FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 8C - Clinical chemistry - Week 6 of treatment - Mean data

STUDY NO.: 235-003-009

MALES

Parameter/units	Study Day	Control Mean	Control SD	Control N	Group 2 Mean	Group 2 SD	Group 2 N	Group 3 Mean	Group 3 SD	Group 3 N	Group 4 Mean	Group 4 SD	Group 4 N
TOTAL PROTEIN g/dl	42	5.72	0.18	4	5.74	0.39	4	6.05	0.49	4	5.91	0.17	4
ALBUMIN %	42	66.90	1.05	4	64.98	1.45	4	63.60	3.63	4	66.65	1.96	4
ALPHA 1 GLOBULIN %	42	4.08	0.33	4	4.25	0.24	4	4.60*	0.14	4	4.05	0.24	4
ALPHA 2 GLOBULIN %	42	6.20	0.50	4	6.30	0.43	4	6.43	1.26	4	7.05	0.79	4
BETA GLOBULIN %	42	8.32	0.65	4	10.95*	1.62	4	9.48	1.76	4	7.73	0.96	4
GAMMA GLOBULIN %	42	14.53	0.87	4	13.53	1.55	4	15.95	2.03	4	14.53	0.69	4
ALBUMIN/GLOBULIN RATIO	42	2.023	0.095	4	1.863	0.121	4	1.768	0.278	4	2.008	0.176	4

Controls from group(s): 1
Data homogeneous by Bartlett's Test — Test of significance is Dunnett's Test
(n) Data nonhomogeneous by Bartlett's Test — Modified t test of significance
* Indicates group mean is significantly different from control at level P = .05
** Indicates group mean is significantly different from control at level P = .01

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A.
(Dr. Alfredo Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 8C - Clinical chemistry - Week 6 of treatment - Mean data

STUDY NO.: 235-003-009

MALES

Parameter/units	Study Day	Control Mean	Control SD	Control N	Group 2 Mean	Group 2 SD	Group 2 N	Group 3 Mean	Group 3 SD	Group 3 N	Group 4 Mean	Group 4 SD	Group 4 N
CHLORIDE mmol/l	42	107.21	2.92	4	106.64	2.75	4	105.17	5.30	4	103.33	3.67	4
SODIUM mmol/l	42	146.125	1.686	4	145.700	1.014	4	146.100	2.245	4	147.200	1.103	4
POTASSIUM mmol/l	42	4.878	0.313	4	4.975	0.172	4	5.070	0.638	4	4.847	0.152	4
CALCIUM mmol/l	42	2.710	0.099	4	2.698	0.024	4	2.668	0.122	4	2.680	0.049	4

Controls from group(s): 1
Data homogeneous by Bartlett's Test — Test of significance is Dunnett's Test
(n) Data nonhomogeneous by Bartlett's Test — Modified t test of significance
* Indicates group mean is significantly different from control at level P = .05
** Indicates group mean is significantly different from control at level P = .01

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A.
(Dr. Alfredo Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 8C - Clinical chemistry - Week 6 of treatment - Mean data

STUDY NO.: 235-003-009

FEMALES

Parameter/units	Study Day	Control Mean	Control SD	Control N	Group 2 Mean	Group 2 SD	Group 2 N	Group 3 Mean	Group 3 SD	Group 3 N	Group 4 Mean	Group 4 SD	Group 4 N
ALKALINE PHOSPHATASE U/l	42	161.90	34.23	4	176.07	38.39	4	175.36	60.97	4	149.90	29.32	4
ALANINE TRANSFERASE U/l	42	19.81	7.01	4	18.20	2.72	4	20.00	4.20	4	17.50	2.59	4
ASPARTATE TRANSFERASE U/l	42	9.91	1.71	4	12.41	2.13	4	13.94*	1.48	4	12.19	0.79	4
UREA mg/dl	42	28.01	4.93	4	29.32	6.13	4	36.76	5.72	4	31.22	4.56	4
GLUCOSE mg/dl	42	93.56	3.18	4	93.71	7.28	4	93.86	3.86	4	89.73	2.18	4
TOTAL BILIRUBIN mg/dl	42	0.1000	0.0245	4	0.0950	0.0129	4	0.0875	0.0096	4	0.1200	0.0141	4
TOTAL CHOLESTEROL mg/dl	42	187.79	35.50	4	133.12**	17.69	4	141.08*	10.65	4	143.74*	9.26	4
CREATININE mg/dl	42	0.79	0.08	4	0.71	0.04	4	0.81	0.12	4	0.83	0.07	4

Controls from group(s): 1
Data homogeneous by Bartlett's Test — Test of significance is Dunnett's Test
(n) Data nonhomogeneous by Bartlett's Test — Modified t test of significance
* Indicates group mean is significantly different from control at level P = .05
** Indicates group mean is significantly different from control at level P = .01

LIFE SCIENCE REGULATION
Roma Toxicology Centre S.p.A.
(Dr. [illegible])

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 8C - Clinical chemistry - Week 6 of treatment - Mean data

STUDY NO.: 235-003-009

FEMALES

Parameter/units	Study Day	Control Mean	Control SD	Control N	Group 2 Mean	Group 2 SD	Group 2 N	Group 3 Mean	Group 3 SD	Group 3 N	Group 4 Mean	Group 4 SD	Group 4 N
TOTAL PROTEIN g/dl	42	5.87	0.16	4	5.57	0.31	4	5.83	0.09	4	5.99	0.19	4
ALBUMIN %	42	67.33	1.78	4	67.55	1.75	4	66.25	3.35	4	66.95	1.97	4
ALPHA 1 GLOBULIN %	42	4.10	0.50	4	4.58	0.31	4	4.40	0.22	4	4.33	0.15	4
ALPHA 2 GLOBULIN %	42	6.47	1.95	4	5.40	1.07	4	5.68	0.52	4	5.58	0.78	4
BETA GLOBULIN %	42	7.35	0.99	4	8.10	0.98	4	7.93	1.63	4	7.20	0.57	4
GAMMA GLOBULIN %	42	14.75	1.17	4	14.48	1.86	4	15.75	1.46	4	15.98	1.24	4
ALBUMIN/GLOBULIN RATIO	42	2.065	0.166	4	2.088	0.168	4	1.985	0.294	4	2.035	0.184	4

Controls from group(s): 1
Data homogeneous by Bartlett's Test — Test of significance is Dunnett's Test
(n) Data nonhomogeneous by Bartlett's Test — Modified t test of significance
* Indicates group mean is significantly different from control at level P = .05
** Indicates group mean is significantly different from control at level P = .01

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A.
(Dr. Alfredo Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 8C - Clinical chemistry - Week 6 of treatment - Mean data

STUDY NO.: 235-003-009

FEMALES

Parameter/units	Study Day	Control Mean	Control SD	Control N	Group 2 Mean	Group 2 SD	Group 2 N	Group 3 Mean	Group 3 SD	Group 3 N	Group 4 Mean	Group 4 SD	Group 4 N
CHLORIDE mmol/l	42	105.24	2.04	4	103.93	2.54	4	103.69	1.52	4	102.92	1.06	4
SODIUM mmol/l	42	147.600	0.986	4	144.775**	1.146	4	144.225**	1.243	4	144.825**	0.659	4
POTASSIUM mmol/l	42	4.843	0.272	4	4.183	0.407	4	4.405	0.169	4	4.685	0.487	4
CALCIUM mmol/l	42	2.653	0.067	4	2.678	0.076	4	2.763	0.079	4	2.713	0.057	4

Controls from group(s): 1
Data homogeneous by Bartlett's Test — Test of significance is Dunnett's Test
(n) Data nonhomogeneous by Bartlett's Test — Modified t test of significance
* Indicates group mean is significantly different from control at level P = .05
** Indicates group mean is significantly different from control at level P = .01

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A.
(Dr. Alfredo Tanzini)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 8D - Clinical chemistry - Week 13 of treatment - Mean data

STUDY NO.: 235-003-009

MALES

Parameter/units	Study Day		Control Mean	Control SD	Control N	Group 2 Mean	Group 2 SD	Group 2 N	Group 3 Mean	Group 3 SD	Group 3 N	Group 4 Mean	Group 4 SD	Group 4 N
ALKALINE PHOSPHATASE U/l	86	(n)	136.07	27.79	4	137.68	35.48	4	167.35	16.39	4	199.96	96.95	4
ALANINE TRANSFERASE U/l	86	(n)	23.62	6.82	4	21.28	1.22	4	22.84	2.42	4	25.52	10.88	4
ASPARTATE TRANSFERASE U/l	86		13.18	0.97	4	11.65	1.22	4	12.83	1.13	4	13.59	2.02	4
UREA mg/dl	86		28.88	4.38	4	28.15	4.52	4	26.98	2.25	4	32.10	4.44	4
GLUCOSE mg/dl	86	(n)	96.36	3.45	4	99.84	1.10	4	101.48	3.38	4	97.65	9.53	4
TOTAL BILIRUBIN mg/dl	86		0.1075	0.0171	4	0.1175	0.0171	4	0.1375	0.0330	4	0.1250	0.0100	4
TOTAL CHOLESTEROL mg/dl	86		132.35	8.77	4	141.29	14.60	4	153.71	12.02	4	137.11	15.14	4
CREATININE mg/dl	86	(n)	0.69	0.07	4	0.74	0.10	4	0.76	0.01	4	0.80	0.06	4

Controls from group(s): 1
Data homogeneous by Bartlett's Test — Test of significance is Dunnett's Test
(n) Data nonhomogeneous by Bartlett's Test — Modified t test of significance
* Indicates group mean is significantly different from control at level P = .05
** Indicates group mean is significantly different from control at level P = .01

LIFE SCIENCES
Roma Toxicology Centre S.p.A.
(Dr. Alfredo Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 8D - Clinical chemistry - Week 13 of treatment - Mean data

STUDY NO.: 235-003-009

MALES

Parameter/units	Study Day		Control Mean	Control SD	Control N	Group 2 Mean	Group 2 SD	Group 2 N	Group 3 Mean	Group 3 SD	Group 3 N	Group 4 Mean	Group 4 SD	Group 4 N
TOTAL PROTEIN g/dl	86		5.44	0.15	4	5.50	0.31	4	5.76	0.32	4	5.56	0.12	4
ALBUMIN %	86		66.45	0.84	4	65.05	2.12	4	63.48	2.74	4	66.20	1.92	4
ALPHA 1 GLOBULIN %	86		4.03	0.31	4	4.23	0.21	4	4.38	0.33	4	4.23	0.26	4
ALPHA 2 GLOBULIN %	86		6.35	0.54	4	6.50	0.52	4	6.40	0.71	4	6.98	0.62	4
BETA GLOBULIN %	86	(n)	8.43	0.13	4	11.60	2.15	4	9.95	1.38	4	8.25	0.89	4
GAMMA GLOBULIN %	86		14.73	0.59	4	12.65	1.65	4	15.80	1.94	4	14.38	0.71	4
ALBUMIN/GLOBULIN RATIO	86		1.983	0.076	4	1.868	0.181	4	1.750	0.194	4	1.965	0.169	4

Controls from group(s): 1
Data homogeneous by Bartlett's Test — Test of significance is Dunnett's Test
(n) Data nonhomogeneous by Bartlett's Test — Modified t test of significance
* Indicates group mean is significantly different from control at level P = .05
** Indicates group mean is significantly different from control at level P = .01

