, MESENTERIC	# Ex 10	0	0	10	0	0	0	0
SKELETAL MUSCLE	# Ex 10	0	0	10	0	0	0	0
SCIATIC NERVE	# Ex 10	0	0	10	0	0	0	0
OVARY	# Ex 10	0	0	10	0	0	0	0
UTERUS	# Ex 10	0	0	10	0	0	0	0
Decidua	1 0.20	0	0	0	0	0	0	0
Dilatation	3 0.50	0	0	3 0.60	0	0	0	0
Hemorrhage	1 0.10	0	0	0	0	0	0	0
Inflammation, acute	1 0.10	0	0	0	0	0	0	0

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Severity Summary Table

DRAFT

PAGE 32

PROJECT ID. NO: TRL098  
 WEEKS: 14-27

FATES: Terminal Sacrifice  
 SEX: FEMALE

GROUP:	1	2	3	4	1 - R	2 - R	3 - R	4 - R
NUMBER OF ANIMALS:	10	10	10	10	10	10	10	9

	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV
TONGUE	# Ex	10	0	0	10	0	0	0	0	0	0	0	0	0
DIAPHRAGM	# Ex	10	0	0	10	0	0	0	0	0	0	0	0	0
RIB	# Ex	10	0	0	10	0	0	0	0	0	0	0	0	0
COSTOCHONDRAL JUNCTION	# Ex	10	0	0	10	0	0	0	0	0	0	0	0	0
STERNUM	# Ex	10	0	0	10	0	0	0	0	0	0	0	0	0
BONE MARROW	# Ex	10	10	10	10	10	0	0	0	0	0	0	9	0
Pigment, hemosiderin		0	0	0	5	0.50	0	0	0	0	0	0	0	0
EYE	# Ex	10	0	0	10	0	0	0	0	0	0	0	0	0
HARDERIAN GLAND	# Ex	10	0	0	10	0	0	0	0	0	0	0	0	0
Infiltrate, cellular		0	0	0	1	0.10	0	0	0	0	0	0	0	0
Inflammation, subacute		1	0.10	0	0	0	0	0	0	0	0	0	0	0

\* Severity calculated by the number of tissues examined.

09-Sep-1993

SECTION IV  
TABULATED ANIMAL DATA

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PROJECT ID: TRL098      GROUP: 1      SEX: MALE  
 WEEKS: 2-27      FATES: Terminal Sacrifice, Natural Death

ANIMAL ID:	0803	0804	0805	0808	0812	0813	0817	0818	0819	0820
BRAIN	N	N	N	N	N	N	N	N	N	N
PITUITARY GLAND		N								
Pars distalis, cyst	-	-	-	-	-	-	-	-	-	P
Pars distalis, vacuo, cytopl	1	-	1	1	1	1	1	1	1	1
SPINAL CORD, THORACIC	N	N	N	N	N	N	N	N	N	N
THYMUS			N	N	N	N	N	N	N	N
Congestion	2	1	-	-	-	-	-	-	-	-
SALIVARY GLAND	N	N	N	N	N	N	N	N	N	N
PANCREAS	N		N	N	N	N	N	N	N	N
Inflammation, chronic	-	1	-	-	-	-	-	-	-	-
ADRENAL GLAND	N				N		N			N
Cortex, vacuolation, cytoplasm	-	1	1	1	-	1	-	2	1	-
TRACHEA	N	N	N	N	N	N	N	N	N	N
THYROID GLAND	N	N	N	N	N	N	N	N	N	N
PARATHYROID GLAND	N	N	N	N	N	N	U	N	N	N

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

**Tabulated Animal Data**

PROJECT ID: TRL098  
 WEEKS: 2-27

GROUP: 1  
 FATES: Terminal Sacrifice, Natural Death

SEX: MALE

DRAFT

PAGE 35

ANIMAL ID:	0803	0804	0805	0808	0812	0813	0817	0818	0819	0820
ESOPHAGUS	N	N	N	N	N	N	N	N	N	N
HEART	N		N	N	N		N		N	
Cardiomyopathy	-	1	-	-	-	1	-	1	-	1
DUODENUM	N	N	N	N	N	N	N	N	N	N
COLON	N	N	N	N	N	N	N	N	N	N
STOMACH	N	N	N	N	N	N	N	N	N	N
LIVER	N	N	N	N	N	N	N			N
Hepatocyte, vacuo, cytoplasm	-	-	-	-	-	-	-	1	-	-
Inflammation, subacute	-	-	-	-	-	-	-	1	1	-
SPLEEN	N	N	N	N	N	N	N	N	N	N
JEJUNUM	N	N	N	N	N	N	N	N	N	N
LUNG						N	N	N		
Alveolar hystiocytosis	-	1	-	-	-	-	-	-	-	-
Hemorrhage	2	-	-	-	1	-	-	-	-	-
Inflammation, perivasc, acute	-	-	1	-	-	-	-	-	-	-
Inflammation, subacute	1	-	-	2	-	-	-	-	1	2
Pigment, hemosiderin	2	-	-	-	-	-	-	-	-	-

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

PROJECT ID: TRL098  
 WEEKS: 2-27

GROUP: 1  
 FATES: Terminal Sacrifice, Natural Death

SEX: MALE

DRAFT

PAGE 36

ANIMAL ID:	0803	0804	0805	0808	0812	0813	0817	0818	0819	0820
KIDNEY		N		N				N	N	N
Nephropathy	1	-	-	-	1	1	1	-	-	-
Renal tubule, dilatation	-	-	1	-	-	-	-	-	-	-
URINARY BLADDER		N	N		N	N			N	N
Calculus	P	-	-	P	-	-	P	-	-	-
Epithelium, ulcer	-	-	-	-	-	-	-	1	-	-
PROSTATE	N	N	N	N		N	N	N	N	N
Inflammation, subacute	-	-	-	-	1	-	-	-	-	-
SKIN	N	N	N	N	N	N	N	N	N	N
MAMMARY GLAND	U	N	N	N	N	N	N	N	N	N
ILEUM	N	N	N	N	N	N	N	N	N	N
CECUM	N	N	N	N	N	N	N	N	N	N
LYMPH NODE, MESENTERIC	N	N	N	N	N	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
SCIATIC NERVE	N	N	N	N	N	N	N	N	N	N

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 37

PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 1  
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

ANIMAL ID:	0803	0804	0805	0808	0812	0813	0817	0818	0819	0820
TESTES	N	N	N	N	N	N	N	N	N	N
EPIDIDYMIS	N	N	N	N	N	N	N	N	N	N
TONGUE	N	N	N	N	N	N	N	N	N	N
DIAPHRAGM	N	N	N	N	N	N	N	N	N	N
RIB	N	N	N	N	N	N	N	N	N	N
COSTOCHONDRAL JUNCTION	N	N	N	N	N	N	N	N	N	N
STERNUM	N	N	N	N	N	N	N	N	N	N
BONE MARROW	N	N	N	N	N	N	N	N	N	N
EYE	N	N	N	N	N	N	N	N	N	N
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

**Tabulated Animal Data**

PROJECT ID: TRL098      GROUP: 2      SEX: MALE  
 WEEKS: 2-27      FATES: Terminal Sacrifice, Natural Death

DRAFT

PAGE 38

ANIMAL ID:	0841	0842	0843	0845	0847	0849	0854	0855	0856	0857
PITUITARY GLAND						U				
Pars distalis, vacuo, cytopl	2	1	1	1	1	-	1	1	1	1
THYROID GLAND	N	N	N	N	N	N	N	N	N	N
LIVER	N	N		N	N			N	N	N
Hepatocyte, vacuo, cytoplasm	-	-	2	-	-	1	1	-	-	-
SPLEEN	N	N	N	N	N	N	N	N	N	N
LUNG	N	N	N	N	N	N	N	N	N	N
KIDNEY	N	N	N	N	N	N	N	N	N	N
BONE MARROW	N	N	N	N	N	N	N	N	N	N

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

**Tabulated Animal Data**

PROJECT ID: TRL098  
 WEEKS: 2-27

GROUP: 3

SEX: MALE

FATES: Terminal Sacrifice, Natural Death

DRAFT

PAGE 39

ANIMAL ID:	0881	0882	0883	0885	0886	0888	0891	0892	0894	0898
<b>PITUITARY GLAND</b>										
Pars distalis, vacuo, cytopl	1	1	1	2	2	2	2	1	1	2
<b>THYROID GLAND</b>	N	N	N	N	N	N	N	N	N	N
<b>LIVER</b>	N	N	N	N	N	N	N	N	N	N
<b>SPLEEN</b>			N	N	N			N	N	N
Hyperplasia	1	1	-	-	-	2	2	-	-	-
<b>LUNG</b>										
Alveolar proteinosis	2	2	2	2	1	2	1	1	2	2
Inflammation, subacute	-	-	1	1	-	1	-	-	-	-
<b>KIDNEY</b>				N	N			N	N	
Nephrosis, hemoglobin	1	1	1	-	-	1	-	-	-	1
Pigment, hemosiderin	-	-	-	-	-	-	-	-	-	1
Renal tubule, epith, regenerat	-	-	-	-	-	-	1	-	-	-
<b>BONE MARROW</b>	N	N	N	N	N	N	N	N	N	N

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

**Tabulated Animal Data**

PROJECT ID: TRL098  
 WEEKS: 2-27

GROUP: 4  
 FATES: Terminal Sacrifice, Natural Death

SEX: MALE

D R A F T

PAGE 40

ANIMAL ID:	0921	0924	0925	0926	0928	0931	0934	0936	0937	0938
<b>BRAIN</b>		N	N	N	N	N	N		N	N
Cerebrum, hemorrhage	1	-	-	-	-	-	-	1	-	-
Medulla, hemorrhage	1	-	-	-	-	-	-	-	-	-
<b>PITUITARY GLAND</b>				N				U	N	
Inflammation, acute	1	-	-	-	-	-	-	-	-	-
Pars distalis, vacuo, cytopl	-	2	1	-	2	1	1	-	-	1
<b>SPINAL CORD, THORACIC</b>	N	N	N	N	N	N	N	N	N	N
<b>THYMUS</b>		N	N	N	N	N	N	N	U	N
Depletion, lymphocyte	4	-	-	-	-	-	-	-	-	-
<b>SALIVARY GLAND</b>	N	N	N	N	N	N	U	N	N	N
<b>PANCREAS</b>	N	N	N	N	N		N	N	N	N
Lobule, degeneration	-	-	-	-	-	1	-	-	-	-
<b>ADRENAL GLAND</b>			N	N	N			N	N	N
Cortex, congestion	-	-	-	-	-	-	1	-	-	-
Cortex, vacuolation, cytoplasm	1	1	-	-	-	1	-	-	-	-
<b>TRACHEA</b>	N	N	N	N	N	N	N	A	N	N
<b>THYROID GLAND</b>	N	N	N	N	N	N	N	A	N	N

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

PROJECT ID: TRL098  
 WEEKS: 2-27

GROUP: 4

SEX: MALE

FATES: Terminal Sacrifice, Natural Death

DRAFT

PAGE 41

ANIMAL ID:	0921	0924	0925	0926	0928	0931	0934	0936	0937	0938
PARATHYROID GLAND	N	N	N	N	N	N	U	N	U	U
ESOPHAGUS	N	N	N	N	N	N	N	N	N	N
HEART			N		N	N	N	N		N
Cardiomyopathy	-	1	-	-	-	-	-	-	-	-
Epicardium, inflam, subacute	3	-	-	-	-	-	-	-	4	-
Inflammation, acute	-	-	-	1	-	-	-	-	-	-
DUODENUM	N	N	N	A	N	N	N	N	N	N
COLON	N	N	N	N	N	N	N	A	N	N
STOMACH	N	N	N	N	N	N	N	N	N	N
LIVER	N	N	N		N		N	N	N	N
Pigment, hemosiderin	-	-	-	1	-	1	-	-	-	-
SPLEEN	N			N			N	N	N	
Hyperplasia	-	2	3	-	2	2	-	-	-	2
JEJUNUM	N	N	N	N	N	N	N	N	N	N