LIFE SCIENCE RESEARCH
Rome Toxicology Centre S.p.A.
(Dr. Alfredo Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 8D - Clinical chemistry - Week 13 of treatment - Mean data

STUDY NO.: 235-003-009

MALES

Parameter/units	Study Day	Control Mean	Control SD	Control N	Group 2 Mean	Group 2 SD	Group 2 N	Group 3 Mean	Group 3 SD	Group 3 N	Group 4 Mean	Group 4 SD	Group 4 N
CHLORIDE mmol/l	86	98.83	3.67	4	99.21	1.05	4	97.24	3.58	4	97.89	1.07	4
SODIUM mmol/l	86	142.875	1.248	4	142.775	0.315	4	142.625	0.900	4	143.225	1.036	4
POTASSIUM mmol/l	86	4.660	0.283	4	4.758	0.160	4	4.727	0.221	4	4.693	0.117	4
CALCIUM mmol/l	86	2.565	0.107	4	2.640	0.032	4	2.620	0.062	4	2.598	0.045	4

Controls from group(s): 1
Data homogeneous by Bartlett's Test — Test of significance is Dunnett's Test
(n) Data nonhomogeneous by Bartlett's Test — Modified t test of significance
* Indicates group mean is significantly different from control at level P = .05
** Indicates group mean is significantly different from control at level P = .01

LITE CONTROL RESEARCH

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 8D - Clinical chemistry - Week 13 of treatment - Mean data

STUDY NO.: 235-003-009

FEMALES

Parameter/units	Study Day		Control Mean	Control SD	N	Group 2 Mean	Group 2 SD	N	Group 3 Mean	Group 3 SD	N	Group 4 Mean	Group 4 SD	N
ALKALINE PHOSPHATASE U/l	86		121.79	23.02	4	125.19	19.35	4	130.44	50.51	4	119.39	21.61	4
ALANINE TRANSFERASE U/l	86		18.00	5.08	4	20.09	4.48	4	20.46	5.22	4	18.23	2.95	4
ASPARTATE TRANSFERASE U/l	86		11.24	1.26	4	14.43	3.22	4	13.47	1.71	4	12.05	1.82	4
UREA mg/dl	86		27.58	6.28	4	29.83	2.45	4	35.48	6.64	4	26.98	5.38	4
GLUCOSE mg/dl	86		96.09	4.71	4	95.61	7.00	4	95.67	8.95	4	96.64	4.71	4
TOTAL BILIRUBIN mg/dl	86	(n)	0.1375	0.0550	4	0.1450	0.0100	4	0.1625	0.0250	4	0.1825	0.0096	4
TOTAL CHOLESTEROL mg/dl	86		157.47	26.87	4	123.45	9.66	4	128.95	20.18	4	130.57	8.94	4
CREATININE mg/dl	86		0.73	0.08	4	0.76	0.06	4	0.87	0.10	4	0.81	0.08	4

Controls from group(s): 1
Data homogeneous by Bartlett's Test — Test of significance is Dunnett's Test
(n) Data nonhomogeneous by Bartlett's Test — Modified t test of significance
* Indicates group mean is significantly different from control at level P = .05
** Indicates group mean is significantly different from control at level P = .01

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A.
(Dr. Alfredo Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 8D - Clinical chemistry - Week 13 of treatment - Mean data

STUDY NO.: 235-003-009

FEMALES

Parameter/units	Study Day	Control Mean	Control SD	Control N	Group 2 Mean	Group 2 SD	Group 2 N	Group 3 Mean	Group 3 SD	Group 3 N	Group 4 Mean	Group 4 SD	Group 4 N
TOTAL PROTEIN g/dl	86	5.48	0.25	4	5.38	0.23	4	5.61	0.27	4	5.58	0.18	4
ALBUMIN %	86	67.55	3.07	4	67.83	1.36	4	65.95	3.86	4	68.43	1.63	4
ALPHA 1 GLOBULIN %	86	4.18	0.71	4	4.78	0.35	4	4.48	0.33	4	4.13	0.13	4
ALPHA 2 GLOBULIN %	86	5.73	1.05	4	4.95	0.33	4	5.48	0.63	4	5.23	0.65	4
BETA GLOBULIN %	86	8.13	0.79	4	8.28	1.23	4	8.28	1.69	4	6.93	0.30	4
GAMMA GLOBULIN %	86	14.40	0.72	4	14.25	2.62	4	15.83	1.89	4	15.30	1.71	4
ALBUMIN/GLOBULIN RATIO	86	2.102	0.286	4	2.115	0.132	4	1.963	0.318	4	2.175	0.161	4

Controls from group(s): 1
Data homogeneous by Bartlett's Test — Test of significance is Dunnett's Test
(n) Data nonhomogeneous by Bartlett's Test — Modified t test of significance
* Indicates group mean is significantly different from control at level P = .05
** Indicates group mean is significantly different from control at level P = .01

Roma Toxicology Centre S.p.A.
(Dr. Alfredo Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 8D - Clinical chemistry - Week 13 of treatment - Mean data

STUDY NO.: 235-003-009

FEMALES

Parameter/units	Study Day	Control Mean	Control SD	Control N	Group 2 Mean	Group 2 SD	Group 2 N	Group 3 Mean	Group 3 SD	Group 3 N	Group 4 Mean	Group 4 SD	Group 4 N
CHLORIDE mmol/l	86	96.66	3.83	4	96.70	1.67	4	96.54	2.31	4	96.11	0.63	4
SODIUM mmol/l	86	143.000	0.750	4	142.750	1.290	4	143.575	1.766	4	141.850	0.505	4
POTASSIUM mmol/l	86	4.380	0.345	4	4.122	0.184	4	4.250	0.161	4	4.403	0.328	4
CALCIUM mmol/l	86	2.572	0.056	4	2.550	0.036	4	2.652	0.080	4	2.555	0.013	4

Controls from group(s): 1
Data homogeneous by Bartlett's Test — Test of significance is Dunnett's Test
(n) Data nonhomogeneous by Bartlett's Test — Modified t test of significance
* Indicates group mean is significantly different from control at level P = .05
** Indicates group mean is significantly different from control at level P = .01

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 9A - Urinalysis - Before treatment - Mean data

STUDY NO.: 235-003-009

MALES

Parameter/units	Study Day	Control Mean	Control SD	Control N	Group 2 Mean	Group 2 SD	Group 2 N	Group 3 Mean	Group 3 SD	Group 3 N	Group 4 Mean	Group 4 SD	Group 4 N
URINE VOLUME (OVERNIGHT) ml	-7	85.0	92.0	4	196.0	138.3	4	114.5	45.9	4	147.5	61.5	4
SPECIFIC GRAVITY g/l	-7	1041.25	10.50	4	1039.50	15.89	4	1047.00	2.71	4	1041.25	20.51	4

Controls from group(s): 1
Data homogeneous by Bartlett's Test — Test of significance is Dunnett's Test
(n) Data nonhomogeneous by Bartlett's Test — Modified t test of significance
* Indicates group mean is significantly different from control at level P = .05
** Indicates group mean is significantly different from control at level P = .01

Roma Tox. Lab. Centro S.p.A.
(Dr. Alfredo Manzato)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 9A - Urinalysis - Before treatment - Mean data

STUDY NO.: 235-003-009

FEMALES

Parameter/units	Study Day	Control Mean	Control SD	Control N	Group 2 Mean	Group 2 SD	Group 2 N	Group 3 Mean	Group 3 SD	Group 3 N	Group 4 Mean	Group 4 SD	Group 4 N
URINE VOLUME (OVERNIGHT) ml	-6	84.3	76.7	4	81.8	66.2	4	115.5	43.0	4	160.0	55.8	4
SPECIFIC GRAVITY g/l	-6	1039.75	9.14	4	1042.50	13.99	4	1032.00	10.23	4	1031.25	15.17	4

Controls from group(s): 1
Data homogeneous by Bartlett's Test — Test of significance is Dunnett's Test
(n) Data nonhomogeneous by Bartlett's Test — Modified t test of significance
* Indicates group mean is significantly different from control at level P = .05
** Indicates group mean is significantly different from control at level P = .01

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A.
(Dr. Alfredo Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 9B - Urinalysis - Week 6 of treatment - Mean data

STUDY NO.: 235-003-009

MALES

Parameter/units	Study Day	Control Mean	Control SD	Control N	Group 2 Mean	Group 2 SD	Group 2 N	Group 3 Mean	Group 3 SD	Group 3 N	Group 4 Mean	Group 4 SD	Group 4 N
URINE VOLUME (OVERNIGHT) ml	38	222.0	145.3	4	216.5	102.4	4	239.0	170.9	4	200.5	72.3	4
SPECIFIC GRAVITY g/l	38	1034.50	11.90	4	1031.00	10.86	4	1032.75	20.17	4	1034.50	16.18	4

Controls from group(s): 1
Data homogeneous by Bartlett's Test — Test of significance is Dunnett's Test
(n) Data nonhomogeneous by Bartlett's Test — Modified t test of significance
* Indicates group mean is significantly different from control at level P = .05
** Indicates group mean is significantly different from control at level P = .01

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A.
(Dr. Alfredo Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 9B - Urinalysis - Week 6 of treatment - Mean data

STUDY NO.: 235-003-009

FEMALES

Parameter/units	Study Day	Control Mean	Control SD	Control N	Group 2 Mean	Group 2 SD	Group 2 N	Group 3 Mean	Group 3 SD	Group 3 N	Group 4 Mean	Group 4 SD	Group 4 N
URINE VOLUME (OVERNIGHT) ml	39	168.5	126.6	4	116.5	72.0	4	152.0	58.7	4	98.5	29.8	4
SPECIFIC GRAVITY g/l	39	1036.25	15.04	4	1049.50	11.27	4	1040.50	8.43	4	1041.75	21.85	4

Controls from group(s): 1
Data homogeneous by Bartlett's Test — Test of significance is Dunnett's Test
(n) Data nonhomogeneous by Bartlett's Test — Modified t test of significance
* Indicates group mean is significantly different from control at level P = .05
** Indicates group mean is significantly different from control at level P = .01

Roma Tox Centre S.p.A
(Dr. Alfredo Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 9C - Urinalysis - Week 13 of treatment - Mean data

STUDY NO.: 235-003-009

MALES

Parameter/units	Study Day	Control Mean	Control SD	Control N	Group 2 Mean	Group 2 SD	Group 2 N	Group 3 Mean	Group 3 SD	Group 3 N	Group 4 Mean	Group 4 SD	Group 4 N
URINE VOLUME (OVERNIGHT) ml	87	147.0	82.1	4	227.5	70.9	4	152.0	105.3	4	156.5	86.3	4
SPECIFIC GRAVITY g/l	87	1054.00	11.58	4	1041.50	13.18	4	1044.75	19.57	4	1033.25	14.05	4

Controls from group(s): 1
Data homogeneous by Bartlett's Test — Test of significance is Dunnett's Test
(n) Data nonhomogeneous by Bartlett's Test — Modified t test of significance
* Indicates group mean is significantly different from control at level P = .05
** Indicates group mean is significantly different from control at level P = .01

LIFE Chemicals Laboratory
Roma Toxicology Centre S.p.A.
(Dr. Alfio Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 9C - Urinalysis - Week 13 of treatment - Mean data

STUDY NO.: 235-003-009

FEMALES

Parameter/units	Study Day	Control Mean	Control SD	Control N	Group 2 Mean	Group 2 SD	Group 2 N	Group 3 Mean	Group 3 SD	Group 3 N	Group 4 Mean	Group 4 SD	Group 4 N
URINE VOLUME (OVERNIGHT) ml	88	124.5	61.6	4	116.0	46.8	4	140.5	56.8	4	117.5	49.8	4
SPECIFIC GRAVITY g/l	88	1043.00	13.56	4	1044.25	9.94	4	1036.25	15.19	4	1039.00	18.09	4

Controls from group(s): 1
Data homogeneous by Bartlett's Test — Test of significance is Dunnett's Test
(n) Data nonhomogeneous by Bartlett's Test — Modified t test of significance
* Indicates group mean is significantly different from control at level P = .05
** Indicates group mean is significantly different from control at level P = .01

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A
(Dr. Alfredo Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 10A - Absolute organ weights (g) - Mean data

STUDY NO.: 235-003-009

MALES

BRAIN Controls from group: 1 Data nonhomogeneous by Bartlett's test (modified T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	81.945	87.610	81.278	77.705
Standard deviation	1.844	8.075	2.503	8.946
Group diff.@ P=.05		13.215	4.960	14.574
Group diff.@ P=.01		24.500	9.195	27.020

Analysis of variance: ratio = 1.73 Df = 3/ 12 probability = 0.213
Note: a * indicates group mean is significantly different from control at level of significance shown.

PITUITARY Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.0733	0.0705	0.0713	0.0700
Standard deviation	0.0079	0.0134	0.0117	0.0107
Group diff.@ P=.05		0.0211	0.0211	0.0211
Group diff.@ P=.01		0.0281	0.0281	0.0281

Analysis of variance: ratio = 0.07 Df = 3/ 12 probability = 0.972
Note: a * indicates group mean is significantly different from control at level of significance shown.

LIFE SCIENCES RESEARCH
Roma Toxicology Centre S.p.A.
(Dr. Alfredo Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 10A - Absolute organ weights (g) - Mean data

STUDY NO.: 235-003-009

MALES

HEART Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	88.473	95.905	88.823	90.080
Standard deviation	2.713	8.984	10.973	7.471
Group diff.@ P=.05		15.423	15.423	15.423
Group diff.@ P=.01		20.587	20.587	20.587

Analysis of variance: ratio = 0.72 Df = 3/ 12 probability = 0.559
Note: a * indicates group mean is significantly different from control at level of significance shown.

LIVER Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	324.350	347.955	332.363	302.663
Standard deviation	24.713	28.555	45.019	49.791
Group diff.@ P=.05		73.068	73.068	73.068
Group diff.@ P=.01		97.535	97.535	97.535

Analysis of variance: ratio = 0.96 Df = 3/ 12 probability = 0.445
Note: a * indicates group mean is significantly different from control at level of significance shown.

LIFE SCIENCE RESEARCH
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FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 10A - Absolute organ weights (g) - Mean data

STUDY NO.: 235-003-009

MALES

LEFT KIDNEY Controls from group: 1 Data nonhomogeneous by Bartlett's test (modified T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	25.603	29.910	24.920	28.760
Standard deviation	2.541	13.757	2.202	15.781
Group diff.@ P=.05		22.321	5.365	25.504
Group diff.@ P=.01		41.383	9.946	47.285

Analysis of variance: ratio = 0.21 Df = 3/ 12 probability = 0.888
Note: a * indicates group mean is significantly different from control at level of significance shown.

RIGHT KIDNEY Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	3	4	3
Mean	25.023	23.607	24.530	20.557
Standard deviation	1.690	0.732	1.196	1.242
Group diff.@ P=.05		2.750	2.546	2.750*
Group diff.@ P=.01		3.734	3.457	3.734*

Analysis of variance: ratio = 7.70 Df = 3/ 10 probability = 0.006
Note: a * indicates group mean is significantly different from control at level of significance shown.

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(Dr. Alfredo Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 10A - Absolute organ weights (g) - Mean data

STUDY NO.: 235-003-009

MALES

LEFT THYROID LOBE Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.4518	0.4128	0.3580	0.4073
Standard deviation	0.0388	0.0942	0.0968	0.0907
Group diff.@ P=.05		0.1587	0.1587	0.1587
Group diff.@ P=.01		0.2119	0.2119	0.2119

Analysis of variance: ratio = 0.85 Df = 3/ 12 probability = 0.497
Note: a * indicates group mean is significantly different from control at level of significance shown.

RIGHT THYROID LOBE Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.4950	0.4848	0.3650	0.4323
Standard deviation	0.0514	0.1013	0.1250	0.0226
Group diff.@ P=.05		0.1616	0.1616	0.1616
Group diff.@ P=.01		0.2157	0.2157	0.2157

Analysis of variance: ratio = 1.96 Df = 3/ 12 probability = 0.174
Note: a * indicates group mean is significantly different from control at level of significance shown.

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A.

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 10A - Absolute organ weights (g) - Mean data

STUDY NO.: 235-003-009

MALES

LEFT ADRENAL Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.5280	0.5353	0.4743	0.5153
Standard deviation	0.1104	0.0799	0.0363	0.0314
Group diff.@ P=.05		0.1371	0.1371	0.1371
Group diff.@ P=.01		0.1830	0.1830	0.1830

Analysis of variance: ratio = 0.57 Df = 3/ 12 probability = 0.649
Note: a * indicates group mean is significantly different from control at level of significance shown.

RIGHT ADRENAL Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.5048	0.6113	0.5388	0.5978
Standard deviation	0.0579	0.1584	0.0652	0.1312
Group diff.@ P=.05		0.2120	0.2120	0.2120
Group diff.@ P=.01		0.2829	0.2829	0.2829

Analysis of variance: ratio = 0.80 Df = 3/ 12 probability = 0.518
Note: a * indicates group mean is significantly different from control at level of significance shown.

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(Dr. Alfredo Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 10A - Absolute organ weights (g) - Mean data

STUDY NO.: 235-003-009

MALES

LEFT TESTIS Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	9.0035	8.0015	7.9633	8.6870
Standard deviation	0.7980	1.2453	1.8963	1.2360
Group diff.@ P=.05		2.5652	2.5652	2.5652
Group diff.@ P=.01		3.4242	3.4242	3.4242

Analysis of variance: ratio = 0.58 Df = 3/ 12 probability = 0.642
Note: a * indicates group mean is significantly different from control at level of significance shown.

RIGHT TESTIS Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	9.6293	7.9548	7.6028	8.5528
Standard deviation	0.7525	0.9137	1.9722	0.4622
Group diff.@ P=.05		2.2258	2.2258	2.2258
Group diff.@ P=.01		2.9710	2.9710	2.9710

Analysis of variance: ratio = 2.29 Df = 3/ 12 probability = 0.130
Note: a * indicates group mean is significantly different from control at level of significance shown.

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FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 10A - Absolute organ weights (g) - Mean data

STUDY NO.: 235-003-009

MALES

SPLEEN Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	33.585	31.823	27.148	29.427
Standard deviation	5.626	2.824	3.290	7.395
Group diff.@ P=.05		9.727	9.727	9.727
Group diff.@ P=.01		12.985	12.985	12.985

Analysis of variance: ratio = 1.20 Df = 3/ 12 probability = 0.352
Note: a * indicates group mean is significantly different from control at level of significance shown.

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FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 10A - Absolute organ weights (g) - Mean data

STUDY NO.: 235-003-009

FEMALES

BRAIN Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	79.331	78.670	78.698	76.850
Standard deviation	1.917	7.329	6.090	2.312
Group diff.@ P=.05		9.478	9.478	9.478
Group diff.@ P=.01		12.652	12.652	12.652

Analysis of variance: ratio = 0.18 Df = 3/ 12 probability = 0.904
Note: a * indicates group mean is significantly different from control at level of significance shown.

PITUITARY Controls from group: 1 Data nonhomogeneous by Bartlett's test (modified T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.1705	0.0658	0.0713	0.0708
Standard deviation	0.2024	0.0075	0.0138	0.0068
Group diff.@ P=.05		0.3231	0.3236	0.3231
Group diff.@ P=.01		0.5990	0.6000	0.5990

Analysis of variance: ratio = 1.00 Df = 3/ 12 probability = 0.429
Note: a * indicates group mean is significantly different from control at level of significance shown.

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FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 10A - Absolute organ weights (g) - Mean data

STUDY NO.: 235-003-009

FEMALES

HEART Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	72.243	75.490	77.693	72.573
Standard deviation	14.404	7.981	6.986	5.742
Group diff.@ P=.05		17.823	17.823	17.823
Group diff.@ P=.01		23.791	23.791	23.791

Analysis of variance: ratio = 0.30 Df = 3/ 12 probability = 0.824
Note: a * indicates group mean is significantly different from control at level of significance shown.

LIVER Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	285.143	256.520	280.325	251.478
Standard deviation	38.667	28.070	28.717	17.743
Group diff.@ P=.05		55.501	55.501	55.501
Group diff.@ P=.01		74.086	74.086	74.086

Analysis of variance: ratio = 1.32 Df = 3/ 12 probability = 0.312
Note: a * indicates group mean is significantly different from control at level of significance shown.

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 10A - Absolute organ weights (g) - Mean data

STUDY NO.: 235-003-009

FEMALES

LEFT KIDNEY Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	24.120	21.052	18.940	20.080
Standard deviation	4.544	2.495	2.456	1.461
Group diff.@ P=.05		5.616	5.616	5.616
Group diff.@ P=.01		7.496	7.496	7.496

Analysis of variance: ratio = 2.26 Df = 3/ 12 probability = 0.134
Note: a * indicates group mean is significantly different from control at level of significance shown.

RIGHT KIDNEY Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	23.058	19.820	18.393	21.133
Standard deviation	3.915	1.773	2.490	2.428
Group diff.@ P=.05		5.245	5.245	5.245
Group diff.@ P=.01		7.001	7.001	7.001

Analysis of variance: ratio = 2.06 Df = 3/ 12 probability = 0.158
Note: a * indicates group mean is significantly different from control at level of significance shown.

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FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 10A - Absolute organ weights (g) - Mean data

STUDY NO.: 235-003-009

FEMALES

LEFT THYROID LOBE Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.3480	0.3583	0.3283	0.3675
Standard deviation	0.0380	0.0449	0.0715	0.0261
Group diff.@ P=.05		0.0912	0.0912	0.0912
Group diff.@ P=.01		0.1218	0.1218	0.1218

Analysis of variance: ratio = 0.49 Df = 3/ 12 probability = 0.698
Note: a * indicates group mean is significantly different from control at level of significance shown.

RIGHT THYROID LOBE Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.3435	0.3490	0.3285	0.3448
Standard deviation	0.0169	0.0549	0.1097	0.0946
Group diff.@ P=.05		0.1479	0.1479	0.1479
Group diff.@ P=.01		0.1974	0.1974	0.1974

Analysis of variance: ratio = 0.05 Df = 3/ 12 probability = 0.978
Note: a * indicates group mean is significantly different from control at level of significance shown.

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(Dr. Alfredo Nanzita)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 10A - Absolute organ weights (g) - Mean data

STUDY NO.: 235-003-009

FEMALES

LEFT ADRENAL Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.5435	0.4960	0.4868	0.5255
Standard deviation	0.0562	0.1355	0.0390	0.0493
Group diff.@ P=.05		0.1514	0.1514	0.1514
Group diff.@ P=.01		0.2021	0.2021	0.2021

Analysis of variance: ratio = 0.43 Df = 3/ 12 probability = 0.736
Note: a * indicates group mean is significantly different from control at level of significance shown.