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

**Tabulated Animal Data**

PROJECT ID: TRL098  
 WEEKS: 2-27

GROUP: 4

SEX: MALE

FATES: Terminal Sacrifice, Natural Death

DRAFT

PAGE 42

ANIMAL ID:	0921	0924	0925	0926	0928	0931	0934	0936	0937	0938
LUNG				N				N		
Alveolar proteinosis	-	3	2	-	3	3	3	-	-	3
Congestion	3	-	-	-	-	-	-	-	-	-
Hemorrhage	2	-	-	-	-	-	-	-	-	-
Inflammation, acute	2	-	-	-	-	-	-	-	-	-
Microthrombosis	3	-	-	-	-	-	-	-	-	-
Pleura, inflammation, subacute	3	-	-	-	-	-	-	-	4	-
KIDNEY	N			N				N	N	
Nephrosis, hemoglobin	-	3	2	-	1	3	2	-	-	2
Pigment, hemosiderin	-	2	3	-	2	2	1	-	-	2
URINARY BLADDER	N	N	N	N	N				N	N
Calculus	-	-	-	-	-	P	P	P	-	-
PROSTATE	N	N	N	N	N	N	N	N	N	N
SKIN	N	N	N	N	N	N	N	N	N	N
MAMMARY GLAND	N	N	N	U	N	N	N	N	N	N
ILEUM	N	N	N	N	N	N	N	A	N	N
CECUM	N	N	N	N	N	N	N	A	N	N
LYMPH NODE, MESENTERIC	N	N	N	N	N	N	U	U	N	N

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

D R A F T

PAGE 43

PROJECT ID: TRL098      GROUP: 4      SEX: MALE  
 WEEKS: 2-27      FATES: Terminal Sacrifice, Natural Death

ANIMAL ID:	0921	0924	0925	0926	0928	0931	0934	0936	0937	0938
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
SCIATIC NERVE	N	N	N	N	N	N	N	N	N	N
TESTES	N	N		N	N	N	N	N		N
Germinal epith, degeneration	-	-	-	-	-	-	-	-	3	-
Seminif tubules, giant cells	-	-	1	-	-	-	-	-	-	-
EPIDIDYMIS	N	N	N	N	N	N	N	N		N
Hypospermia	-	-	-	-	-	-	-	-	3	-
TONGUE	N	N	N	N	N	N	N	N	N	N
DIAPHRAGM		U	N		N	N	N			N
Inflammation, acute	-	-	-	1	-	-	-	2	-	-
Inflammation, subacute	3	-	-	-	-	-	-	-	3	-
RIB	N	N	N	N	N	N	N	N	N	N
COSTOCHONDRAL JUNCTION	N	N	U	N	N	N	N	N	N	N
STERNUM	N	N	N	N	N	N	N	N	N	N
BONE MARROW	N	N		N		N	N	N	N	N
Pigment, hemosiderin	-	-	1	-	1	-	-	-	-	-

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 44

PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 4

SEX: MALE

FATES: Terminal Sacrifice, Natural Death

ANIMAL ID:	0921	0924	0925	0926	0928	0931	0934	0936	0937	0933
EYE	N	N	N	A	N	N	N	A	N	N
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

**Tabulated Animal Data**

PROJECT ID: TRL098  
 WEEKS: 2-27

GROUP: 1 - R

SEX: MALE

FATES: Terminal Sacrifice, Natural Death

DRAFT

PAGE 45

ANIMAL ID:	0801	0802	0806	0807	0809	0810	0811	0814	0815	0816
<b>PITUITARY GLAND</b>										
Pars distalis, vacuo, cytopl	1	1	2	1	1	1	1	2	1	2
Pars intermedia, cyst	-	-	-	-	-	-	P	-	-	-
<b>THYROID GLAND</b>										
	N	N	N	N	N	N	N	N	N	N
<b>LIVER</b>										
Lobular hyperplasia	2	-	-	-	-	-	-	-	-	-
Periportal, infiltr, cellular	-	-	-	-	-	-	1	-	-	-
<b>SPLEEN</b>										
	N	N	N	N	N	N	N	N	N	N
<b>LUNG</b>										
Hemorrhage	-	-	-	1	-	-	-	-	-	1
Inflammation, subacute	-	-	-	-	-	-	-	1	-	1
<b>KIDNEY</b>										
Cortex, cyst	-	-	-	-	-	-	-	-	-	P
Nephropathy	-	-	1	-	-	-	-	-	1	-
Renal tubule, epith, regenerat	-	-	-	-	-	1	-	-	-	-
<b>BONE MARROW</b>										
	N	N	N	N	N	N	N	N	N	N

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 46

PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 2 - R

SEX: MALE

FATES: Terminal Sacrifice, Natural Death

ANIMAL ID:	0844	0846	0848	0850	0851	0852	0853	0858	0859	0860
LUNG		N		N	N					
Hemorrhage	-	-	-	-	-	1	1	-	1	1
Inflammation, subacute	1	-	1	-	-	-	-	1	-	-
Pigment, hemosiderin	-	-	-	-	-	-	-	-	-	1

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 47

PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 3 - R

SEX: MALE

FATES: Terminal Sacrifice, Natural Death

ANIMAL ID:	0884	0887	0889	0890	0893	0895	0896	0897	0899	0900
LUNG					N					
Hemorrhage	-	-	1	-	-	-	-	-	-	1
Inflammation, chronic	-	1	-	1	-	1	1	-	1	-
Inflammation, subacute	-	-	1	1	-	-	-	1	-	-
Pigment, hemosiderin	1	1	-	2	-	1	1	1	1	-

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 48

PROJECT ID: TRL098      GROUP: 4 - R      SEX: MALE  
 WEEKS: 2-27            FATES: Terminal Sacrifice, Natural Death

ANIMAL ID:	0922	0923	0927	0929	0930	0932	0933	0935	0939	0940
<b>PITUITARY GLAND</b>						N				
Pars distalis, hyperplasia	-	-	-	-	-	-	1	-	-	-
Pars distalis, vacuo, cytopl	1	1	1	1	1	-	1	2	1	1
Rathke's cleft, tubulr hyperpl	-	-	-	-	-	-	-	1	-	-
<b>THYROID GLAND</b>	N	N	N	N	N	N	N	N	N	N
<b>LIVER</b>	N		N	N	N	N	N	N	N	N
Hepatocyte, vacuo, cytoplasm	-	1	-	-	-	-	-	-	-	-
<b>SPLEEN</b>	N	N	N	N	N	N	N	N	N	
Pigment, hemosiderin	-	-	-	-	-	-	-	-	-	1
<b>LUNG</b>					N					N
Alveolar epithelium, hyperpl	-	-	-	-	-	1	-	-	-	-
Alveolar hystiocytosis	-	-	1	-	-	1	1	-	-	-
Inflammation, chronic	-	-	-	-	-	-	2	-	-	-
Inflammation, subacute	1	1	-	-	-	-	-	-	-	-
Pigment, hemosiderin	1	1	1	1	-	1	1	1	1	-
<b>KIDNEY</b>		N	N	N			N	N	N	
Infiltrate, cellular	-	-	-	-	1	-	-	-	-	-
Nephropathy	-	-	-	-	-	-	-	-	-	1
Pigment, hemosiderin	1	-	-	-	-	1	-	-	-	-
<b>BONE MARROW</b>	N	N	N	N	N	N	N	N	N	N

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

**Tabulated Animal Data**

PROJECT ID: TRL098  
 WEEKS: 2-27

GROUP: 1

SEX: FEMALE

FATES: Terminal Sacrifice, Natural Death

DRAFT

PAGE 49

ANIMAL ID:	0821	0822	0825	0826	0828	0829	0832	0833	0838	0839
BRAIN	N	N	N	N	N	N	N	N	N	N
PITUITARY GLAND	N	N	N	N	N		N	N	N	N
Pars distalis, cyst	-	-	-	-	-	P	-	-	-	-
SPINAL CORD, THORACIC	N	N	N	N	N	N	N	N	N	N
THYMUS	N	N	N	N	N	N	N	N	N	N
SALIVARY GLAND	N	N	N	N	N	N	N	N	N	N
PANCREAS	N	N	N	N	N	N	N	N	N	N
ADRENAL GLAND	N	N	N	N	N	N	N		N	N
Cortex, cystic degeneration	-	-	-	-	-	-	-	1	-	-
TRACHEA	N	N	N	N	N	N	N	N	N	N
THYROID GLAND	N	N	N	N	N	N	N	N	N	N
PARATHYROID GLAND	N	N	N	N	N	N	N	N		U
Fibrosis	-	-	-	-	-	-	-	-	2	-
ESOPHAGUS	N	N	N	N	N	N	N	N	N	N

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

**Tabulated Animal Data**

DRAFT

PAGE 50

PROJECT ID: TRL098  
 WEEKS: 2-27

GROUP: 1

SEX: FEMALE

FATES: Terminal Sacrifice, Natural Death

ANIMAL ID:	0821	0822	0825	0826	0828	0829	0832	0833	0838	0839
HEART	N	N	N	N		N	N	N	N	N
Hemorrhage	-	-	-	-	1	-	-	-	-	-
DUODENUM	N	N	N	N	N	N	N	N	N	N
COLON	N	N	N	N	N	N	N	N	N	N
STOMACH	N	N	N		N	N	N	N	N	N
Non-glandular, inflammation	-	-	-	1	-	-	-	-	-	-
LIVER	N	N	N	N	N		N			N
Inflammation, subacute	-	-	-	-	-	1	-	1	1	-
SPLEEN	N	N	N	N	N	N	N	N	N	N
JEJUNUM	N	N	N	N	N	N	N	N	N	N
LUNG			N		N	N	N	N	N	N
Hemorrhage	-	1	-	-	-	-	-	-	-	-
Inflammation, subacute	1	-	-	1	-	-	-	-	-	-
KIDNEY	N			N	N					
Nephrocalcinosis	-	1	1	-	-	2	1	1	1	2
URINARY BLADDER	N	N	N	N	N	N	N	N	N	N

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

**Tabulated Animal Data**

DRAFT

PAGE 51

PROJECT ID: TRL098  
 WEEKS: 2-27

GROUP: 1

SEX: FEMALE

FATES: Terminal Sacrifice, Natural Death

ANIMAL ID:	0821	0822	0825	0826	0828	0829	0832	0833	0838	0839
SKIN	N	N	N	N	N	N	N	N	N	N
MAMMARY GLAND	U	N	N	N	N	N	N	N	N	N
ILEUM	N	N	N	N	N	N	N	N	N	N
CECUM	N	N	N	N	N	N	N	N	N	N
LYMPH NODE, MESENTERIC	N	N	N	N	N	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
SCIATIC NERVE	N	N	N	N	N	N	N	N	N	N
OVARY	N	N	N	N	N	N	N	N	N	N
UTERUS		N	N			N				N
Decidua	2	-	-	-	-	-	-	-	-	-
Dilatation	-	-	-	2	-	-	-	2	1	-
Hemorrhage	-	-	-	-	1	-	-	-	-	-
Inflammation, acute	-	-	-	-	-	-	1	-	-	-
TONGUE	N	N	N	N	N	N	N	N	N	N

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

**Tabulated Animal Data**

PROJECT ID: TRL098  
 WEEKS: 2-27

GROUP: 1  
 FATES: Terminal Sacrifice, Natural Death

SEX: FEMALE

D R A F T

PAGE 52

ANIMAL ID:	0821	0822	0825	0826	0828	0829	0832	0833	0838	0839
DIAPHRAGM	N	N	N	N	N	N	N	N	N	N
RIB	N	N	N	N	N	N	N	N	N	N
COSTOCHONDRAL JUNCTION	N	N	N	N	N	N	N	N	N	N
STERNUM	N	N	N	N	N	N	N	N	N	N
BONE MARROW	N	N	N	N	N	N	N	N	N	N
EYE	N	N	N	N	N	N	N	N	N	N
HARDERIAN GLAND Inflammation, subacute	N	N	N	N		N	N	N	N	N
	-	-	-	-	1	-	-	-	-	-

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 53

PROJECT ID: TRL098      GROUP: 1      SEX: FEMALE  
WEEKS: 2-27      FATES: Terminal Sacrifice, Natural Death

ANIMAL ID:	0821	0822	0825	0826	0828	0829	0832	0833	0838	0839
OTHER TISSUES AND LESIONS:										
SKIN, HEAD - Inflamm, chronic	-	-	-	-	-	-	2	-	-	-

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

**Tabulated Animal Data**

DRAFT

PAGE 54

PROJECT ID: TRL098      GROUP: 2      SEX: FEMALE  
 WEEKS: 2-27      FATES: Terminal Sacrifice, Natural Death

ANIMAL ID:	0862	0863	0865	0866	0869	0870	0872	0875	0876	0878
PITUITARY GLAND	N	N	N	N	N	N	N	N	N	N
THYROID GLAND	N	N	N	N	N	N	N	N	N	N
LIVER		N	N	N	N	N	N	N	N	N
Basophilic focus	1	-	-	-	-	-	-	-	-	-
Periportal, infiltr, cellular	1	-	-	-	-	-	-	-	-	-
SPLEEN	N	N	N	N	N	N	N	N	N	N
LUNG	N	N	N	N	N	N	N	N	N	N
KIDNEY	N			N		N	N			
Nephrocalcinosis	-	1	1	-	1	-	-	1	1	1
BONE MARROW	N	N	N	N	N	N	N	N	N	N