RIGHT ADRENAL Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.5155	0.5108	0.5488	0.5243
Standard deviation	0.0606	0.1225	0.0841	0.0805
Group diff.@ P=.05		0.1704	0.1704	0.1704
Group diff.@ P=.01		0.2274	0.2274	0.2274

Analysis of variance: ratio = 0.14 Df = 3/ 12 probability = 0.930
Note: a * indicates group mean is significantly different from control at level of significance shown.

Roma Toxicology Centre S.p.A.

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 10A - Absolute organ weights (g) - Mean data

STUDY NO.: 235-003-009

FEMALES

LEFT OVARY Controls from group: 1 Data nonhomogeneous by Bartlett's test (modified T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.8645	0.3605	0.4558	0.3735
Standard deviation	1.0780	0.0470	0.2100	0.0965
Group diff.@ P=.05		1.7216	1.7523	1.7268
Group diff.@ P=.01		3.1918	3.2487	3.2015

Analysis of variance: ratio = 0.74 Df = 3/ 12 probability = 0.549
Note: a * indicates group mean is significantly different from control at level of significance shown.

RIGHT OVARY Controls from group: 1 Data nonhomogeneous by Bartlett's test (modified T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.5798	0.3283	0.4388	0.3473
Standard deviation	0.5656	0.0342	0.1649	0.0915
Group diff.@ P=.05		0.9041	0.9400	0.9142
Group diff.@ P=.01		1.6762	1.7428	1.6948

Analysis of variance: ratio = 0.59 Df = 3/ 12 probability = 0.635
Note: a * indicates group mean is significantly different from control at level of significance shown.

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A.

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 10A - Absolute organ weights (g) - Mean data

STUDY NO.: 235-003-009

FEMALES

SPLEEN Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	24.210	35.155	28.550	28.645
Standard deviation	2.644	9.329	5.634	4.160
Group diff.@ P=.05		11.347	11.347	11.347
Group diff.@ P=.01		15.147	15.147	15.147

Analysis of variance: ratio = 2.28 Df = 3/ 12 probability = 0.131
Note: a * indicates group mean is significantly different from control at level of significance shown.

UTERUS Controls from group: 1 Data nonhomogeneous by Bartlett's test (modified T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	4.2197	1.7978	4.7127	1.5928
Standard deviation	4.5687	0.4255	5.4047	0.2790
Group diff.@ P=.05		7.3212	11.2918	7.3032
Group diff.@ P=.01		13.5733	20.9346	13.5400

Analysis of variance: ratio = 0.83 Df = 3/ 12 probability = 0.505
Note: a * indicates group mean is significantly different from control at level of significance shown.

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Rome Toxicology Centre S.p.A.

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 10B - Relative organ weights+ - Mean data

STUDY NO.: 235-003-009

MALES

BRAIN — Controls from group: 1 — Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.709	0.721	0.736	0.732
Standard deviation	0.028	0.073	0.079	0.033
Group diff.@ P=.05		0.110	0.110	0.110
Group diff.@ P=.01		0.147	0.147	0.147

Analysis of variance: ratio = 0.18 Df = 3/ 12 probability = 0.908
Note: a * indicates group mean is significantly different from control at level of significance shown.

PITUITARY — Controls from group: 1 — Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.0006	0.0006	0.0006	0.0007
Standard deviation	0.0001	0.0001	0.0001	0.0001
Group diff.@ P=.05		0.0002	0.0002	0.0002
Group diff.@ P=.01		0.0003	0.0003	0.0003

Analysis of variance: ratio = 0.44 Df = 3/ 12 probability = 0.730
Note: a * indicates group mean is significantly different from control at level of significance shown.

+ Expressed as % organ to body weight ratio

Rhône Tox Drug Centre S.p.A.

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 10B - Relative organ weights+ - Mean data

STUDY NO.: 235-003-009

MALES

HEART Controls from group: 1 Data nonhomogeneous by Bartlett's test (modified T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.765	0.787	0.803	0.853
Standard deviation	0.016	0.033	0.114	0.080
Group diff.@ P=.05		0.059	0.183	0.130
Group diff.@ P=.01		0.110	0.340	0.240

Analysis of variance: ratio = 1.09 Df = 3/ 12 probability = 0.393
Note: a * indicates group mean is significantly different from control at level of significance shown.

LIVER Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	2.808	2.864	2.995	2.839
Standard deviation	0.261	0.261	0.366	0.193
Group diff.@ P=.05		0.526	0.526	0.526
Group diff.@ P=.01		0.702	0.702	0.702

Analysis of variance: ratio = 0.35 Df = 3/ 12 probability = 0.790
Note: a * indicates group mean is significantly different from control at level of significance shown.

+ Expressed as % organ to body weight ratio

LIFE SCIENCE RESEARCH
Rome Texas

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 10B - Relative organ weights+ - Mean data

STUDY NO.: 235-003-009

MALES

LEFT KIDNEY Controls from group: 1 Data nonhomogeneous by Bartlett's test (modified T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.222	0.243	0.224	0.265
Standard deviation	0.023	0.097	0.009	0.118
Group diff.@ P=.05		0.159	0.040	0.193
Group diff.@ P=.01		0.295	0.074	0.357

Analysis of variance: ratio = 0.27 Df = 3/ 12 probability = 0.849
Note: a * indicates group mean is significantly different from control at level of significance shown.

RIGHT KIDNEY Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	3	4	3
Mean	0.216	0.199	0.222	0.203
Standard deviation	0.016	0.002	0.023	0.026
Group diff.@ P=.05		0.041	0.038	0.041
Group diff.@ P=.01		0.056	0.051	0.056

Analysis of variance: ratio = 1.07 Df = 3/ 10 probability = 0.406
Note: a * indicates group mean is significantly different from control at level of significance shown.

+ Expressed as % organ to body weight ratio

LIFE SCIENCE RESEARCH
Rama Toxicology Centre S.p.A.

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 10B - Relative organ weights+ - Mean data

STUDY NO.: 235-003-009

MALES

LEFT THYROID LOBE Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.0039	0.0034	0.0032	0.0039
Standard deviation	0.0004	0.0006	0.0006	0.0011
Group diff.@ P=.05		0.0013	0.0013	0.0013
Group diff.@ P=.01		0.0018	0.0018	0.0018

Analysis of variance: ratio = 1.08 Df = 3/ 12 probability = 0.396
Note: a * indicates group mean is significantly different from control at level of significance shown.

RIGHT THYROID LOBE Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.0043	0.0040	0.0032	0.0041
Standard deviation	0.0004	0.0006	0.0009	0.0005
Group diff.@ P=.05		0.0012	0.0012	0.0012
Group diff.@ P=.01		0.0016	0.0016	0.0016

Analysis of variance: ratio = 2.22 Df = 3/ 12 probability = 0.138
Note: a * indicates group mean is significantly different from control at level of significance shown.

+ Expressed as % organ to body weight ratio

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FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 10B - Relative organ weights+ - Mean data

STUDY NO.: 235-003-009

MALES

LEFT ADRENAL Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.0046	0.0044	0.0043	0.0049
Standard deviation	0.0010	0.0005	0.0008	0.0007
Group diff.@ P=.05		0.0015	0.0015	0.0015
Group diff.@ P=.01		0.0020	0.0020	0.0020

Analysis of variance: ratio = 0.46 Df = 3/ 12 probability = 0.721
Note: a * indicates group mean is significantly different from control at level of significance shown.

RIGHT ADRENAL Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.0044	0.0050	0.0049	0.0056
Standard deviation	0.0006	0.0010	0.0011	0.0008
Group diff.@ P=.05		0.0017	0.0017	0.0017
Group diff.@ P=.01		0.0022	0.0022	0.0022

Analysis of variance: ratio = 1.30 Df = 3/ 12 probability = 0.320
Note: a * indicates group mean is significantly different from control at level of significance shown.

+ Expressed as % organ to body weight ratio

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FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 10B - Relative organ weights+ - Mean data

STUDY NO.: 235-003-009

MALES

LEFT TESTIS Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.0779	0.0656	0.0707	0.0817
Standard deviation	0.0078	0.0083	0.0107	0.0047
Group diff.@ P=.05		0.0154	0.0154	0.0154
Group diff.@ P=.01		0.0206	0.0206	0.0206

Analysis of variance: ratio = 3.11 Df = 3/ 12 probability = 0.066
Note: a * indicates group mean is significantly different from control at level of significance shown.

RIGHT TESTIS Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.0832	0.0654	0.0674	0.0811
Standard deviation	0.0052	0.0067	0.0116	0.0079
Group diff.@ P=.05		0.0155*	0.0155*	0.0155
Group diff.@ P=.01		0.0207	0.0207	0.0207

Analysis of variance: ratio = 5.05 Df = 3/ 12 probability = 0.017
Note: a * indicates group mean is significantly different from control at level of significance shown.

+ Expressed as % organ to body weight ratio

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FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 10B - Relative organ weights+ - Mean data

STUDY NO.: 235-003-009

MALES

SPLEEN Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.292	0.261	0.246	0.274
Standard deviation	0.059	0.017	0.038	0.042
Group diff.@ P=.05		0.079	0.079	0.079
Group diff.@ P=.01		0.106	0.106	0.106

Analysis of variance: ratio = 0.88 Df = 3/ 12 probability = 0.482
Note: a * indicates group mean is significantly different from control at level of significance shown.

+ Expressed as % organ to body weight ratio

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(Dr. Alfredo Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 10B - Relative organ weights+ - Mean data

STUDY NO.: 235-003-009

FEMALES

BRAIN Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.828	0.875	0.848	0.829
Standard deviation	0.096	0.128	0.075	0.020
Group diff.@ P=.05		0.168	0.168	0.168
Group diff.@ P=.01		0.225	0.225	0.225

Analysis of variance: ratio = 0.25 Df = 3/ 12 probability = 0.860
Note: a * indicates group mean is significantly different from control at level of significance shown.

PITUITARY Controls from group: 1 Data nonhomogeneous by Bartlett's test (modified T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.0018	0.0007	0.0008	0.0008
Standard deviation	0.0021	0.0001	0.0001	0.0001
Group diff.@ P=.05		0.0033	0.0033	0.0033
Group diff.@ P=.01		0.0061	0.0061	0.0061

Analysis of variance: ratio = 0.94 Df = 3/ 12 probability = 0.451
Note: a * indicates group mean is significantly different from control at level of significance shown.

+ Expressed as % organ to body weight ratio

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FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 10B - Relative organ weights+ - Mean data

STUDY NO.: 235-003-009

FEMALES

HEART Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.743	0.835	0.835	0.782
Standard deviation	0.103	0.081	0.043	0.056
Group diff.@ P=.05		0.142	0.142	0.142
Group diff.@ P=.01		0.189	0.189	0.189

Analysis of variance: ratio = 1.43 Df = 3/ 12 probability = 0.282
Note: a * indicates group mean is significantly different from control at level of significance shown.

LIVER Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	2.942	2.828	3.011	2.711
Standard deviation	0.126	0.175	0.166	0.178
Group diff.@ P=.05		0.308	0.308	0.308
Group diff.@ P=.01		0.412	0.412	0.412

Analysis of variance: ratio = 2.63 Df = 3/ 12 probability = 0.097
Note: a * indicates group mean is significantly different from control at level of significance shown.

+ Expressed as % organ to body weight ratio

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FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 10B - Relative organ weights+ - Mean data

STUDY NO.: 235-003-009

FEMALES

LEFT THYROID LOBE Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.0036	0.0040	0.0035	0.0040
Standard deviation	0.0006	0.0007	0.0005	0.0003
Group diff.@ P=.05		0.0010	0.0010	0.0010
Group diff.@ P=.01		0.0014	0.0014	0.0014

Analysis of variance: ratio = 0.83 Df = 3/ 12 probability = 0.504
Note: a * indicates group mean is significantly different from control at level of significance shown.

RIGHT THYROID LOBE Controls from group: 1 Data homogeneous by Bartlett's test (Dunnett's T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.0036	0.0038	0.0035	0.0037
Standard deviation	0.0005	0.0003	0.0011	0.0010
Group diff.@ P=.05		0.0015	0.0015	0.0015
Group diff.@ P=.01		0.0020	0.0020	0.0020

Analysis of variance: ratio = 0.13 Df = 3/ 12 probability = 0.939
Note: a * indicates group mean is significantly different from control at level of significance shown.

+ Expressed as % organ to body weight ratio

LIFE SCIENCE RESEARCH

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 10B - Relative organ weights+ - Mean data

STUDY NO.: 235-003-009

FEMALES

LEFT OVARY Controls from group: 1 Data nonhomogeneous by Bartlett's test (modified T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.0081	0.0040	0.0049	0.0040
Standard deviation	0.0091	0.0007	0.0020	0.0010
Group diff.@ P=.05		0.0145	0.0148	0.0145
Group diff.@ P=.01		0.0269	0.0274	0.0270

Analysis of variance: ratio = 0.69 Df = 3/ 12 probability = 0.577
Note: a * indicates group mean is significantly different from control at level of significance shown.

RIGHT OVARY Controls from group: 1 Data nonhomogeneous by Bartlett's test (modified T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.0056	0.0036	0.0047	0.0037
Standard deviation	0.0046	0.0003	0.0015	0.0010
Group diff.@ P=.05		0.0074	0.0077	0.0075
Group diff.@ P=.01		0.0137	0.0143	0.0140

Analysis of variance: ratio = 0.53 Df = 3/ 12 probability = 0.670
Note: a * indicates group mean is significantly different from control at level of significance shown.

+ Expressed as % organ to body weight ratio

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 10B - Relative organ weights+ - Mean data

STUDY NO.: 235-003-009

FEMALES

SPLEEN Controls from group: 1 Data nonhomogeneous by Bartlett's test (modified T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.250	0.382	0.304	0.309
Standard deviation	0.008	0.073	0.035	0.044
Group diff.@ P=.05		0.117*	0.058	0.071
Group diff.@ P=.01		0.216	0.107	0.132

Analysis of variance: ratio = 5.53 Df = 3/ 12 probability = 0.013
Note: a * indicates group mean is significantly different from control at level of significance shown.

UTERUS Controls from group: 1 Data nonhomogeneous by Bartlett's test (modified T test)

Group	Control	2	3	4
Number/group	4	4	4	4
Mean	0.0402	0.0202	0.0478	0.0172
Standard deviation	0.0378	0.0060	0.0519	0.0030
Group diff.@ P=.05		0.0610	0.1024	0.0604
Group diff.@ P=.01		0.1131	0.1898	0.1121

Analysis of variance: ratio = 0.86 Df = 3/ 12 probability = 0.488
Note: a * indicates group mean is significantly different from control at level of significance shown.

+ Expressed as % organ to body weight ratio

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 11 - Macroscopic observations - Group incidence

STUDY NO.: 235-003-009

	-- Males --				-- Females --			
Group:	Control	2	3	4	Control	2	3	4
Number in group:	4	4	4	4	4	4	4	4
Duodenum								
Abnormal area(s)	0	0	0	0	0	0	1	0
Gall Bladder								
Abnormal Contents	0	1	0	2	2	1	1	0
Ileum								
Abnormal colour	0	0	1	0	0	0	0	0
Injection sites								
Abnormal colour	3	4	3	4	1	2	2	3
Inj site control								
Abnormal colour	0	0	0	0	0	0	0	1
Jejunum								
Abnormal Area(s)	0	0	0	0	0	0	1	1
Kidneys								
Abnormal size	0	1	0	1	0	0	0	0
Not present	0	1	0	1	0	0	0	0
Lymph nodes								
Abnormal colour	0	1	2	0	1	1	2	0
Abnormal size	0	0	1	0	0	1	0	0

LIFE SCIENCE RESEARCH

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 11 - Macroscopic observations - Group incidence

STUDY NO.: 235-003-009

	-- Males --				-- Females --			
Group:	Control	2	3	4	Control	2	3	4
Number in group:	4	4	4	4	4	4	4	4
Lungs								
Not collapsed	0	2	0	0	0	0	0	0
Abnormal Area(s)	0	2	3	0	1	0	2	0
Abnormal consistency	0	1	0	0	0	0	0	0
Mesenteric nodes								
Abnormal Colour	0	0	0	0	0	1	1	0
Peribronch nodes								
Abnormal size	0	1	0	0	0	0	0	0
Prostate gland								
Abnormal size	0	1	0	0	0	0	0	0
Skin								
Abnormal Colour	0	0	0	1	0	0	0	0
Abnormal areas	0	0	1	0	0	0	0	0
Submandib nodes								
Abnormal colour	0	0	0	0	1	0	0	0
Spleen								
Abnormal Shape	0	0	0	0	0	1	0	0
Abnormal Area(s)	0	1	0	0	0	0	0	0
Whole body								
No abnormalities detected	1	0	1	0	1	0	1	1

LIFE SCIENCE RESEARCH
Toxicology Centre S.p.A
(Alfredo Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 12 - Microscopic observation - Group incidence

STUDY NO.: 235-003-009

Controls from group(s): 1

Tissues With Diagnoses	Animal sex:	-- Animals Affected -- Males --				-- Females --			
	Group:	Control	2	3	4	Control	2	3	4
	No. in group:	4	4	4	4	4	4	4	4
Adrenals	Number examined:	4	4	4	4	4	4	4	4
GRANULOMA/S		0	0	0	0	1	0	0	0
Caecum	Number examined:	4	4	4	4	4	4	4	4
MUCOSAL CONGESTION		0	1	0	0	0	0	0	0
Colon	Number examined:	4	4	4	4	4	4	4	4
MUCOSAL CONGESTION		0	1	0	1	0	0	0	0
Duodenum	Number examined:	4	4	4	4	4	4	4	4
NO SIGNIFICANT LESION		0	0	0	0	0	0	1	0
Gall Bladder	Number examined:	4	4	4	4	4	4	4	4
NO SIGNIFICANT LESION		0	1	0	1	2	1	1	0
MUCOSAL CONGESTION		0	0	0	1	0	0	0	0
Ileum	Number examined:	4	4	4	4	4	4	4	4
MUCOSAL CONGESTION		0	0	1	0	0	0	0	0
Inj site control	Number examined:	4	4	4	4	4	4	4	4
HAEMORRHAGE		0	0	2	0	0	0	0	0
NO SIGNIFICANT LESION		0	0	0	0	0	0	0	1
Injection sites	Number examined:	4	4	4	4	4	4	4	4
SCAB/S		1	0	0	0	0	0	0	0
HAEMORRHAGE		3	3	2	4	2	4	3	2
ACUTE INFLAMMATION		1	0	0	2	0	0	0	0
LYMPHOCYTIC INFILTRATION		1	0	0	0	1	0	0	0
NO SIGNIFICANT LESION		0	1	2	0	0	0	0	0
CHRONIC INFLAMMATION		0	0	0	0	0	0	1	1

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 12 - Microscopic observation - Group incidence

STUDY NO.: 235-003-009

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Females --			
	Group:	Control	2	3	4	Control	2	3	4
Tissues With Diagnoses	No. in group:	4	4	4	4	4	4	4	4
Jejunum	Number examined:	4	4	4	4	4	4	4	4
MUCOSAL CONGESTION		0	0	0	0	0	0	1	1
VILLOUS NECROSIS		0	0	0	0	0	0	1	0
Kidneys	Number examined:	4	4	4	4	4	4	4	4
LYMPHOCYTIC INFILTRATION		1	0	0	1	0	0	0	0
GRANULOMA/S		0	0	0	0	1	0	0	0
HYPERPLASIA		0	1	0	1	0	0	0	0
CHRONIC INTERSTITIAL NEPHRITIS		0	0	1	0	0	0	0	1
TUBULAR DILATATION		0	0	0	1	0	0	0	0
Liver	Number examined:	4	4	4	4	4	3	4	4
CHRONIC INFLAMMATION		2	0	1	0	0	0	0	1
PERIVASCULAR LYMPHOCYTIC INFILTRATION		0	0	0	0	0	1	0	0
Lungs	Number examined:	4	4	4	4	4	4	4	4
CHRONIC INFLAMMATION		1	0	1	3	3	0	0	0
PERIVASCULAR LYMPHOCYTIC INFILTRATION		0	0	1	0	1	0	0	0
NO SIGNIFICANT LESION		0	2	0	0	0	0	2	0
BRONCHOPNEUMONIA		0	0	1	0	0	0	0	0
BLOOD IN BRONCHI/ALVEOLI		0	1	1	0	0	0	0	0
Mesenteric nodes	Number examined:	4	4	4	4	4	4	4	4
NO SIGNIFICANT LESION		0	0	0	0	0	1	0	0
HAEMORRHAGE		0	0	0	0	0	0	1	0
Parathyroid gl.	Number examined:	4	4	4	4	4	4	4	4
BRANCHIAL CYST/S		0	0	3	0	0	0	0	1

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FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

TABLE 12 - Microscopic observation - Group incidence

STUDY NO.: 235-003-009

Controls from group(s): 1	Animal sex:	-- Animals Affected --							
		-- Males --				-- Females --			
	Group:	Control	2	3	4	Control	2	3	4
Tissues With Diagnoses	No. in group:	4	4	4	4	4	4	4	4
Peribronc.nodes .....Number examined:		4	4	4	4	4	4	4	4
NO SIGNIFICANT LESION		0	1	0	0	0	0	0	0
Pituitary .....Number examined:		3	4	4	4	4	4	4	4
CRANIO-PHARYNGEAL CYST/S		0	1	1	0	0	1	0	0
CHRONIC INFLAMMATION		0	0	1	0	0	0	0	0
Prostate gland .....Number examined:		4	4	4	4	4	4	4	4
HYPOPLASIA		0	1	0	0	0	0	0	0
Submandibular ln .....Number examined:		4	4	4	4	4	4	4	4
BROWN PIGMENTATION		0	0	1	2	1	1	0	0
Skin .....Number examined:		4	4	4	4	4	4	4	4
ULCERATION		0	0	1	0	0	0	0	0
ACUTE INFLAMMATION		0	0	1	0	0	0	0	0
SCAB FORMATION		0	0	1	0	0	0	0	0
NO SIGNIFICANT LESION		0	0	0	1	0	0	0	0
Spleen .....Number examined:		4	4	4	4	4	4	4	4
HAEMORRHAGE		0	1	0	0	0	0	0	0
NO SIGNIFICANT LESION		0	0	0	0	0	1	0	0
B- HAEMANGIOMA		0	0	1	0	0	0	0	0
Thyroid gland .....Number examined:		4	4	4	4	4	4	4	4
GRANULOMA		0	0	1	0	0	0	0	0
Lymph nodes .....Number examined:		0	1	2	0	1	2	2	0
HAEMORRHAGE		0	1	2	0	1	1	1	0
NO SIGNIFICANT LESION		0	0	1	0	0	1	1	0

Note: Entries flagged with a - (minus) are significantly different from control at the 0.05 level using the Kolmogorov-Smirnov two tailed test.