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

**Tabulated Animal Data**

PROJECT ID: TRL098  
 WEEKS: 2-27

GROUP: 3

SEX: FEMALE

D R A F T

PAGE 55

FATES: Terminal Sacrifice, Natural Death

ANIMAL ID:	0903	0905	0906	0907	0910	0911	0913	0914	0917	0920
PITUITARY GLAND	N	N	N	N	N	N	N	N	N	N
THYROID GLAND	N	N	N	N	N	N	N	N	N	N
LIVER	N	N	N	N				N	N	N
Infiltrate, cellular	-	-	-	-	1	1	1	-	-	-
Pigment, hemosiderin	-	-	-	-	1	1	-	-	-	-
SPLEEN	N	N	N	N	N	N	N	N	N	N
LUNG										
Alveolar proteinosis	2	2	1	2	2	2	1	1	1	2
Inflammation, subacute	-	-	-	1	1	1	-	-	1	1
KIDNEY			N					N	N	
Nephrocalcinosis	1	1	-	1	1	-	1	-	-	-
Nephrosis, hemoglobin	-	-	-	1	1	-	1	-	-	1
Pigment, hemosiderin	-	-	-	1	-	1	-	-	-	-
BONE MARROW	N	N	N	N	N	N	N	N	N	N

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

D R A F T

PAGE 56

PROJECT ID: TRL098  
 WEEKS: 2-27

GROUP: 4

SEX: FEMALE

FATES: Terminal Sacrifice, Natural Death

ANIMAL ID:	0943	0945	0946	0947	0948	0950	0951	0952	0955	0958
BRAIN	N	N	N	N	N	N	N	N	N	N
PITUITARY GLAND Pars distalis, cyst	N	N	N	N	N	N	N	N	N	N
	-	-	-	-	-	-	-	P	-	-
SPINAL CORD, THORACIC	N	N	N	N	N	N	N	N	N	N
THYMUS	N	N	N	N	N	N	N	N	N	N
SALIVARY GLAND	N	N	N	N	N	N	N	N	N	N
PANCREAS	N	N	N	N	N	N	N	N	N	N
ADRENAL GLAND Cortex, pigment, lipofuscin	N	N	N	N	N	N	N	N	N	N
	-	-	-	-	-	-	-	-	1	1
TRACHEA	N	N	N	N	N	N	N	N	N	N
THYROID GLAND	N	N	N	N	N	N	N	N	N	N
PARATHYROID GLAND	N	N	N	N	N	N	N	N	N	N
ESOPHAGUS	N	N	N	N	N	N	N	N	N	N

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

D R A F T

PAGE 57

PROJECT ID: TRL098  
 WEEKS: 2-27

GROUP: 4

SEX: FEMALE

FATES: Terminal Sacrifice, Natural Death

ANIMAL ID:	0943	0945	0946	0947	0948	0950	0951	0952	0955	0958
HEART	N	N	N	N	N		N		N	N
Cardiomyopathy	-	-	-	-	-	1	-	1	-	-
DUODENUM	N	N	N	N	N	N	N	N	N	N
COLON	N	N	N	N	N	N	N	N	N	N
STOMACH	N	N	N	N	N	N	N	N	N	N
LIVER	N	N	N	N	N	N	N	N	N	N
SPLEEN				N				N		
Hyperplasia	2	2	2	-	2	2	2	-	2	1
JEJUNUM	N	N	N	N	N	N	N	N	N	N
LUNG										
Alveolar proteinosis	3	2	3	3	1	3	2	2	2	1
Inflammation, acute	-	-	-	1	-	-	-	-	1	-
Inflammation, subacute	-	-	-	-	-	1	-	-	-	-
KIDNEY										
Nephrocalcinosis	-	-	-	-	1	1	1	-	1	-
Nephrosis, hemoglobin	1	2	2	1	2	1	2	1	2	1
Pigment, hemosiderin	2	3	2	2	2	2	3	2	2	2

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 58

PROJECT ID: TRL098      GROUP: 4      SEX: FEMALE  
 WEEKS: 2-27      FATES: Terminal Sacrifice, Natural Death

ANIMAL ID:	0943	0945	0946	0947	0948	0950	0951	0952	0955	0958
URINARY BLADDER	N	N	N	N	N	N	N	N	N	N
SKIN	N	N	N	N	N	N	N	N	N	N
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N
ILEUM	N	N	N	N	N	N	N	N	N	N
CECUM	N	N	N	N	N	N	N	N	N	N
LYMPH NODE, MESENTERIC	N	N	N	N	N	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
SCIATIC NERVE	N	N	N	N	N	N	N	N	N	N
OVARY	N	N	N	N	N	N	N	N	N	N
UTERUS Dilatation	2	2	-	-	-	-	-	2	-	-
TONGUE	N	N	N	N	N	N	N	N	N	N

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 59

PROJECT ID: TRL098      GROUP: 4      SEX: FEMALE  
WEEKS: 2-27      FATES: Terminal Sacrifice, Natural Death

ANIMAL ID:	0943	0945	0946	0947	0948	0950	0951	0952	0955	0958
DIAPHRAGM	N	N	N	N	N	N	N	N	N	N
RIB	N	N	N	N	N	N	N	N	N	N
COSTOCHONDRAL JUNCTION	N	N	N	N	N	N	N	N	N	N
STERNUM	N	N	N	N	N	N	N	N	N	N
BONE MARROW	N			N	N				N	N
Pigment, hemosiderin	-	1	1	-	-	1	1	1	-	-
EYE	N	N	N	N	N	N	N	N	N	N
HARDERIAN GLAND		N	N	N	N	N	N	N	N	N
Infiltrate, cellular	1	-	-	-	-	-	-	-	-	-

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 60

PROJECT ID: TRL098      GROUP: 4      SEX: FEMALE  
WEEKS: 2-27      FATES: Terminal Sacrifice, Natural Death

ANIMAL ID:	0943	0945	0946	0947	0948	0950	0951	0952	0955	0958
OTHER TISSUES AND LESIONS:										
SKIN, EAR - Inflamm, granulomat	-	-	-	-	4	-	-	-	-	-
SKIN - Granuloma, foreign body	-	-	-	-	-	-	3	-	-	-

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

D R A F T

PAGE 61

PROJECT ID: TRL098      GROUP: 1 - R      SEX: FEMALE  
 WEEKS: 2-27            FATES: Terminal Sacrifice, Natural Death

ANIMAL ID:	0823	0824	0827	0830	0831	0834	0835	0836	0837	0840
PITUITARY GLAND		N	N	N	N	N	U			
Pars distalis, adenoma	P	-	-	-	-	-	-	-	P	-
Pars distalis, vacuo, cytopl	-	-	-	-	-	-	-	1	-	1
Pars intermedia, cyst	P	-	-	-	-	-	-	-	-	-
THYROID GLAND	N	N	N	N	N	N	N	N	N	N
LIVER	N	N	N	N	N	N	N	N		N
Hepatocyte, vacuo, cytoplasm	-	-	-	-	-	-	-	-	1	-
SPLEEN	N	N	N	N	N	N	N	N	N	N
LUNG	N	N	N	N	N	N	N	N	N	N
KIDNEY	N				N			N		
Nephrocalcinosis	-	1	1	1	-	1	-	-	1	1
Renal tubule, casts, proteinic	-	-	-	-	-	-	1	-	-	-
BONE MARROW	N	N	N	N	N	N	N	N	N	N

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 62

PROJECT ID: TRL098      GROUP: 2 - R      SEX: FEMALE  
WEEKS: 2-27      FATES: Terminal Sacrifice, Natural Death

ANIMAL ID:	0861	0864	0867	0868	0871	0873	0874	0877	0879	0880
LUNG	N	N	N	N	N	N		N	N	N
Hemorrhage	-	-	-	-	-	-	1	-	-	-

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 63

PROJECT ID: TRL098      GROUP: 3 - R      SEX: FEMALE  
WEEKS: 2-27      FATES: Terminal Sacrifice, Natural Death

ANIMAL ID:	0901	0902	0904	0908	0909	0912	0915	0916	0918	0919
LUNG			N							
Inflammation, chronic	1	2	-	1	-	-	2	2	2	1
Inflammation, subacute	-	-	-	1	-	-	-	-	-	-
Pigment, hemosiderin	1	2	-	-	1	2	2	1	1	2

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 64

PROJECT ID: TRL098      GROUP: 4 - R      SEX: FEMALE  
 WEEKS: 2-27            FATES: Terminal Sacrifice, Natural Death

ANIMAL ID:	0941	0942	0944	0949	0953	0954	0956	0957	0959	0960
BRAIN	*	*	*	*	*	*	N	*	*	*
PITUITARY GLAND	N	N	N	N	N	N	N	N	N	N
SPINAL CORD, THORACIC	*	*	*	*	*	*	N	*	*	*
THYMUS	*	*	*	*	*	*		*	*	*
Congestion	-	-	-	-	-	-	1	-	-	-
SALIVARY GLAND	*	*	*	*	*	*	N	*	*	*
PANCREAS	*	*	*	*	*	*	N	*	*	*
ADRENAL GLAND	*	*	*	*	*	*	N	*	*	*
TRACHEA	*	*	*	*	*	*	N	*	*	*
THYROID GLAND	N	N	N	N	N	N	N	N	N	N
PARATHYROID GLAND	*	*	*	*	*	*	U	*	*	*
ESOPHAGUS	*	*	*	*	*	*	N	*	*	*

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

**Tabulated Animal Data**

D R A F T

PAGE 65

PROJECT ID: TRL098      GROUP: 4 - R      SEX: FEMALE  
 WEEKS: 2-27      FATES: Terminal Sacrifice, Natural Death

ANIMAL ID:	0941	0942	0944	0949	0953	0954	0956	0957	0959	0960
HEART	*	*	*	*	*	*	N	*	*	*
DUODENUM	*	*	*	*	*	*	N	*	*	*
COLON	*	*	*	*	*	*	N	*	*	*
STOMACH	*	*	*	*	*	*	N	*	*	*
LIVER		N			N	N	N	N		N
Bile duct, hyperplasia	2	-	1	2	-	-	-	-	1	-
Periportal, infiltr, cellular	-	-	1	-	-	-	-	-	-	-
Portal, fibrosis	1	-	-	-	-	-	-	-	-	-
SPLEEN	N	N	N	N	N	N		N		N
Pigment, hemosiderin	-	-	-	-	-	-	-	-	1	-
Serosa, inflammation, chronic	-	-	-	-	-	-	2	-	-	-
JEJUNUM	*	*	*	*	*	*	N	*	*	*
LUNG										
Alveolar hystiocytosis	1	-	-	-	-	1	-	1	-	-
Alveolar proteinosis	-	-	-	-	-	-	3	-	-	-
Inflammation, chronic	1	-	-	-	1	1	-	2	-	1
Inflammation, subacute	-	-	-	-	-	-	1	-	-	-
Pigment, hemosiderin	2	1	1	1	1	1	-	1	1	1

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
 THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
 TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

D R A F T

PAGE 66

PROJECT ID: TRL098  
 WEEKS: 2-27

GROUP: 4 - R

SEX: FEMALE

FATES: Terminal Sacrifice, Natural Death

ANIMAL ID:	0941	0942	0944	0949	0953	0954	0956	0957	0959	0960
KIDNEY			N	N						
Cortex, cyst	-	-	-	-	-	-	-	P	-	-
Nephrocalcinosis	1	1	-	-	1	1	1	2	1	1
Nephropathy	-	-	-	-	-	-	-	-	1	-
Pigment, hemosiderin	-	-	-	-	-	1	2	-	-	-
URINARY BLADDER	*	*	*	*	*	*	N	*	*	*
SKIN	*	*	*	*	*	*	N	*	*	*
MAMMARY GLAND	*	*	*	*	*	*	U	*	*	*
ILEUM	*	*	*	*	*	*	N	*	*	*
CECUM	*	*	*	*	*	*	N	*	*	*
LYMPH NODE, MESENTERIC	*	*	*	*	*	*	N	*	*	*
SKELETAL MUSCLE	*	*	*	*	*	*	N	*	*	*
SCIATIC NERVE	*	*	*	*	*	*	U	*	*	*
OVARY	*	*	*	*	*	*	N	*	*	*

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 67

PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 4 - R

SEX: FEMALE

FATES: Terminal Sacrifice, Natural Death

ANIMAL ID:	0941	0942	0944	0949	0953	0954	0956	0957	0959	0960
UTERUS	*	*	*	*	*	*	N	*	*	*
TONGUE	*	*	*	*	*	*	N	*	*	*
DIAPHRAGM	*	*	*	*	*	*	N	*	*	*
RIB	*	*	*	*	*	*	N	*	*	*
COSTOCHONDRAL JUNCTION	*	*	*	*	*	*	N	*	*	*
STERNUM	*	*	*	*	*	*	N	*	*	*
BONE MARROW	N	N	N	N	N	N	N	N	N	N
EYE	*	*	*	*	*	*	N	*	*	*
HARDERIAN GLAND	*	*	*	*	*	*	N	*	*	*