Section 4)

Attachment no. 3

LSR-RTC S.p.A.:

Chronic Toxicity of Fructose-1,6-Diphosphate,

1991

VOL. II

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DATE 15/5/1991

FDP

13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

LSR-RTC Study No.: 235-003-009

LSR-RTC Report No.: 235-003-009/T/080/90

FINAL REPORT

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TO: ISTITUTO RICERCHE FARMACOBIOLOGICHE
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FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 1 - Body weights (kg) - Individual data

STUDY NO.: 235-003-009

MALES

Animal number	Group		Day of Study -14	-7	1	4	8	11	15
2350002	1		8.98	9.22	9.38	9.56	9.62	9.74	9.98
2350004	1		8.44	8.77	9.36	9.26	9.52	9.78	9.86
2350006	1		8.64	8.48	8.89	9.32	9.72	9.41	9.49
2350008	1		8.10	7.98	8.05	8.10	8.32	8.58	8.60
		N	4	4	4	4	4	4	4
		Mean	8.540	8.613	8.920	9.060	9.295	9.378	9.483
		SD	0.368	0.520	0.623	0.653	0.655	0.557	0.624
2350010	2		8.54	8.86	9.14	9.38	9.56	9.80	10.05
2350012	2		9.00	9.00	9.32	9.38	9.58	9.64	9.67
2350014	2		8.64	8.70	9.05	9.10	9.32	9.62	9.47
2350016	2		8.40	8.70	8.38	8.40	8.60	8.71	8.72
		N	4	4	4	4	4	4	4
		Mean	8.645	8.815	8.973	9.065	9.265	9.443	9.478
		SD	0.256	0.145	0.411	0.463	0.459	0.495	0.559
2350018	3		7.42	7.28	7.92	8.21	8.44	8.70	8.81
2350020	3		8.84	8.60	9.36	9.38	9.70	9.74	9.87
2350022	3		7.70	7.18	7.54	7.56	7.84	7.99	7.99
2350024	3		8.46	8.50	8.91	8.94	9.20	9.45	9.44
		N	4	4	4	4	4	4	4
		Mean	8.105	7.890	8.433	8.523	8.795	8.970	9.028
		SD	0.658	0.764	0.846	0.803	0.821	0.787	0.817
2350026	4		8.54	8.57	9.04	9.16	9.34	9.38	9.43
2350028	4		9.00	8.83	9.26	9.36	9.48	9.56	9.81
2350030	4		7.52	7.16	7.55	7.68	7.80	8.03	7.86
2350032	4		8.68	8.72	8.89	8.94	9.10	9.16	9.15
		N	4	4	4	4	4	4	4
		Mean	8.435	8.320	8.685	8.785	8.930	9.033	9.063
		SD	0.640	0.781	0.772	0.756	0.770	0.688	0.846

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Roma Toxicology Centre

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 1 - Body weights (kg) - Individual data

STUDY NO.: 235-003-009

MALES

Animal number	Group		Day of Study 18	22	25	29	36	43	50
2350002	1		10.11	10.29	10.32	10.38	10.54	10.66	10.86
2350004	1		10.00	10.09	10.27	10.22	10.48	10.60	10.98
2350006	1		9.57	10.00	10.32	10.40	10.51	10.58	10.92
2350008	1		8.66	8.86	9.28	9.34	9.32	9.64	9.82
		N	4	4	4	4	4	4	4
		Mean	9.585	9.810	10.047	10.085	10.213	10.370	10.645
		SD	0.659	0.645	0.512	0.503	0.595	0.488	0.552
2350010	2		10.30	10.45	10.61	10.96	11.06	11.38	11.62
2350012	2		9.80	9.96	10.01	10.12	10.47	10.78	10.82
2350014	2		9.84	9.95	10.20	10.34	10.64	10.90	11.02
2350016	2		9.00	9.08	9.26	9.38	9.24	9.80	9.96
		N	4	4	4	4	4	4	4
		Mean	9.735	9.860	10.020	10.200	10.353	10.715	10.855
		SD	0.540	0.570	0.565	0.652	0.782	0.663	0.687
2350018	3		9.02	9.18	9.31	9.64	9.72	10.02	10.25
2350020	3		10.25	10.56	10.34	10.40	10.88	11.18	11.30
2350022	3		8.26	8.52	8.43	8.60	8.62	8.82	8.88
2350024	3		9.55	9.65	9.98	9.96	10.12	10.58	10.87
		N	4	4	4	4	4	4	4
		Mean	9.270	9.478	9.515	9.650	9.835	10.150	10.325
		SD	0.841	0.858	0.840	0.766	0.942	1.005	1.055
2350026	4		9.63	9.69	9.79	9.92	9.96	10.10	10.10
2350028	4		10.15	10.10	10.14	10.40	10.66	10.66	10.94
2350030	4		8.16	8.52	8.56	8.60	8.68	8.88	9.04
2350032	4		9.29	9.55	9.67	9.70	9.68	9.91	10.12
		N	4	4	4	4	4	4	4
		Mean	9.307	9.465	9.540	9.655	9.745	9.888	10.050
		SD	0.843	0.672	0.683	0.762	0.821	0.743	0.779

002

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A.

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 1 - Body weights (kg) - Individual data

STUDY NO.: 235-003-009

MALES

Animal number	Group		Day of Study 57	64	71	78	85	92
2350002	1		11.01	11.68	11.58	11.70	11.78	11.90
2350004	1		10.78	11.06	11.10	11.34	11.28	11.54
2350006	1		11.44	11.68	12.10	11.89	12.20	11.92
2350008	1		10.04	10.38	10.34	10.50	10.86	10.88
		N	4	4	4	4	4	4
		Mean	10.818	11.200	11.280	11.358	11.530	11.560
		SD	0.586	0.620	0.748	0.615	0.584	0.486
2350010	2		12.10	12.26	12.58	12.70	12.80	13.06
2350012	2		11.20	11.28	11.42	11.60	11.74	11.90
2350014	2		11.52	11.80	11.74	11.97	12.34	12.50
2350016	2		10.22	10.51	10.52	10.78	11.20	11.01
		N	4	4	4	4	4	4
		Mean	11.260	11.463	11.565	11.762	12.020	12.118
		SD	0.787	0.751	0.851	0.799	0.698	0.877
2350018	3		10.62	11.02	11.18	11.30	11.34	11.52
2350020	3		11.36	11.69	12.14	12.32	12.66	12.68
2350022	3		9.37	9.24	9.66	9.46	9.78	9.48
2350024	3		11.06	11.48	11.48	11.66	11.90	12.00
		N	4	4	4	4	4	4
		Mean	10.602	10.858	11.115	11.185	11.420	11.420
		SD	0.876	1.114	1.050	1.225	1.220	1.378
2350026	4		10.38	10.68	10.62	10.76	10.90	11.24
2350028	4		11.56	11.80	11.42	11.72	11.70	11.82
2350030	4		9.28	9.42	9.46	9.58	9.72	9.78
2350032	4		10.24	10.40	10.54	10.60	10.62	10.68
		N	4	4	4	4	4	4
		Mean	10.365	10.575	10.510	10.665	10.735	10.880
		SD	0.935	0.979	0.805	0.876	0.817	0.869

003

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 1 - Body weights (kg) - Individual data

STUDY NO.: 235-003-009

FEMALES

Animal number	Group		Day of Study -14	-7	1	4	8	11	15
2350001	1		6.96	7.36	7.70	7.64	8.19	8.06	7.87
2350003	1		7.34	7.57	7.70	7.82	8.02	7.84	7.84
2350005	1		7.86	7.84	8.02	8.50	8.60	8.61	8.60
2350007	1		7.80	8.12	8.44	8.40	8.20	8.25	8.53
		N	4	4	4	4	4	4	4
		Mean	7.490	7.723	7.965	8.090	8.253	8.190	8.210
		SD	0.423	0.330	0.351	0.424	0.246	0.326	0.411
2350009	2		6.62	6.38	6.38	6.50	6.68	6.72	6.79
2350011	2		8.36	8.00	8.26	8.32	8.46	8.54	8.56
2350013	2		7.68	7.62	7.73	7.62	7.86	7.93	8.00
2350015	2		7.02	7.00	7.12	7.26	7.42	7.63	7.55
		N	4	4	4	4	4	4	4
		Mean	7.420	7.250	7.373	7.425	7.605	7.705	7.725
		SD	0.764	0.711	0.809	0.758	0.750	0.758	0.748
2350017	3		7.60	7.82	7.92	8.10	8.46	8.48	8.72
2350019	3		7.96	8.06	8.08	8.18	8.38	8.46	8.60
2350021	3		7.20	7.48	7.44	7.68	7.62	7.35	7.68
2350023	3		6.70	6.68	6.95	6.92	6.84	7.13	6.93
		N	4	4	4	4	4	4	4
		Mean	7.365	7.510	7.598	7.720	7.825	7.855	7.983
		SD	0.541	0.602	0.510	0.577	0.758	0.716	0.842
2350025	4		7.00	7.22	7.52	7.54	7.86	7.88	7.84
2350027	4		8.02	8.25	8.12	8.10	8.22	8.48	8.50
2350029	4		7.52	7.54	7.60	7.68	7.76	7.83	7.76
2350031	4		7.54	7.40	7.77	7.80	7.94	7.68	7.86
		N	4	4	4	4	4	4	4
		Mean	7.520	7.602	7.753	7.780	7.945	7.968	7.990
		SD	0.417	0.451	0.266	0.238	0.198	0.352	0.343

001

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A.