09-Sep-1993

SECTION V

CORRELATION OF GROSS AND MICROSCOPIC (MICRO) FINDINGS

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 1  
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 69

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ANIMAL ID: 0803                      PATHOLOGY ID. NO: TI098-0803      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0804                      PATHOLOGY ID. NO: TI098-0804      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 0805                      PATHOLOGY ID. NO: TI098-0805      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 0808                      PATHOLOGY ID. NO: TI098-0808      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 1  
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 70

ANIMAL ID: 0812                      PATHOLOGY ID. NO: TI098-0812      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0813                      PATHOLOGY ID. NO: TI098-0813      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0817                      PATHOLOGY ID. NO: TI098-0817      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0818                      PATHOLOGY ID. NO: TI098-0818      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 1  
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 71

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ANIMAL ID: 0819                      PATHOLOGY ID. NO: TI098-0819      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0820                      PATHOLOGY ID. NO: TI098-0820      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 2  
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 72

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ANIMAL ID: 0841                      PATHOLOGY ID. NO: TI098-0841      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 0842                      PATHOLOGY ID. NO: TI098-0842      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0843                      PATHOLOGY ID. NO: TI098-0843      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>SPLEEN - SMALL, 28X8 MM

No corresponding lesion

---

ANIMAL ID: 0845                      PATHOLOGY ID. NO: TI098-0845      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 2  
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 73

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ANIMAL ID: 0847                      PATHOLOGY ID. NO: TI098-0847      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0849                      PATHOLOGY ID. NO: TI098-0849      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0854                      PATHOLOGY ID. NO: TI098-0854      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0855                      PATHOLOGY ID. NO: TI098-0855      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 2  
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 74

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ANIMAL ID: 0856  
ANIMAL FATE: Terminal Sacrifice

PATHOLOGY ID. NO: TI098-0856 PATHOLOGIST: MJT

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LIVER, PARENCHYMA - LESION, MOTTLED

No corresponding lesion

>ADRENAL GLAND, BILATERAL - SMALL,  
1.5X2.0 MM

Not required by protocol

---

ANIMAL ID: 0857  
ANIMAL FATE: Terminal Sacrifice

PATHOLOGY ID. NO: TI098-0857 PATHOLOGIST: MJT

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 3  
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 75

ANIMAL ID: 0881                      PATHOLOGY ID. NO: TI098-0881      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,  
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

ANIMAL ID: 0882                      PATHOLOGY ID. NO: TI098-0882      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,  
IRREGULAR, WHITE, FIRM

LUNG- Alveolar proteinosis

ANIMAL ID: 0883                      PATHOLOGY ID. NO: TI098-0883      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,  
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 3  
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 76

ANIMAL ID: 0885                      PATHOLOGY ID. NO: TI098-0885      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,  
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

ANIMAL ID: 0886                      PATHOLOGY ID. NO: TI098-0886      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,  
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

ANIMAL ID: 0888                      PATHOLOGY ID. NO: TI098-0888      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,  
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 3  
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 77

ANIMAL ID: 0891                      PATHOLOGY ID. NO: TI098-0891      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>SKIN, THORACIC, LEFT, SUBCUTANEOUS  
TISSUE - MASS, SINGLE, PLAQUE,  
16X12X9 MM

Not required by protocol

>TESTES, BILATERAL - SMALL

Not required by protocol

>EPIDIDYMIS, BILATERAL - SMALL

Not required by protocol

>LUNG, PLEURA - LESION, MULTIPLE,  
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

ANIMAL ID: 0892                      PATHOLOGY ID. NO: TI098-0892      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LYMPH NODE, MANDIBULAR - ENLARGED,  
2, TAN, 8X5X5 MM

Not required by protocol

>LUNG, PLEURA - LESION, MULTIPLE,  
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 3  
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 78

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ANIMAL ID: 0894                      PATHOLOGY ID. NO: TI098-0894      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,  
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

>ADRENAL GLAND, UNILATERAL - SMALL,  
1.5X2.0 MM

Not required by protocol

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ANIMAL ID: 0898                      PATHOLOGY ID. NO: TI098-0898      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,  
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 4  
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 79

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ANIMAL ID: 0921  
ANIMAL FATE: Natural Death

PATHOLOGY ID. NO: TI098-0921 PATHOLOGIST: MJT

WEEKS ON TEST: 2

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>HEART, EPICARDIUM - LESION,  
DIFFUSE, WHITE

HEART- Epicardium, inflam,  
subacute

>LUNG, LEFT - DIFFUSE, BLACK

LUNG- Pleura, inflammation,  
subacute

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ANIMAL ID: 0924  
ANIMAL FATE: Terminal Sacrifice

PATHOLOGY ID. NO: TI098-0924 PATHOLOGIST: MJT

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0925  
ANIMAL FATE: Terminal Sacrifice

PATHOLOGY ID. NO: TI098-0925 PATHOLOGIST: MJT

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>SPLEEN - ENLARGED

SPLEEN- Hyperplasia

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 4  
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 80

ANIMAL ID: 0926  
ANIMAL FATE: Natural Death

PATHOLOGY ID. NO: TI098-0926 PATHOLOGIST: MJT

WEEKS ON TEST: 2

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0928  
ANIMAL FATE: Terminal Sacrifice

PATHOLOGY ID. NO: TI098-0928 PATHOLOGIST: MJT

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,  
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

ANIMAL ID: 0931  
ANIMAL FATE: Terminal Sacrifice

PATHOLOGY ID. NO: TI098-0931 PATHOLOGIST: MJT

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,  
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 4  
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 81

ANIMAL ID: 0934                      PATHOLOGY ID. NO: TI098-0934      PATHOLOGIST: MJT  
ANIMAL FATE: Natural Death

WEEKS ON TEST: 8

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0936                      PATHOLOGY ID. NO: TI098-0936      PATHOLOGIST: MJT  
ANIMAL FATE: Natural Death

WEEKS ON TEST: 2

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0937                      PATHOLOGY ID. NO: TI098-0937      PATHOLOGIST: MJT  
ANIMAL FATE: Natural Death

WEEKS ON TEST: 2

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>HEART, EPICARDIUM - LESION,  
DIFFUSE, WHITE

HEART- Epicardium, inflam,  
subacute

>LUNG, PLEURA - LESION, DIFFUSE,  
WHITE

LUNG- Pleura, inflammation,  
subacute

>TESTES, CAPSULE - FOCUS, RED

No corresponding lesion

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Correlation of Gross & Micro Findings

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 4  
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 32

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ANIMAL ID: 0938

PATHOLOGY ID. NO: TI098-0938 PATHOLOGIST: MJT

ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,  
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 1 - R  
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 83

ANIMAL ID: 0801                      PATHOLOGY ID. NO: TI098-0801      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:                      RELATED HISTOPATHOLOGY:

>LIVER, MEDIAN LOBE - MASS, 25X18X15      LIVER- Lobular hyperplasia  
MM

ANIMAL ID: 0802                      PATHOLOGY ID. NO: TI098-0802      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:                      RELATED HISTOPATHOLOGY:

ANIMAL ID: 0806                      PATHOLOGY ID. NO: TI098-0806      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:                      RELATED HISTOPATHOLOGY:

ANIMAL ID: 0807                      PATHOLOGY ID. NO: TI098-0807      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:                      RELATED HISTOPATHOLOGY:

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 1 - R  
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 84

ANIMAL ID: 0809                      PATHOLOGY ID. NO: TI098-0809      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0810                      PATHOLOGY ID. NO: TI098-0810      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0811                      PATHOLOGY ID. NO: TI098-0811      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>KIDNEY, BILATERAL - LESION,  
MULTIPLE, IRREGULAR, MOTTLED

No corresponding lesion

ANIMAL ID: 0814                      PATHOLOGY ID. NO: TI098-0814      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, DIAPHRAGMATIC LOBE - LESION,  
DIFFUSE, PALE

No corresponding lesion

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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 1 - R  
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 85

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ANIMAL ID: 0815                      PATHOLOGY ID. NO: TI098-0815      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0816                      PATHOLOGY ID. NO: TI098-0816      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 2 - R                      SEX: MALE  
FATES: Terminal Sacrifice, Natural Death

PAGE 86

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ANIMAL ID: 0844                      PATHOLOGY ID. NO: TI098-0844      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0846                      PATHOLOGY ID. NO: TI098-0846      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0848                      PATHOLOGY ID. NO: TI098-0848      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0850                      PATHOLOGY ID. NO: TI098-0850      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 2 - R  
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 87

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ANIMAL ID: 0851                      PATHOLOGY ID. NO: TI098-0851      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 0852                      PATHOLOGY ID. NO: TI098-0852      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0853                      PATHOLOGY ID. NO: TI098-0853      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0858                      PATHOLOGY ID. NO: TI098-0858      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 2 - R                      SEX: MALE  
FATES: Terminal Sacrifice, Natural Death

PAGE 88

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ANIMAL ID: 0859                      PATHOLOGY ID. NO: TI098-0859      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0860                      PATHOLOGY ID. NO: TI098-0860      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>KIDNEY, BILATERAL - LESION, MOTTLED      Not required by protocol

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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 3 - R  
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 89

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ANIMAL ID: 0884                      PATHOLOGY ID. NO: TI098-0884      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0887                      PATHOLOGY ID. NO: TI098-0887      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0889                      PATHOLOGY ID. NO: TI098-0889      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0890                      PATHOLOGY ID. NO: TI098-0890      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 3 - R  
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 90

ANIMAL ID: 0893                      PATHOLOGY ID. NO: TI098-0893      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0895                      PATHOLOGY ID. NO: TI098-0895      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,  
IRREGULAR, WHITE

LUNG- Inflammation, chronic

ANIMAL ID: 0896                      PATHOLOGY ID. NO: TI098-0896      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0897                      PATHOLOGY ID. NO: TI098-0897      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>KIDNEY, BILATERAL - LESION,  
MULTIPLE, IRREGULAR, MOTTLED

Not required by protocol

09-Sep-1993

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WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 3 - R                      SEX: MALE  
FATES: Terminal Sacrifice, Natural Death

PAGE 91

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ANIMAL ID: 0899                      PATHOLOGY ID. NO: TI098-0899      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>EYE, RIGHT - LESION, OPAQUE

Not required by protocol

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ANIMAL ID: 0900                      PATHOLOGY ID. NO: TI098-0900      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 4 - R  
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 92

ANIMAL ID: 0922                      PATHOLOGY ID. NO: TI098-0922      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0923                      PATHOLOGY ID. NO: TI098-0923      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0927                      PATHOLOGY ID. NO: TI098-0927      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0929                      PATHOLOGY ID. NO: TI098-0929      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 4 - R                      SEX: MALE  
FATES: Terminal Sacrifice, Natural Death

PAGE 93

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ANIMAL ID: 0930                      PATHOLOGY ID. NO: TI098-0930      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0932                      PATHOLOGY ID. NO: TI098-0932      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0933                      PATHOLOGY ID. NO: TI098-0933      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0935                      PATHOLOGY ID. NO: TI098-0935      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 4 - R  
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 94

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ANIMAL ID: 0939                      PATHOLOGY ID. NO: TI098-0939    PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0940                      PATHOLOGY ID. NO: TI098-0940    PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>MESENTERY, FAT - LESION, SINGLE,  
OVAL, RED, 8X6X2 MM

Not required by protocol

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09-Sep-1993

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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 1  
SEX: FEMALE  
FATES: Terminal Sacrifice, Natural Death

PAGE 95

ANIMAL ID: 0821                      PATHOLOGY ID. NO: TI098-0821      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>UTERUS, BILATERAL - DIVERTICULUM,  
MULTIPLE, OVAL

UTERUS- Deciduoma

ANIMAL ID: 0822                      PATHOLOGY ID. NO: TI098-0822      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0825                      PATHOLOGY ID. NO: TI098-0825      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0826                      PATHOLOGY ID. NO: TI098-0826      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098                      GROUP: 1                      SEX: FEMALE                      PAGE 96  
WEEKS: 2-27                      FATES: Terminal Sacrifice, Natural Death

ANIMAL ID: 0828                      PATHOLOGY ID. NO: TI098-0828                      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:                      RELATED HISTOPATHOLOGY:

ANIMAL ID: 0829                      PATHOLOGY ID. NO: TI098-0829                      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:                      RELATED HISTOPATHOLOGY:

ANIMAL ID: 0832                      PATHOLOGY ID. NO: TI098-0832                      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:                      RELATED HISTOPATHOLOGY:

>SKIN, HEAD - SCAR, 20X15 MM                      SKIN, HEAD - Inflammation, chronic

ANIMAL ID: 0833                      PATHOLOGY ID. NO: TI098-0833                      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:                      RELATED HISTOPATHOLOGY:

>UTERUS, BILATERAL - DILATATION                      UTERUS- Dilatation

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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 1  
FATES: Terminal Sacrifice, Natural Death

SEX: FEMALE

PAGE 97

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ANIMAL ID: 0838

PATHOLOGY ID. NO: TI098-0838 PATHOLOGIST: MJT

ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0839

PATHOLOGY ID. NO: TI098-0839 PATHOLOGIST: MJT

ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 2  
FATES: Terminal Sacrifice, Natural Death

SEX: FEMALE

PAGE 98

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ANIMAL ID: 0862                      PATHOLOGY ID. NO: TI098-0862      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0863                      PATHOLOGY ID. NO: TI098-0863      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0865                      PATHOLOGY ID. NO: TI098-0865      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0866                      PATHOLOGY ID. NO: TI098-0866      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098                      GROUP: 2                      SEX: FEMALE                      PAGE 99  
WEEKS: 2-27                      FATES: Terminal Sacrifice, Natural Death

ANIMAL ID: 0869                      PATHOLOGY ID. NO: TI098-0869                      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice                      WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:                      RELATED HISTOPATHOLOGY:

ANIMAL ID: 0870                      PATHOLOGY ID. NO: TI098-0870                      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice                      WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:                      RELATED HISTOPATHOLOGY:

ANIMAL ID: 0872                      PATHOLOGY ID. NO: TI098-0872                      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice                      WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:                      RELATED HISTOPATHOLOGY:

ANIMAL ID: 0875                      PATHOLOGY ID. NO: TI098-0875                      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice                      WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:                      RELATED HISTOPATHOLOGY:

>UTERUS, BILATERAL - DILATATION                      Not required by protocol

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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098                      GROUP: 2                      SEX: FEMALE                      PAGE 100  
WEEKS: 2-27                      FATES: Terminal Sacrifice, Natural Death

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ANIMAL ID: 0876                      PATHOLOGY ID. NO: TI098-0876                      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice                      WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:                      RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0878                      PATHOLOGY ID. NO: TI098-0878                      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice                      WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:                      RELATED HISTOPATHOLOGY:

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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 3  
FATES: Terminal Sacrifice, Natural Death

SEX: FEMALE

PAGE 101

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ANIMAL ID: 0903                      PATHOLOGY ID. NO: TI098-0903      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0905                      PATHOLOGY ID. NO: TI098-0905      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,  
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

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ANIMAL ID: 0906                      PATHOLOGY ID. NO: TI098-0906      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,  
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 3  
FATES: Terminal Sacrifice, Natural Death

SEX: FEMALE

PAGE 102

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ANIMAL ID: 0907                      PATHOLOGY ID. NO: TI098-0907      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,  
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

---

ANIMAL ID: 0910                      PATHOLOGY ID. NO: TI098-0910      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,  
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

---

ANIMAL ID: 0911                      PATHOLOGY ID. NO: TI098-0911      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,  
IRREGULAR, WHITE, FIRM

LUNG- Alveolar proteinosis

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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098                      GROUP: 3                      SEX: FEMALE                      PAGE 103  
WEEKS: 2-27                      FATES: Terminal Sacrifice, Natural Death

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ANIMAL ID: 0913                      PATHOLOGY ID. NO: TI098-0913                      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice                      WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:                      RELATED HISTOPATHOLOGY:  
>LUNG, PLEURA - LESION, MULTIPLE,                      LUNG- Alveolar proteinosis  
IRREGULAR, WHITE

---

ANIMAL ID: 0914                      PATHOLOGY ID. NO: TI098-0914                      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice                      WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:                      RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0917                      PATHOLOGY ID. NO: TI098-0917                      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice                      WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:                      RELATED HISTOPATHOLOGY:  
>LUNG, PLEURA - LESION, MULTIPLE,                      LUNG- Alveolar proteinosis  
IRREGULAR, WHITE

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WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098                      GROUP: 4                      SEX: FEMALE                      PAGE 107  
WEEKS: 2-27                      FATES: Terminal Sacrifice, Natural Death

ANIMAL ID: 0951                      PATHOLOGY ID. NO: TI098-0951                      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice                      WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:                      RELATED HISTOPATHOLOGY:  
>SKIN, SUBCUTANEOUS TISSUE - MASS,                      SKIN - Granuloma, foreign body  
SINGLE, PLAQUE, TAN, 3X4 MM  
>LUNG, PLEURA - LESION, MULTIPLE,                      LUNG- Alveolar proteinosis  
IRREGULAR, WHITE, FIRM

ANIMAL ID: 0952                      PATHOLOGY ID. NO: TI098-0952                      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice                      WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:                      RELATED HISTOPATHOLOGY:  
>LUNG, PLEURA - LESION, MULTIPLE,                      LUNG- Alveolar proteinosis  
IRREGULAR, WHITE, FIRM

ANIMAL ID: 0955                      PATHOLOGY ID. NO: TI098-0955                      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice                      WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:                      RELATED HISTOPATHOLOGY:

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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 4  
FATES: Terminal Sacrifice, Natural Death

SEX: FEMALE

PAGE 108

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ANIMAL ID: 0958

PATHOLOGY ID. NO: TI098-0958 PATHOLOGIST: MJT

ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,  
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

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10-Sep-1993



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WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 1 - R  
FATES: Terminal Sacrifice, Natural Death

SEX: FEMALE

PAGE 110

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ANIMAL ID: 0831                      PATHOLOGY ID. NO: TI098-0831      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0834                      PATHOLOGY ID. NO: TI098-0834      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0835                      PATHOLOGY ID. NO: TI098-0835      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 0836                      PATHOLOGY ID. NO: TI098-0836      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 1 - R  
FATES: Terminal Sacrifice, Natural Death

SEX: FEMALE

PAGE 111

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ANIMAL ID: 0837  
ANIMAL FATE: Terminal Sacrifice

PATHOLOGY ID. NO: TI098-0837

PATHOLOGIST: MJT

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>PITUITARY GLAND - ENLARGED, 5X4 MM

PITUITARY GLAND- Pars distalis,  
adenoma

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ANIMAL ID: 0840  
ANIMAL FATE: Terminal Sacrifice

PATHOLOGY ID. NO: TI098-0840

PATHOLOGIST: MJT

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 2 - R  
FATES: Terminal Sacrifice, Natural Death

SEX: FEMALE

PAGE 112

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ANIMAL ID: 0861                      PATHOLOGY ID. NO: TI098-0861      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0864                      PATHOLOGY ID. NO: TI098-0864      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0867                      PATHOLOGY ID. NO: TI098-0867      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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ANIMAL ID: 0868                      PATHOLOGY ID. NO: TI098-0868      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>EYE, RIGHT - LESION, OPAQUE

Not required by protocol

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09-Sep-1993

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098                      GROUP: 2 - R                      SEX: FEMALE                      PAGE 113  
WEEKS: 2-27                      FATES: Terminal Sacrifice, Natural Death

ANIMAL ID: 0871                      PATHOLOGY ID. NO: TI098-0871                      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice  
WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:                      RELATED HISTOPATHOLOGY:  
>EAR, BILATERAL - LESION                      Not required by protocol

ANIMAL ID: 0873                      PATHOLOGY ID. NO: TI098-0873                      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice  
WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:                      RELATED HISTOPATHOLOGY:

ANIMAL ID: 0874                      PATHOLOGY ID. NO: TI098-0874                      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice  
WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:                      RELATED HISTOPATHOLOGY:

ANIMAL ID: 0877                      PATHOLOGY ID. NO: TI098-0877                      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice  
WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:                      RELATED HISTOPATHOLOGY:

09-Sep-1993

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 2 - R                      SEX: FEMALE  
FATES: Terminal Sacrifice, Natural Death

PAGE 114

---

ANIMAL ID: 0879                      PATHOLOGY ID. NO: TI098-0879      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 0880                      PATHOLOGY ID. NO: TI098-0880      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LIVER, CAPSULE - MASS, SINGLE,  
OVAL, WHITE, 1X2 MM

Not required by protocol

---

09-Sep-1993

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

---

Correlation of Gross & Micro Findings

DRAFT

---

PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 3 - R                      SEX: FEMALE  
FATES: Terminal Sacrifice, Natural Death

PAGE 115

---

ANIMAL ID: 0901                      PATHOLOGY ID. NO: TI098-0901      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,  
IRREGULAR, WHITE

LUNG- Inflammation, chronic

---

ANIMAL ID: 0902                      PATHOLOGY ID. NO: TI098-0902      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,  
IRREGULAR, WHITE

LUNG- Inflammation, chronic

---

ANIMAL ID: 0904                      PATHOLOGY ID. NO: TI098-0904      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 3 - R  
FATES: Terminal Sacrifice, Natural Death

SEX: FEMALE

PAGE 116

---

ANIMAL ID: 0908                      PATHOLOGY ID. NO: TI098-0908      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>UTERUS, BILATERAL - DILATATION

Not required by protocol

---

ANIMAL ID: 0909                      PATHOLOGY ID. NO: TI098-0909      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 0912                      PATHOLOGY ID. NO: TI098-0912      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>PITUITARY GLAND - ENLARGED

Not required by protocol

---

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 3 - R                      SEX: FEMALE  
FATES: Terminal Sacrifice, Natural Death

PAGE 117

---

ANIMAL ID: 0915                      PATHOLOGY ID. NO: TI098-0915      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,  
IRREGULAR, WHITE

LUNG- Inflammation, chronic

---

ANIMAL ID: 0916                      PATHOLOGY ID. NO: TI098-0916      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,  
IRREGULAR, WHITE

LUNG- Inflammation, chronic

---

ANIMAL ID: 0918                      PATHOLOGY ID. NO: TI098-0918      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>EYE, LEFT - LESION, 1, OPAQUE

Not required by protocol

>LUNG, PLEURA - LESION, MULTIPLE,  
IRREGULAR, WHITE

LUNG- Inflammation, chronic

---

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

---

Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 3 - R                      SEX: FEMALE  
FATES: Terminal Sacrifice, Natural Death

PAGE 118

---

ANIMAL ID: 0919                      PATHOLOGY ID. NO: TI098-0919      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,  
IRREGULAR, WHITE

LUNG- Inflammation, chronic

---

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

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Correlation of Gross & Micro Findings

DRAFT

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PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 4 - R  
FATES: Terminal Sacrifice, Natural Death

SEX: FEMALE

PAGE 119

---

ANIMAL ID: 0941                      PATHOLOGY ID. NO: TI098-0941      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 0942                      PATHOLOGY ID. NO: TI098-0942      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 0944                      PATHOLOGY ID. NO: TI098-0944      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

---

ANIMAL ID: 0949                      PATHOLOGY ID. NO: TI098-0949      PATHOLOGIST: MJT  
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 4 - R  
FATES: Terminal Sacrifice, Natural Death

SEX: FEMALE

PAGE 120

ANIMAL ID: 0953  
ANIMAL FATE: Terminal Sacrifice

PATHOLOGY ID. NO: TI098-0953

PATHOLOGIST: MJT  
WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0954  
ANIMAL FATE: Terminal Sacrifice

PATHOLOGY ID. NO: TI098-0954

PATHOLOGIST: MJT  
WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,  
IRREGULAR, WHITE

LUNG- Inflammation, chronic

ANIMAL ID: 0956  
ANIMAL FATE: Natural Death

PATHOLOGY ID. NO: TI098-0956

PATHOLOGIST: MJT  
WEEKS ON TEST: 16

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, WHITE

LUNG- Alveolar proteinosis

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.  
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605  
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS  
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098  
WEEKS: 2-27

GROUP: 4 - R  
FATES: Terminal Sacrifice, Natural Death

SEX: FEMALE

PAGE 121

ANIMAL ID: 0957  
ANIMAL FATE: Terminal Sacrifice

PATHOLOGY ID. NO: TI098-0957

PATHOLOGIST: MJT  
WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,  
IRREGULAR, WHITE

LUNG- Inflammation, chronic

ANIMAL ID: 0959  
ANIMAL FATE: Terminal Sacrifice

PATHOLOGY ID. NO: TI098-0959

PATHOLOGIST: MJT  
WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0960  
ANIMAL FATE: Terminal Sacrifice

PATHOLOGY ID. NO: TI098-0960

PATHOLOGIST: MJT  
WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>SPLEEN, CAPSULE - CYST, SINGLE,  
LOBULATED, CLEAR, WATERY

No corresponding lesion

09-Sep-1993

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
** 04/15/93	Microtomy	04/15/93
* 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
** 09/10/93	Individual Animal Data	09/10/93
** 09/10/93	Data Entry	09/10/93
** 09/10/93	Computer-Generated Tables	09/10/93
** 09/10/93	Draft Pathology Report	09/10/93
** 09/28/93	Second Draft Pathology Report	09/28/93

\*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

09/28/93

Date

Thirteen Week Oral Toxicity Study of WR238605 with a Thirteen Week Recovery Period in Rats, TRL Study Number 098.