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 1 - Body weights (kg) - Individual data

STUDY NO.: 235-003-009

FEMALES

Animal number	Group		Day of Study 18	22	25	29	36	43	50
2350001	1		7.89	8.21	8.61	8.50	8.70	8.67	9.08
2350003	1		8.04	7.94	7.96	8.00	8.08	8.08	8.30
2350005	1		8.80	8.90	9.09	9.22	9.22	9.64	9.88
2350007	1		8.71	8.89	8.82	8.98	9.14	9.30	9.50
		N	4	4	4	4	4	4	4
		Mean	8.360	8.485	8.620	8.675	8.785	8.923	9.190
		SD	0.462	0.486	0.482	0.540	0.523	0.691	0.677
2350009	2		7.09	7.26	7.38	7.34	7.35	7.46	7.74
2350011	2		8.83	8.80	8.94	9.02	9.12	9.32	9.43
2350013	2		8.20	8.22	8.26	8.40	8.68	8.82	9.12
2350015	2		7.70	7.85	7.74	7.92	8.02	8.14	8.52
		N	4	4	4	4	4	4	4
		Mean	7.955	8.033	8.080	8.170	8.293	8.435	8.703
		SD	0.739	0.647	0.678	0.713	0.774	0.810	0.745
2350017	3		8.75	9.04	9.08	9.26	9.40	9.72	9.74
2350019	3		8.89	8.65	8.72	8.82	8.96	9.12	9.46
2350021	3		7.96	8.08	8.20	8.36	8.32	8.60	8.82
2350023	3		6.96	7.14	7.09	7.08	6.98	7.24	7.20
		N	4	4	4	4	4	4	4
		Mean	8.140	8.227	8.273	8.380	8.415	8.670	8.805
		SD	0.887	0.825	0.867	0.941	1.054	1.057	1.137
2350025	4		8.27	8.22	8.31	8.14	8.30	8.26	8.34
2350027	4		8.45	8.90	8.91	8.96	8.72	8.84	8.94
2350029	4		8.07	8.22	8.24	8.28	8.10	8.20	8.46
2350031	4		8.26	7.64	8.10	7.90	8.40	8.48	8.24
		N	4	4	4	4	4	4	4
		Mean	8.263	8.246	8.390	8.320	8.380	8.445	8.495
		SD	0.155	0.515	0.357	0.455	0.259	0.290	0.310

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A.
Dr. Alfredo Nunziata

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 1 - Body weights (kg) - Individual data

STUDY NO.: 235-003-009

FEMALES

Animal number	Group		Day of Study 57	64	71	78	85	92
2350001	1		8.74	9.26	9.24	9.02	9.20	9.22
2350003	1		8.14	8.44	8.30	8.44	8.32	8.34
2350005	1		9.90	10.14	10.62	10.66	11.22	11.40
2350007	1		9.61	9.86	9.86	10.02	9.90	10.00
		N	4	4	4	4	4	4
		Mean	9.097	9.425	9.505	9.535	9.660	9.740
		SD	0.806	0.752	0.982	0.994	1.225	1.298
2350009	2		7.56	7.88	7.92	7.70	7.80	7.88
2350011	2		9.52	9.86	10.04	10.20	10.38	10.20
2350013	2		9.20	9.50	9.60	9.80	9.84	9.88
2350015	2		8.74	8.92	9.10	9.12	9.46	9.24
		N	4	4	4	4	4	4
		Mean	8.755	9.040	9.165	9.205	9.370	9.300
		SD	0.859	0.865	0.915	1.098	1.113	1.027
2350017	3		9.66	10.22	10.06	10.10	10.30	10.20
2350019	3		9.36	9.54	9.64	9.72	9.56	9.70
2350021	3		8.80	9.01	9.40	9.42	9.58	9.64
2350023	3		7.26	7.60	7.80	7.82	7.78	7.60
		N	4	4	4	4	4	4
		Mean	8.770	9.093	9.225	9.265	9.305	9.285
		SD	1.068	1.111	0.988	1.003	1.073	1.151
2350025	4		8.36	8.60	9.08	9.14	8.98	9.20
2350027	4		9.26	9.36	9.38	9.50	9.72	9.58
2350029	4		8.58	8.68	9.01	8.97	9.20	9.00
2350031	4		8.62	8.78	9.00	8.82	8.90	9.26
		N	4	4	4	4	4	4
		Mean	8.705	8.855	9.118	9.108	9.200	9.260
		SD	0.387	0.345	0.179	0.292	0.369	0.241

LIFE SCIENCE RESEARCH
Roma Toxicology Center S.p.A.

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 2 - Food consumption+ (g/dog/day) - Individual data

STUDY NO.: 235-003-009

MALES

Animal number	Group		Day of Study -7	1	8	15	22	29	36	43
2350002	1		352.4	400.0	400.0	400.0	400.0	400.0	395.7	400.0
2350004	1		336.3	376.0	400.0	400.0	363.7	364.9	361.7	317.7
2350006	1		276.4	357.1	345.4	304.3	326.4	361.6	390.9	301.3
2350008	1		326.4	374.6	396.3	400.0	400.0	400.0	400.0	400.0
		N	4	4	4	4	4	4	4	4
		Mean	322.89	376.93	385.43	376.07	372.54	381.61	387.07	354.75
		SD	32.78	17.61	26.72	47.86	35.18	21.28	17.31	52.68
2350010	2		376.9	386.3	400.0	400.0	400.0	400.0	400.0	400.0
2350012	2		366.9	394.6	400.0	400.0	400.0	400.0	400.0	400.0
2350014	2		346.4	378.3	400.0	400.0	400.0	400.0	400.0	400.0
2350016	2		305.7	400.0	400.0	400.0	400.0	373.7	400.0	400.0
		N	4	4	4	4	4	4	4	4
		Mean	348.96	389.79	400.00	400.00	400.00	393.43	400.00	400.00
		SD	31.49	9.52	0.00	0.00	0.00	13.14	0.00	0.00
2350018	3		289.7	372.3	400.0	391.4	389.6	400.0	400.0	400.0
2350020	3		358.7	394.1	400.0	400.0	400.0	400.0	400.0	400.0
2350022	3		294.7	378.3	400.0	400.0	400.0	400.0	400.0	385.4
2350024	3		344.3	400.0	400.0	400.0	400.0	400.0	400.0	400.0
		N	4	4	4	4	4	4	4	4
		Mean	321.86	386.18	400.00	397.86	397.39	400.00	400.00	396.36
		SD	34.79	13.04	0.00	4.28	5.21	0.00	0.00	7.29
2350026	4		319.6	358.6	400.0	400.0	400.0	400.0	400.0	370.7
2350028	4		365.0	400.0	400.0	400.0	400.0	400.0	400.0	400.0
2350030	4		236.3	372.7	330.4	293.6	341.0	296.6	373.1	323.7
2350032	4		333.9	394.3	400.0	400.0	400.0	400.0	400.0	380.0
		N	4	4	4	4	4	4	4	4
		Mean	313.68	381.39	382.61	373.39	385.25	374.14	393.29	368.61
		SD	54.97	19.22	34.79	53.21	29.50	51.71	13.43	32.33

+ Mean daily food consumption for the previous 7 days

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A.

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 2 - Food consumption+ (g/dog/day) - Individual data

STUDY NO.: 235-003-009

MALES

Animal number	Group		Day of Study 50	57	64	71	78	85	92
2350002	1		400.0	400.0	400.0	400.0	400.0	400.0	400.0
2350004	1		378.3	315.0	363.7	302.6	349.4	323.0	323.4
2350006	1		400.0	400.0	381.0	358.1	365.0	364.3	325.6
2350008	1		400.0	400.0	400.0	400.0	400.0	400.0	400.0
		N	4	4	4	4	4	4	4
		Mean	394.57	378.75	386.18	365.18	378.61	371.82	362.25
		SD	10.86	42.50	17.45	46.17	25.51	36.64	43.60
2350010	2		400.0	400.0	400.0	400.0	400.0	400.0	368.9
2350012	2		400.0	400.0	400.0	400.0	400.0	400.0	395.1
2350014	2		400.0	400.0	400.0	400.0	400.0	400.0	400.0
2350016	2		400.0	400.0	400.0	400.0	400.0	400.0	400.0
		N	4	4	4	4	4	4	4
		Mean	400.00	400.00	400.00	400.00	400.00	400.00	391.00
		SD	0.00	0.00	0.00	0.00	0.00	0.00	14.94
2350018	3		400.0	400.0	400.0	400.0	400.0	324.6	326.7
2350020	3		400.0	400.0	400.0	400.0	400.0	400.0	400.0
2350022	3		400.0	400.0	397.1	397.1	387.1	400.0	384.1
2350024	3		400.0	400.0	400.0	400.0	400.0	400.0	400.0
		N	4	4	4	4	4	4	4
		Mean	400.00	400.00	399.29	399.29	396.79	381.14	377.71
		SD	0.00	0.00	1.44	1.44	6.43	37.71	34.81
2350026	4		394.3	400.0	400.0	400.0	400.0	395.0	343.7
2350028	4		400.0	400.0	400.0	400.0	400.0	400.0	356.4
2350030	4		357.1	363.3	340.6	327.9	316.7	323.7	280.0
2350032	4		400.0	400.0	400.0	400.0	400.0	400.0	378.9
		N	4	4	4	4	4	4	4
		Mean	387.86	390.82	385.14	381.96	379.18	379.68	339.75
		SD	20.65	18.36	29.71	36.07	41.64	37.38	42.40

+ Mean daily food consumption for the previous 7 days

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A.
(Dr. Alfredo Nihasiase)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 2 - Food consumption+ (g/dog/day) - Individual data

STUDY NO.: 235-003-009

FEMALES

Animal number	Group		Day of Study -7	1	8	15	22	29	36	43
2350001	1		311.0	326.4	365.0	309.0	322.1	304.4	325.4	302.0
2350003	1		340.0	328.3	336.0	364.7	313.9	318.0	347.7	280.4
2350005	1		345.7	338.6	398.6	400.0	400.0	391.4	392.9	395.7
2350007	1		315.9	306.0	360.0	400.0	373.0	343.0	394.6	330.9
		N	4	4	4	4	4	4	4	4
		Mean	328.14	324.82	364.89	368.43	352.25	339.21	365.14	327.25
		SD	17.26	13.64	25.77	42.97	41.20	38.30	34.23	50.10
2350009	2		291.9	306.6	344.9	324.6	385.3	367.0	348.1	318.6
2350011	2		343.3	351.7	400.0	400.0	386.7	400.0	400.0	371.4
2350013	2		343.7	382.1	400.0	400.0	400.0	400.0	395.3	400.0
2350015	2		283.4	308.7	341.6	383.0	313.0	370.9	392.3	352.4
		N	4	4	4	4	4	4	4	4
		Mean	315.57	337.29	371.61	376.89	371.25	384.46	383.93	360.61
		SD	32.43	36.42	32.81	35.79	39.39	18.01	24.07	34.17
2350017	3		366.9	350.1	400.0	389.0	400.0	400.0	389.6	393.4
2350019	3		303.7	289.4	306.4	309.3	304.1	297.9	324.6	307.4
2350021	3		367.1	340.9	400.0	354.7	400.0	391.4	400.0	396.4
2350023	3		289.7	285.1	323.1	346.1	314.0	312.7	348.1	234.7
		N	4	4	4	4	4	4	4	4
		Mean	331.86	316.39	357.39	349.79	354.54	350.50	365.57	333.00
		SD	40.98	33.87	49.67	32.74	52.65	52.68	35.34	77.44
2350025	4		289.7	315.7	346.7	328.4	336.6	382.7	382.3	335.3
2350027	4		326.1	282.9	324.6	332.4	360.1	348.9	340.4	312.1
2350029	4		349.3	349.3	363.9	400.0	400.0	392.6	400.0	367.1
2350031	4		265.4	321.9	340.4	252.1	228.4	290.1	392.4	277.0
		N	4	4	4	4	4	4	4	4
		Mean	307.64	317.43	343.89	328.25	331.29	353.57	378.79	322.89
		SD	37.33	27.28	16.25	60.44	73.40	46.24	26.58	38.01

+ Mean daily food consumption for the previous 7 days

009

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A.