# Pathology Associates, Inc.

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BONE MARROW EVALUATION REPORT  
FOR

DRAFT

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

STUDY NUMBER 098

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

DRAFT

I. Bone Marrow Evaluation Narrative

## BONE MARROW EVALUATION REPORT

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

#### 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 rats given WR 238605 orally by gavage once daily for at least thirteen weeks.

#### EXPERIMENTAL DESIGN AND METHODS

Eighty male and eighty female rats 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	10 + 10*	10 + 10*
2	0.5	10 + 10*	10 + 10*
3	6.0	10 + 10*	10 + 10*
4	18.0	10 + 10*	10 + 10*

\*Recovery Animals.

Surviving animals designated for the Day 91 and 92 necropsies were necropsied in random order on Days 91 and 92. The remainder of the animals were held for a thirteen week recovery period at which time they were necropsied.

Bone marrow smears were prepared (and fixed in methanol) from the femur of each animal at all necropsies. The bone marrow smears from animals in the high dose (Group 4) and control (Group 1) groups were stained with a Modified 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. Five high dose male animals (#0921, #0926, #0934, #0936 and #0937) died prior to the Day 91/92 necropsies and bone marrow smears were not prepared for these animals.

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

## 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 sex and dose group 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 from male and female high dose and control animals on Days 91 and 92 in this study were within normal limits.

## CONCLUSION

Under the conditions of this study, WR 238605 did not result in a treatment-related effect in the M:E Ratio of the femoral bone marrow of male and female treated rats at Days 91 and 92.

---

Lynda L. Pippin, DVM  
June 14, 1993

DRAFT

II. M:E Ratio Group Summary Tables

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

SUMMARY REPORT  
TEST: M:E RATIO

STUDY: 098  
STUDY NO: 098BM

SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

PERIOD(s): Week 14

Group: 1F : 0 mg base/kg/day  
MEAN 1.59  
SD 0.062  
N 10

DRAFT

Group: 2F : 0.5 mg base/kg/day  
MEAN NA  
SD NA  
N 0

Group: 3F : 6.0 mg base/kg/day  
MEAN NA  
SD NA  
N 0

Group: 4F : 18.0 mg base/kg/day  
MEAN 1.59  
SD 0.074  
N 10

NA-Not Applicable

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

SUMMARY REPORT  
TEST: M:E RATIO

STUDY: 098  
STUDY NO: 098BM

SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

PERIOD(s): Week 14

Group: 1M : 0 mg base/kg/day  
MEAN 1.55  
SD 0.066  
N 10

Group: 2M : 0.5 mg base/kg/day  
MEAN NA  
SD NA  
N 0

Group: 3M : 6.0 mg base/kg/day  
MEAN NA  
SD NA  
N 0

Group: 4M : 18.0 mg base/kg/day  
MEAN 1.55  
SD 0.066  
N 5

DRAFT

NA-Not Applicable

DRAFT

III. Individual Animal M:E Ratio Data

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

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: M:E RATIO

STUDY ID: 098  
STUDY NO: 0988M  
ABBR: M:E RATIO

SEX: MALE

UNITS: -

ANIMAL ID Week 14

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

801	--
802	--
803	1.59
804	1.48
805	1.66
806	--
807	--
808	1.50
809	--
810	--
811	--
812	1.55
813	1.46
814	--
815	--
816	--
817	1.60
818	1.51
819	1.63
820	1.54

MEAN	1.55
SD	0.066
N	10

DRAFT

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

841	--
842	--
843	--
844	--
845	--
846	--
847	--
848	--
849	--
850	--
851	--
852	--
853	--
854	--
855	--
856	--
857	--
858	--
859	--
860	--

MEAN	NA
SD	NA
N	0

(--)-Data Unavailable

NA-Not Applicable

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

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: M:E RATIO

STUDY ID: 098  
STUDY NO: 098BM  
ABBR: M:E RATIO

SEX: MALE

UNITS: -

ANIMAL ID Week 14

GROUP: 3M:6.0 mg base/kg/day

881	--
882	--
883	--
884	--
885	--
886	--
887	--
888	--
889	--
890	--
891	--
892	--
893	--
894	--
895	--
896	--
897	--
898	--
899	--
900	--

MEAN	NA
SD	NA
N	0

D R A F T

GROUP: 4M:18.0 mg base/kg/day

921	--
922	--
923	--
924	1.65
925	1.49
926	--
927	--
928	1.53
929	--
930	--
931	1.50
932	--
933	--
934	--
935	--
936	--
937	--
938	1.58
939	--
940	--

MEAN	1.55
SD	0.066
N	5

(--)-Data Unavailable

NA-Not Applicable

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

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: M:E RATIO

STUDY ID: 098  
STUDY NO: 0988M  
ASBR: M:E RATIO

SEX: FEMALE

UNITS: -

ANIMAL ID Week 14

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

821	1.63
822	1.53
823	--
824	--
825	1.58
826	1.67
827	--
828	1.55
829	1.49
830	--
831	--
832	1.65
833	1.54
834	--
835	--
836	--
837	--
838	1.56
839	1.66
840	--
MEAN	1.59
SD	0.062
N	10

DRAFT

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

861	--
862	--
863	--
864	--
865	--
866	--
867	--
868	--
869	--
870	--
871	--
872	--
873	--
874	--
875	--
876	--
877	--
878	--
879	--
880	--
MEAN	NA
SD	NA
N	0

(--)-Data Unavailable

NA-Not Applicable

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

INDIVIDUAL ANIMAL REPORT BY GROUP  
TEST: M:E RATIO

STUDY ID: 098  
STUDY NO: 0988M  
ASBR: M:E RATIO

SEX: FEMALE  
UNITS: -

ANIMAL ID Week 14

GROUP: 3F:6.0 mg base/kg/day

901	--
902	--
903	--
904	--
905	--
906	--
907	--
908	--
909	--
910	--
911	--
912	--
913	--
914	--
915	--
916	--
917	--
918	--
919	--
920	--

MEAN	NA
SD	NA
N	0

DRAFT

GROUP: 4F:18.0 mg base/kg/day

941	--
942	--
943	1.63
944	--
945	1.51
946	1.66
947	1.56
948	1.46
949	--
950	1.67
951	1.56
952	1.62
953	--
954	--
955	1.53
956	--
957	--
958	1.67
959	--
960	--

MEAN	1.59
SD	0.074
N	10

(--)-Data Unavailable

NA-Not Applicable

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

SUMMARY REPORT  
 TEST: M:E RATIO

STUDY: 098  
 STUDY NO: 098BM

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 -99%- HI				
1M	10	15.52	1.55	0.066				TREATMENTS	3	0.0000	0.0000
2M	NA	0.00	0.00	NA				ERROR	13	0.0572	0.0044
3M	NA	0.00	0.00	NA							
4M	5	7.75	1.55	0.066				TOTAL	16	0.0572	

F Ratio = 0.00 'F' table values F.01 = 9.07 F.05 = 4.67  
 Coeff. Var. % = 4.274 Dunnett's 'T' table values P.01 = 3.01 P.05 = 2.16

DRAFT

NA-Not Applicable

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

SUMMARY REPORT  
 TEST: M:E RATIO

STUDY: 098  
 STUDY NO: 098BM

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 -99%- HI				
1F	10	15.86	1.59	0.062				TREATMENTS	3	0.0000	0.0000
2F	NA	0.00	0.00	NA				ERROR	18	0.0839	0.0047
3F	NA	0.00	0.00	NA							
4F	10	15.87	1.59	0.074				TOTAL	21	0.0839	

F Ratio = 0.00 'F' table values F.01 = 8.28 F.05 = 4.41  
 Coeff. Var. % = 4.302 Dunnett's 'T' table values P.01 = 2.88 P.05 = 2.10

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NA-Not Applicable

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IV. Individual Animal Data Sheets

INDIVIDUAL BONE MARROW M:E RATIO DATA

Group 1

Vehicle Control: 0 mg base/kg/day

ANIMAL NO.	0821	0822	0825	0826	0828	0829	0832	0833	0838	0839
	310:190	302:198	306:194	313:187	304:196	299:201	311:189	303:197	305:195	312:188
RATIO	1.63:1.00	1.53:1.00	1.58:1.00	1.67:1.00	1.55:1.00	1.49:1.00	1.65:1.00	1.54:1.00	1.56:1.00	1.66:1.00

Group 4

High-Dose: 18.0 mg base/kg/day

ANIMAL NO.	0943	0945	0946	0947	0948	0950	0951	0952	0955	0958
	310:190	301:199	312:188	305:195	297:203	313:187	305:195	309:191	302:198	313:187
RATIO	1.63:1.00	1.51:1.00	1.66:1.00	1.56:1.00	1.46:1.00	1.67:1.00	1.56:1.00	1.62:1.00	1.53:1.00	1.67:1.00

INDIVIDUAL BONE MARROW M:E RATIO DATA

Group 1

Vehicle Control: 0 mg base/kg/day

ANIMAL NO.	0803	0804	0805	0808	0812	0813	0817	0818	0819	0820
	307:193	298:202	312:188	300:200	304:196	297:203	308:192	301:199	310:190	303:197
RATIO	1.59:1.00	1.48:1.00	1.66:1.00	1.50:1.00	1.55:1.00	1.46:1.00	1.60:1.00	1.51:1.00	1.63:1.00	1.54:1.00

Group 4

High-Dose: 18.0 mg base/kg/day

ANIMAL NO.	0921	0924	0925	0926	0928	0931	0934	0936	0937	0938
	ED	311:189	299:201	ED	302:198	300:200	ED	ED	ED	306:194
RATIO		1.65:1.00	1.49:1.00		1.53:1.00	1.50:1.00				1.58:1.00

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V. Quality Assurance Statement



# Pathology Associates, Inc.

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

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## QUALITY ASSURANCE STATEMENT

This histopathology project with the exception of statistical analysis tables (Sections II and III) provided by the testing facility, Toxicology Research Laboratory (TRL), 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 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.

<u>Date of Inspection</u>	<u>Phase Inspected</u>	<u>Date Findings Reported to Management/ Study Pathologist</u>
06/14/93	Individual Animal Data Sheets	06/14/93
06/14/93	Individual M:E Ratio Tables	06/14/93
06/14/93	Draft Bone Marrow Evaluation Report	06/14/93

*Carol C. Hoffman*

Quality Assurance Specialist

*06/29/93*

Date

TRL Study No. 098  
Thirteen Week Oral Toxicity Study of WR 238605 With a Thirteen Week Recovery Period in Rats

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Appendix 11  
Pre-test Clinical Pathology Data

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

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PRETEST ANIMAL CLINICAL CHEMISTRY REPORT  
 PERIOD: PRETEST

STUDY ID: 098P

SEX: MALE

ANIMAL ID	ALT U/L	AST U/L	TP g/dL	ALB g/dL	TBA mg/dL	ALKP U/L	LDH U/L	CK U/L
GROUP: PRETEST								
18	67	104	6.1	3.5	89.0	276	291	183
45	72	122	7.0	3.9	99.2	388	88	261
48	87	122	6.8	3.7	41.1	291	96	241
56	74	115	6.8	3.9	146.9	266	270	284
75	95	QNS	7.4	4.0	237.7	304	98	202
MEAN	79	116	6.8	3.8	122.8	305	169	234
SD	11.6	8.5	0.47	0.20	74.43	48.6	102.5	41.5
N	5	4	5	5	5	5	5	5

*ml = 25-200*

QNS-Quantity Not Sufficient

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

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PRETEST ANIMAL CLINICAL CHEMISTRY REPORT  
 PERIOD: PRETEST

STUDY ID: 098P

SEX: MALE

ANIMAL ID	BUN mg/dL	CREA mg/dL	NA mmol/L	K mmol/L	CL mEq/L	CA mg/dL	IP mg/dL	GLU mg/dL
GROUP: PRETEST								
18	12.5	0.41	139	6.24	113	10.7	10.4	127
45	10.6	0.37	147	6.38	110	11.2	12.3	132
48	8.0	0.43	139	6.52	110	11.0	11.9	125
56	12.7	0.36	140	6.78	112	11.6	12.9	161
75	10.9	0.45	143	6.87	111	12.0	12.3	192
MEAN	10.9	0.40	142	6.56	111	11.3	12.0	147
SD	1.89	0.038	3.4	0.265	1.3	0.51	0.94	28.8
N	5	5	5	5	5	5	5	5

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

DRAFT

PRETEST ANIMAL CLINICAL CHEMISTRY REPORT  
 PERIOD: PRETEST

STUDY ID: 098P

SEX: FEMALE

ANIMAL ID	ALT U/L	AST U/L	TP g/dL	ALB g/dL	TBA mg/dL	ALKP U/L	LDH U/L	CK U/L
GROUP: PRETEST								
117	63	131	7.1	3.8	112.8	258	167	544
143	58	112	7.1	4.0	123.8	261	118	344
152	61	99	7.7	4.4	72.3	233	54	88
184	50	120	7.9	4.4	21.7	200	<del>212</del>	181
197	75	148	6.7	4.0	301.1	257	<del>367</del>	524
MEAN	61	122	7.3	4.1	126.3	242	184	336
SD	9.1	18.6	0.49	0.27	105.59	25.9	118.1	202.6
N	5	5	5	5	5	5	5	5

*ml = 25-200*

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

DRAFT

PRETEST ANIMAL CLINICAL CHEMISTRY REPORT  
PERIOD: PRETEST

STUDY ID: 098P

SEX: FEMALE

ANIMAL ID	BUN mg/dL	CREA mg/dL	NA mmol/L	K mmol/L	CL mEq/L	CA mg/dL	IP mg/dL	GLU mg/dL
GROUP: PRETEST								
117	10.0	0.49	143	6.92	111	11.9	11.5	175
143	8.9	0.42	143	6.99	111	12.4	10.7	150
152	13.6	0.40	143	6.12	110	11.8	10.3	138
184	16.9	0.45	145	6.14	117	12.3	10.5	129
197	10.9	0.45	137	6.63	108	11.3	10.3	133
MEAN	12.1	0.44	142	6.56	111	11.9	10.7	145
SD	3.22	0.034	3.0	0.415	3.4	0.44	0.50	18.5
N	5	5	5	5	5	5	5	5

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

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PRETEST ANIMAL HEMATOLOGY REPORT  
 PERIOD: PRETEST

STUDY ID: 098P

SEX: MALE

ANIMAL ID	RBC 10 <sup>6</sup> /cmm	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RETICS %RBCs	HB %
GROUP: PRETEST								
18	6.36	14.0	41.3	64.9	22.0	33.9	3.4	0.0
45	6.38	13.7	40.8	63.9	21.5	33.6	1.9	0.0
48	6.68	14.5	42.1	63.0	21.7	34.4	3.4	0.0
56	6.50	16.4	42.6	65.5	25.2	38.5	2.7	0.0
75	6.82	15.5	44.1	64.7	22.7	35.1	2.6	0.0
MEAN	6.55	14.8	42.2	64.4	22.6	35.1	2.8	0.0
SD	0.198	1.12	1.28	0.97	1.51	1.98	0.63	0.00
N	5	5	5	5	5	5	5	5

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

DRAFT

PRETEST ANIMAL HEMATOLOGY REPORT  
PERIOD: PRETEST

STUDY ID: 098P

SEX: MALE

ANIMAL ID	PLT 10 <sup>3</sup> /ccm	WBC 10 <sup>3</sup> /cmm
-----------	-----------------------------	-----------------------------

GROUP: PRETEST

18	1141	22.0
45	1075	11.4
48	1136	13.1
56	1309	16.1
75	1396	21.6

MEAN	1211	16.8
SD	135.0	4.83
N	5	5

WBC corrected for NRBC = or > 10

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

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PRETEST ANIMAL HEMATOLOGY REPORT  
PERIOD: PRETEST

STUDY ID: 098P

SEX: MALE

ANIMAL ID	%METHGB %	APTT sec
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GROUP: PRETEST

2	0.5	11.5
32	1.0	10.4
58	0.4	8.9
85	0.3	10.3
95	0.7	16.1

MEAN	0.6	11.4
SD	0.28	2.76
N	5	5

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

D R A F T

WHITE DIFFERENTIAL DATA

STUDY ID: 098P

GROUP: PRETEST

SEX: MALE

ANIMAL ID		PRETEST	
		REL	ABS
18	Nucleated Red Cells	0	
	M. Neutrophils	5	1.1
	I. Neutrophils	0	0.0
	Lymphocytes	92	20.2
	Monocytes	3	0.7
	Eosinophils	0	0.0
	Basophils	0	0.0
	WBC		22.0
45	Nucleated Red Cells	0	
	M. Neutrophils	6	0.7
	I. Neutrophils	0	0.0
	Lymphocytes	88	10.0
	Monocytes	6	0.7
	Eosinophils	0	0.0
	Basophils	0	0.0
	WBC		11.4
48	Nucleated Red Cells	0	
	M. Neutrophils	12	1.6
	I. Neutrophils	0	0.0
	Lymphocytes	81	10.6
	Monocytes	5	0.7
	Eosinophils	2	0.3
	Basophils	0	0.0
	WBC		13.1
56	Nucleated Red Cells	0	
	M. Neutrophils	14	2.3
	I. Neutrophils	0	0.0
	Lymphocytes	77	12.4
	Monocytes	8	1.3
	Eosinophils	1	0.2
	Basophils	0	0.0
	WBC		16.1

NRBC Corrected After-10

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

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WHITE DIFFERENTIAL DATA

STUDY ID: 098P

GROUP: PRETEST

SEX: MALE

ANIMAL ID		PRETEST	
		REL	ABS
75	Nucleated Red Cells	0	
	M. Neutrophils	8	1.7
	I. Neutrophils	0	0.0
	Lymphocytes	87	18.8
	Monocytes	4	0.9
	Eosinophils	1	0.2
	Basophils	0	0.0
	WBC		21.6

NRBC Corrected After-10

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

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MORPHOLOGY OBSERVATIONS

STUDY ID: 098P

GROUP: PRETEST

SEX: MALE

ANIMAL ID	PRETEST
18	Anisocytosis,Slight; Polychromasia, Moderate;Target Cells,Slight
45	Polychromasia,Slight Target Cells,Slight; Macrocytes,Slight
48	Anisocytosis,Slight; Polychromasia,Slight
56	Polychromasia,Slight Macrocytes,Slight
75	Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight

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

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PRETEST ANIMAL HEMATOLOGY REPORT  
 PERIOD: PRETEST

STUDY ID: 098P

SEX: FEMALE

ANIMAL ID	RBC 10 <sup>6</sup> /cmm	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RETICS %RBCs	HB %
GROUP: PRETEST								
117	7.21	15.0	43.9	60.9	20.8	34.2	2.3	0.0
143	6.21	13.3	38.9	62.6	21.4	34.2	0.8	0.0
152	6.93	14.5	41.6	60.0	20.9	34.9	1.4	0.0
184	6.85	14.4	41.2	60.1	21.0	35.0	2.0	0.0
197	6.77	14.8	42.6	62.9	21.9	34.7	2.9	0.0
MEAN	6.79	14.4	41.6	61.3	21.2	34.6	1.9	0.0
SD	0.366	0.66	1.85	1.37	0.45	0.38	0.81	0.00
N	5	5	5	5	5	5	5	5

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

DRAFT

PRETEST ANIMAL HEMATOLOGY REPORT  
PERIOD: PRETEST

STUDY ID: 098P

SEX: FEMALE

ANIMAL ID	PLT 10 <sup>3</sup> /ccm	WBC 10 <sup>3</sup> /cmm
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GROUP: PRETEST

117	768	12.1
143	1097	12.3
152	1049	21.5
184	1012	15.5
197	1195	12.7

MEAN	1024	14.8
SD	158.8	3.98
N	5	5

WBC corrected for NRBC = or > 10

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

DRAFT

PRETEST ANIMAL HEMATOLOGY REPORT  
PERIOD: PRETEST

STUDY ID: 098P

SEX: FEMALE

ANIMAL ID	%METHGB %	APTT sec
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GROUP: PRETEST

105	0.7	9.5
107	0.3	8.1
166	0.7	10.3
174	0.4	8.6
188	1.1	10.1

MEAN	0.6	9.3
SD	0.31	0.95
N	5	5

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

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: 098P

GROUP: PRETEST

SEX: FEMALE

ANIMAL ID		PRETEST	
		REL	ABS
117	Nucleated Red Cells	0	
	M. Neutrophils	7	0.8
	I. Neutrophils	0	0.0
	Lymphocytes	81	9.8
	Monocytes	12	1.5
	Eosinophils	0	0.0
	Basophils	0	0.0
	WBC		12.1
143	Nucleated Red Cells	0	
	M. Neutrophils	8	1.0
	I. Neutrophils	0	0.0
	Lymphocytes	89	10.9
	Monocytes	3	0.4
	Eosinophils	0	0.0
	Basophils	0	0.0
	WBC		12.3
152	Nucleated Red Cells	0	
	M. Neutrophils	6	1.3
	I. Neutrophils	0	0.0
	Lymphocytes	92	19.8
	Monocytes	1	0.2
	Eosinophils	1	0.2
	Basophils	0	0.0
	WBC		21.5
184	Nucleated Red Cells	0	
	M. Neutrophils	16	2.5
	I. Neutrophils	0	0.0
	Lymphocytes	79	12.2
	Monocytes	4	0.6
	Eosinophils	1	0.2
	Basophils	0	0.0
	WBC		15.5

NRBC Corrected After-10

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

WHITE DIFFERENTIAL DATA

STUDY ID: 098P

GROUP: PRETEST

SEX: FEMALE

ANIMAL ID		PRETEST	
		REL	ABS
197	Nucleated Red Cells	0	
	M. Neutrophils	16	2.0
	I. Neutrophils	0	0.0
	Lymphocytes	80	10.2
	Monocytes	4	0.5
	Eosinophils	0	0.0
	Basophils	0	0.0
	WBC		12.7

NRBC Corrected After-10

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

DRAFT

MORPHOLOGY OBSERVATIONS

STUDY ID: 098P

GROUP: PRETEST

SEX: FEMALE

ANIMAL ID	PRETEST
117	Anisocytosis,Slight; Polychromasia,Slight Large Platelets, Slight
143	Polychromasia, Moderate;Macrocytes, Moderate
152	Anisocytosis,Slight; Polychromasia,Slight
184	Anisocytosis, Moderate; Polychromasia,Slight
197	Anisocytosis,Slight; Polychromasia,Slight

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Appendix 12  
Protocol and Protocol Amendments

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

1.0 PURPOSE OF THE STUDY:

The purpose of this study is to determine specific target organ toxicity, dose-response relationships, and a no adverse effect level of WR 238605 in CD® rats following thirteen weeks of daily administration by gavage. 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: 12/17/92  
4.3 Proposed Necropsy Dates: 3/18,19/93; 6/17,18/93  
4.4 Proposed Study Completion Date  
(Draft Study Report): 9/17/93

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5.0 TEST ARTICLE

- 5.1 Name or Code No.: WR238605 succinate
- 5.2 IRL 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.
Analytical Chemist	Ian R. Tebbett, Ph.D.
Clinical Veterinarian	James E. Artwohl, D.V.M., Ph.D., D.A.C.L.A.M.
Veterinarian Support	Documented in raw data
Ophthalmologist	Samuel J. Vainisi, D.V.M., D.A.C.V.O.
Tox. Lab Supervisor	Soudabeh Soura, B.S.
Lead Technician	Nancy Dinger, B.S.
Clinical Pathology	Maria Lang, A.H.T., C.V.T.
Chemistry Specialist	Thomas Tolhurst, B.S.
Quality Assurance	Ronald C. Schoenbeck

7.0 TEST SYSTEM:

- 7.1 Species: Rat
- 7.2 Strain: CD® (Virus Antibody Free)
- 7.3 Number and Sex: 80 Males and 80 Females

# DRAFT

Contract No.: DAMD17-92-C-2001  
Task Order No.: UIC-5B  
Study No.: 098

- 7.4 Age of Animals: Approximately 7 weeks old at dosing initiation.
- 7.5 Weight of Animals: Approximately 200 - 250 g (males) and approximately 150 - 200 g (females) at dosing initiation.
- 7.6 Source of Animals: Charles River Breeding Laboratories. The specific breeding facility will be documented in the raw data.
- 7.7 Justification for Selection of Test System: The rat is a standard and accepted rodent species for 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 study-unique quarantine/pretest number. During the animal selection process, each animal will be assigned an animal number unique to it within the population making up the study. This number will appear as an ear tag and will also appear on a cage card visible on the front of each cage. The cage card will additionally contain the study number, test article identification, treatment group number and dose level. Cage cards will be color-coded as a function of treatment group. Raw data records and specimens will also be identified by the unique test animal number.
- 7.9 Housing: The animals will be housed in an AAALAC-accredited facility. Animals will be singly housed in polycarbonate cages with Anderson-bed-a-cob bedding (Heinold, Kankakee, Illinois) in a temperature (65-78°F) and humidity (approx. 40-70%) controlled room with a 14 hour light/10 hour dark cycle. The cage size, 840 cm area and 20 cm height, is adequate to house rats at the upper weight range as described in the Guide for the Care and Use of Laboratory Animals, DHEW (NIH) No. 86.23. All animals will be routinely transferred to clean cages with fresh bedding once weekly.
- 7.10 Quarantine Procedure: Animals will be quarantined for approximately one week. During that time, the animals will be observed daily for signs of illness or death, and all unusual observations will be reported to the Study Director, Toxicologist or Clinical Veterinarian. Animals will be examined during quarantine and approved for use by the Clinical Veterinarian prior to being placed on test. Any sickly animals will be eliminated prior to the test animal selection process. If a selected animal appears sickly prior to initiation of treatment, it will be replaced by a healthy animal prior to initiation of treatment under the direction of the Study Director or Toxicologist. In addition, during the quarantine/pretest, hematology and clinical chemistry parameters (see Section 8.7.6) will be measured for five rats/sex to determine the suitability of the rat shipment for use in this study. These rats, however, will not be used in the dosing portion of the study. Quarantine release will be documented on the Clinical Veterinarian Log by the veterinarian prior to study initiation.

- 7.11 Food: Purina Certified Rodent Chow No. 5002 (Ralston Purina Company, St. Louis, MO) will be provided *ad libitum* from arrival until termination, except during an approximate 16-20 hour fast prior to blood collection for clinical pathology and/or necropsy.
- 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 bimonthly comprehensive chemical analyses of Chicago water are documented in files maintained by Quality Assurance.

8.0 EXPERIMENTAL DESIGN:

8.1 Treatment Groups:

<u>Treatment Group</u>	<u>Dose Level (mg base/kg/day)</u>	<u>Number of Males</u>	<u>Number of Females</u>
1	0	10 + 10*	10 + 10*
2	0.5	10 + 10*	10 + 10*
3	6.0	10 + 10*	10 + 10*
4	18.0	10 + 10*	10 + 10*

\*Recovery Animals

Dose levels were supplied by the Sponsor based on the results of a 28-day gavage rat study, and are extrapolations from that shorter-term toxicology study.

Ten animals/sex/group will be necropsied after the thirteen week treatment period. The remaining animals indicated above 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 by gavage once daily starting with Day 0 for at least thirteen weeks. Control animals will receive the test article vehicle (aqueous 1% methylcellulose/0.4% Tween 80). The animals to be sacrificed after the 13 week treatment period will be dosed up to and including the day prior to their scheduled necropsy on Days 91 and 92. The recovery animals will be dosed for 91 days. Dosing volume will be 5 ml/kg, adjusted on the basis of each animal's most recent body weight. The actual volume (ml) administered will be documented in the raw data.

# DRAFT

Contract No.: DAMD17-92-C-2001  
Task Order No.: UIC-5B  
Study No.: 098

- 8.3 Justification of Route(s): Oral treatment is the intended clinical route of administration and is specified by the Sponsor.
- 8.4 Procedure to Control Bias during the Assignment of Animals to Treatment Groups: During the quarantine/pretest period, the animals will be randomized by sex into the four groups shown in Section 8.1 using a computer-generated randomization procedure on the basis of body weight.
- 8.5 Test Article Vehicle: Aqueous 1% methylcellulose/0.4% 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 5 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 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 -1, on Day 0, and weekly thereafter.
- 8.7.3 Body Weight: Body weights of all animals will be recorded at randomization in Week -1, on Day 0, weekly thereafter, and at scheduled necropsy.
- 8.7.4 Food Consumption: Food consumption for all animals will be measured weekly commencing in Week -1.
- 8.7.5 Ophthalmologic Examinations: All rats will be examined by indirect ophthalmoscopy prior to study initiation and during Week 13, and in Week 26 for the recovery animals.

DRAFT

8.7.6 Clinical Pathology: Hematology and clinical chemistry parameters will be measured for 10 animals/sex/group during Weeks 2, 4, 8 and 13, and in Weeks 16, 21 and 27 (at necropsy) for the recovery groups. The recovery animals will be routinely used throughout the study for these measurements. The overnight fasted animals will be anesthetized by carbon dioxide inhalation, and approximately 1.5 - 2.0 ml of blood will be collected from the orbital sinus to measure the following parameters. The samples will be processed in the same random order as collected.

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	Heinz Bodies
Reticulocyte counts	Platelet count
	<sup>b</sup> Methemoglobin

<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

Albumin	Creatine kinase
Albumin/Globulin Ratio (calculated)	Chloride
Alkaline phosphatase	Glucose
Alanine aminotransferase (ALT/SGPT)	Globulin (calculated)
Aspartate aminotransferase (AST/SGOT)	Inorganic phosphorus
Calcium	Lactate dehydrogenase
Creatinine	Potassium
	Sodium
	Total bile acids
	Total protein
	Urea nitrogen (BUN)

Activated partial thromboplastin time will be measured for all rats from blood samples collected from the vena cava at their scheduled necropsy in Weeks 14 and 27. Clinical chemistry and hematology tests and activated partial thromboplastin time will be measured for 5 rats/sex during the quarantine/pretest period.

8.7.7 Plasma Drug Levels: Blood samples will be obtained at scheduled necropsy from the vena cava to provide approximately 1 ml of plasma for drug level measurements. The samples will be collected after blood is obtained for activated partial thromboplastin time. The plasma samples will subsequently be shipped to Dr. Emil Lin for analysis as specified by the Sponsor. The results will not be included in the Study Report.

# DRAFT

Contract No.: DAMD17-92-C-2001  
Task Order No.: UIC-5B  
Study No.: 098

8.7.8 Pathology: All animals which die on test or are sacrificed if moribund will be necropsied on that day. For surviving animals, 10 animals/sex/group will be sacrificed and necropsied in random order over two consecutive days (Days 91 and 92). The remaining animals will be held for a 13 week recovery period. They will be sacrificed and necropsied at the onset of Week 27.

Euthanasia will be accomplished by carbon dioxide asphyxiation, and an extensive necropsy will be performed under the direction and supervision of the pathologist. Terminal body weights will be collected prior to routine sacrifice.

The necropsy procedure will be a thorough and systematic examination and dissection of the animal viscera and carcass, and collection and fixation of the following tissues/organs in 10% neutral buffered formalin.

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

\*Weighed at scheduled necropsy. Paired organs will be weighed as a unit.

All tissues and organs collected at necropsy will be examined microscopically for all high dose and control animals sacrificed after 13 weeks of treatment. In addition, animals found dead or subjected to a moribund sacrifice will also be processed for microscopic examination. If treatment-related lesions are observed at the high dose, those tissues/organs will be examined microscopically for mid and low dose animals sacrificed in Week 14, and for control and high dose (and mid and low dose if necessary) recovery animals.

DRAFT

Contract No.: DAMD17-92-C-2001  
Task Order No.: UIC-5B  
Study No.: 098

Femoral bone marrow smears will be prepared for all animals at scheduled necropsy and for moribund sacrificed animals. The myeloid:erythroid (M:E) ratio will be determined for control and high dose animals at the Week 14 necropsy. If treatment-related changes are seen, M:E ratios will be determined from mid and low dose animals at Week 14, and from control and high dose (and mid and low dose as necessary) recovery animals.

8.7.9 Statistical Analyses: For each sex, Analysis of Variance tests will be conducted on body weight, food consumption, hematology, clinical chemistry and organ weight data. Organ weight analysis will consider absolute weights and weights relative to body weight. If a significant F ratio is obtained ( $p \leq 0.05$ ), Dunnett's t test will be used for pair-wise comparisons to the control group. Frequency data such as incidence of mortality, gross necropsy observations and tissues 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 study, except those that are generated as direct computer input, shall be recorded directly, promptly, and accurately in ink in bound books with prenumbered pages or on worksheets that shall be bound during or at the conclusion of the nonclinical laboratory study. All appropriate computer and machine output shall be bound during or at the conclusion of the study. All data entries shall be dated on the day of entry and signed or initialed by the person entering the data. Any changes in entries for whatever reason (e.g., to correct an error or transposition) shall be made so as not to obscure the original entry, shall indicate the reason for such change, and shall be dated and signed or identified at the time of data input. In computer driven collection systems, the operator responsible for direct input shall be identified at the time of data input. Any changes in computer entries for whatever reason (e.g., to correct an error or transposition) shall be made in such manner so as not to obscure the original entry, if possible, shall indicate the reason for such change, and shall be dated and the responsible individual shall be identified.

All recorded data shall be reviewed, signed, and dated by a knowledgeable person, other than the person making the entry, to assure adherence to procedures and to verify observations.

Upon completion of the study and submission of the final report, all raw data, documentation, specimens, test article reserves and other materials necessary to reconstruct the study will be stored in the TRL archives

DRAFT

Contract No.: DAMD17-92-C-2001  
Task Order No.: UIC-5B  
Study No.: 098

maintained by Quality Assurance, unless specified by the Sponsor.

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-5B  
Study No.: 098

11.0 PROTOCOL APPROVAL:

STUDY DIRECTOR:

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

9/1/92  
Date

QUALITY ASSURANCE:

Ronald Schöenbeck  
Ronald Schöenbeck

9/1/92  
Date

SPONSOR APPROVAL:

George Schieferstein  
George Schieferstein, Ph.D.  
Contracting Officer's  
Representative (COR)

9/2/92  
Date

COMMENTS FROM THE COR:

PROTOCOL AMENDMENT

DRAFT

Study No.: 098

Title: Thirteen Week Oral Toxicity Study of WR238605 with a Thirteen Week Recovery Period in Rats

1. Page 1 Section 4.0

Change the study dates as follows:

4.2 Proposed Initiation of Dosing: 12/17/92

4.3 Proposed Necropsy Date: 3/18,19/93; 6/17,18/93

4.4 Proposed Study Completion Date  
(Draft Study Report): 9/17/93

Reason: Delay in study start.

2. Page 2 Section 6.0

Change "Technician Teresa O'Neill, B.S." to "Lead Technician Nancy Dinger, B.S."

Reason: Mistake in protocol.

3. Page 6 Section 8.7.6

A. Change the blood collection weekly timepoints for clinical pathology measurements from "3, 5, 9, 13, 16, 18, 22 and 27" to "2, 4, 8, 13, 16, 21 and 27."

Reason: Sponsor request.

B. Add total bile acids (TBA) to the clinical chemistry list.

Reason: Inadvertently omitted from protocol.

C. Change "abdominal aorta" to "vena cava" in the last sentence which describes the collection of blood for activated partial thromboplastin time.

Reason: Mistake in protocol.

D. Add the following sentence at the end of the section:

"Clinical chemistry and hematology tests and activated partial thromboplastin time will be measured for 5 rats/sex during the quarantine/pretest period."

PROTOCOL AMENDMENT

DRAFT

Study No.: 098

Title: Thirteen Week Oral Toxicity Study of WR238605 with a Thirteen Week Recovery Period in Rats

Reason: Clarification of procedures.

4. Page 6 Section 8.7.7

Change "abdominal aorta" to "vena cava" as the source of blood collection in the first sentence.

Reason: Mistake in protocol.

5. Page 7 Section 8.7.8

Add "sternum with marrow" to the tissue list.

Reason: Inadvertently omitted from the protocol.

6. Page 8 Section 8.7.8

Change the first sentence as follows:

"Femoral bone marrow smears will be prepared for all animals at scheduled necropsy and for moribund sacrificed animals."

Reason: Clarification of protocol.

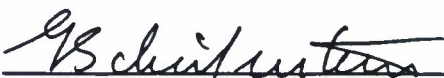
APPROVALS:

STUDY DIRECTOR:

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

12/21/92  
Date

SPONSOR APPROVAL:

  
George Schieferstein, Ph.D.  
Contracting Officer's  
Representative (COR)

12/23/92  
Date

PROTOCOL AMENDMENT

DRAFT

Study No.: 098

Title: Thirteen Week Oral Toxicity Study of WR238605 with a Thirteen Week Recovery Period in Rats

7. 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)

5/2/93  
Date

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Appendix 13  
Study Deviations

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

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Study Deviations\*

<u>Deviation Type</u>	<u>Specific Deviation</u>	<u>Effect on Study</u>
Protocol	On several occasions the temperature deviated outside the specified range in the animal room(s.) The temperature deviations ranged from -0 to +3°F, outside the specified ranges.	None. These minimal sporadic occurrences were not considered to have had an impact on the outcome of the study.
Protocol	In an attempt to identify unknown pigment (hemosiderin or lipofuscin) present in the alveolar macrophages in the lungs of recovery rats, Perl's and acid-fast staining of lung sections were performed.	These stains allowed the identification of pigment as hemosiderin.

\*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