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 2 - Food consumption+ (g/dog/day) - Individual data

STUDY NO.: 235-003-009

FEMALES

Animal number	Group		Day of Study 50	57	64	71	78	85	92
2350001	1		376.1	275.1	375.4	322.3	311.0	307.4	290.4
2350003	1		306.7	266.6	276.4	322.7	304.1	274.7	259.3
2350005	1		392.9	383.6	389.4	394.3	400.0	397.1	372.1
2350007	1		375.7	370.1	377.9	341.6	343.6	296.3	323.0
		N	4	4	4	4	4	4	4
		Mean	362.86	323.86	354.79	345.21	339.68	318.89	311.21
		SD	38.27	61.54	52.59	33.93	43.74	53.91	48.23
2350009	2		357.7	334.9	319.3	330.7	326.9	280.6	313.1
2350011	2		395.7	400.0	398.6	400.0	400.0	400.0	331.6
2350013	2		395.7	400.0	400.0	400.0	400.0	400.0	400.0
2350015	2		395.7	372.9	384.3	352.7	338.6	293.9	289.4
		N	4	4	4	4	4	4	4
		Mean	386.21	376.93	375.54	370.86	366.36	343.61	333.54
		SD	19.00	30.83	38.16	34.83	39.14	65.34	47.55
2350017	3		385.7	400.0	400.0	400.0	387.9	400.0	343.9
2350019	3		392.1	340.3	335.7	377.7	384.4	309.4	347.7
2350021	3		400.0	400.0	395.7	381.7	400.0	340.0	350.7
2350023	3		324.3	308.3	294.1	311.0	316.4	291.0	264.3
		N	4	4	4	4	4	4	4
		Mean	375.54	362.14	356.39	367.61	372.18	335.11	326.64
		SD	34.66	45.62	50.83	38.97	37.76	47.75	41.67
2350025	4		342.3	308.9	381.4	400.0	359.9	345.0	329.4
2350027	4		360.0	361.6	335.0	345.9	366.9	348.3	321.9
2350029	4		400.0	400.0	400.0	388.3	380.0	340.6	308.6
2350031	4		280.0	330.7	340.7	372.0	322.1	237.7	312.1
		N	4	4	4	4	4	4	4
		Mean	345.57	350.29	364.29	376.54	357.21	317.89	318.00
		SD	49.94	39.57	31.53	23.45	24.83	53.55	9.46

+ Mean daily food consumption for the previous 7 days

010

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Roma Toxicology Center S.p.A.
(Dr. Alfredo Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 3A - Water consumption (g/dog/day) - Before treatment [1] - Individual data

STUDY NO.: 235-003-009

MALES

Animal number	Group		Day of Study -14	-13	-12
2350002	1		783.0	1573.0	1373.0
2350004	1		740.0	908.0	1728.0
2350006	1		229.0	741.0	1151.0
2350008	1		1284.0	562.0	1586.0
		N	4	4	4
		Mean	759.00	946.00	1459.50
		SD	431.07	441.23	252.16
2350010	2		159.0	1034.0	72.0
2350012	2		411.0	1086.0	374.0
2350014	2		253.0	90.0	662.0
2350016	2		174.0	236.0	1126.0
		N	4	4	4
		Mean	249.25	611.50	558.50
		SD	115.45	521.73	448.51
2350018	3		369.0	109.0	285.0
2350020	3		1874.0	952.0	1137.0
2350022	3		135.0	96.0	1098.0
2350024	3		201.0	297.0	1110.0
		N	4	4	4
		Mean	644.75	363.50	907.50
		SD	825.40	402.94	415.32
2350026	4		293.0	1135.0	1934.0
2350028	4		648.0	664.0	1786.0
2350030	4		348.0	453.0	1029.0
2350032	4		1036.0	773.0	1176.0
		N	4	4	4
		Mean	581.25	756.25	1481.25
		SD	340.95	285.31	445.56

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(Dr. Alfredo Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 3A - Water consumption (g/dog/day) - Before treatment [1] - Individual data

STUDY NO.: 235-003-009

FEMALES

Animal number	Group		Day of Study -14	-13	-12
2350001	1		567.0	882.0	1245.0
2350003	1		343.0	929.0	1192.0
2350005	1		752.0	822.0	860.0
2350007	1		221.0	726.0	951.0
		N	4	4	4
		Mean	470.75	839.75	1062.00
		SD	235.98	87.57	185.75
2350009	2		413.0	550.0	569.0
2350011	2		614.0	861.0	720.0
2350013	2		536.0	608.0	995.0
2350015	2		631.0	668.0	1311.0
		N	4	4	4
		Mean	548.50	671.75	898.75
		SD	99.35	135.05	326.55
2350017	3		493.0	952.0	956.0
2350019	3		1667.0	546.0	1438.0
2350021	3		391.0	640.0	1168.0
2350023	3		1415.0	741.0	1032.0
		N	4	4	4
		Mean	991.50	719.75	1148.50
		SD	644.14	174.11	211.99
2350025	4		1138.0	517.0	643.0
2350027	4		269.0	617.0	1484.0
2350029	4		568.0	599.0	1212.0
2350031	4		925.0	1122.0	930.0
		N	4	4	4
		Mean	725.00	713.75	1067.25
		SD	384.34	275.62	362.15

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LIFE SCIENCE RESEARCH
Roma Tavola

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 3B - Water consumption (g/dog/day) - Before treatment [2] - Individual data

STUDY NO.: 235-003-009

MALES

Animal number	Group		Day of Study -6	-5	-4
2350002	1		989.0	1771.0	956.0
2350004	1		725.0	549.0	848.0
2350006	1		432.0	667.0	835.0
2350008	1		284.0	817.0	1095.0
		N	4	4	4
		Mean	607.50	951.00	933.50
		SD	313.48	557.56	120.56
2350010	2		928.0	1490.0	833.0
2350012	2		533.0	1073.0	1390.0
2350014	2		330.0	526.0	80.0
2350016	2		232.0	428.0	244.0
		N	4	4	4
		Mean	505.75	879.25	636.75
		SD	308.15	496.31	597.25
2350018	3		683.0	921.0	1105.0
2350020	3		1507.0	1643.0	1857.0
2350022	3		285.0	788.0	145.0
2350024	3		256.0	1302.0	312.0
		N	4	4	4
		Mean	682.75	1163.50	854.75
		SD	583.01	386.83	788.55
2350026	4		588.0	1122.0	967.0
2350028	4		359.0	777.0	785.0
2350030	4		1012.0	1131.0	2190.0
2350032	4		1084.0	802.0	1106.0
		N	4	4	4
		Mean	760.75	958.00	1262.00
		SD	345.86	194.87	632.48

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FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 3B - Water consumption (g/dog/day) - Before treatment [2] - Individual data

STUDY NO.: 235-003-009

FEMALES

Animal number	Group		Day of Study -6	-5	-4
2350001	1		407.0	953.0	836.0
2350003	1		481.0	850.0	636.0
2350005	1		1377.0	2151.0	1725.0
2350007	1		452.0	917.0	1004.0
		N	4	4	4
		Mean	679.25	1217.75	1050.25
		SD	466.16	623.63	474.32
2350009	2		531.0	578.0	1073.0
2350011	2		463.0	797.0	785.0
2350013	2		1439.0	847.0	1238.0
2350015	2		566.0	635.0	668.0
		N	4	4	4
		Mean	749.75	714.25	941.00
		SD	461.49	128.21	261.09
2350017	3		650.0	800.0	981.0
2350019	3		1003.0	974.0	689.0
2350021	3		727.0	636.0	930.0
2350023	3		430.0	786.0	723.0
		N	4	4	4
		Mean	702.50	799.00	830.75
		SD	236.58	138.28	146.21
2350025	4		570.0	798.0	706.0
2350027	4		920.0	842.0	1465.0
2350029	4		1738.0	798.0	1092.0
2350031	4		751.0	827.0	733.0
		N	4	4	4
		Mean	994.75	816.25	999.00
		SD	515.70	21.95	357.03

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(Dr. Alfredo Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 3C - Water consumption (g/dog/day) - Week 1 - Individual data

STUDY NO.: 235-003-009

MALES

Animal number	Group		Day of Study 2	3	4
2350002	1		1295.0	1084.0	650.0
2350004	1		849.0	907.0	115.0
2350006	1		722.0	739.0	749.0
2350008	1		808.0	982.0	878.0
		N	4	4	4
		Mean	918.50	928.00	598.00
		SD	256.52	145.39	335.26
2350010	2		724.0	896.0	1177.0
2350012	2		244.0	1007.0	1173.0
2350014	2		92.0	660.0	915.0
2350016	2		88.0	637.0	744.0
		N	4	4	4
		Mean	287.00	800.00	1002.25
		SD	300.25	180.95	211.34
2350018	3		2216.0	2009.0	1824.0
2350020	3		2069.0	1676.0	2213.0
2350022	3		450.0	880.0	810.0
2350024	3		278.0	1051.0	1268.0
		N	4	4	4
		Mean	1253.25	1404.00	1528.75
		SD	1030.96	528.90	616.43
2350026	4		977.0	1127.0	1153.0
2350028	4		673.0	838.0	969.0
2350030	4		2209.0	601.0	800.0
2350032	4		1111.0	1028.0	1224.0
		N	4	4	4
		Mean	1242.50	898.50	1036.50
		SD	669.88	231.77	190.80

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FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 3C - Water consumption (g/dog/day) - Week 1 - Individual data

STUDY NO.: 235-003-009

FEMALES

Animal number	Group		Day of Study 2	3	4
2350001	1		531.0	567.0	988.0
2350003	1		563.0	527.0	1420.0
2350005	1		2217.0	1994.0	1576.0
2350007	1		766.0	522.0	717.0
		N	4	4	4
		Mean	1019.25	902.50	1175.25
		SD	805.25	727.95	393.94
2350009	2		751.0	505.0	868.0
2350011	2		603.0	759.0	816.0
2350013	2		1016.0	911.0	866.0
2350015	2		531.0	621.0	702.0
		N	4	4	4
		Mean	725.25	699.00	813.00
		SD	214.38	175.37	77.81
2350017	3		844.0	964.0	1071.0
2350019	3		847.0	614.0	752.0
2350021	3		844.0	890.0	634.0
2350023	3		826.0	724.0	659.0
		N	4	4	4
		Mean	840.25	798.00	779.00
		SD	9.60	158.48	201.18
2350025	4		918.0	795.0	1675.0
2350027	4		830.0	574.0	666.0
2350029	4		784.0	488.0	690.0
2350031	4		692.0	669.0	589.0
		N	4	4	4
		Mean	806.00	631.50	905.00
		SD	94.16	131.70	515.14

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(Dr. Alfredo Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 3D - Water consumption (g/dog/day) - Week 7 - Individual data

STUDY NO.: 235-003-009

MALES

Animal number	Group		Day of Study 43	44	45
2350002	1		1047.0	1021.0	2095.0
2350004	1		760.0	1415.0	659.0
2350006	1		714.0	707.0	839.0
2350008	1		824.0	735.0	919.0
		N	4	4	4
		Mean	836.25	969.50	1128.00
		SD	147.56	329.15	653.77
2350010	2		698.0	1513.0	1295.0
2350012	2		392.0	1532.0	1957.0
2350014	2		852.0	991.0	1090.0
2350016	2		413.0	937.0	981.0
		N	4	4	4
		Mean	588.75	1243.25	1330.75
		SD	224.23	323.30	437.32
2350018	3		1694.0	2182.0	909.0
2350020	3		1100.0	1398.0	1815.0
2350022	3		827.0	1094.0	1084.0
2350024	3		692.0	1107.0	1078.0
		N	4	4	4
		Mean	1078.25	1445.25	1221.50
		SD	444.20	510.82	403.90
2350026	4		513.0	962.0	1828.0
2350028	4		595.0	1196.0	1341.0
2350030	4		964.0	945.0	876.0
2350032	4		1375.0	587.0	1086.0
		N	4	4	4
		Mean	861.75	922.50	1282.75
		SD	394.40	251.28	410.22

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Ricerche Nunziatella

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 3D - Water consumption (g/dog/day) - Week 7 -- Individual data

STUDY NO.: 235-003-009

FEMALES

Animal number	Group		Day of Study 43	44	45
2350001	1		985.0	774.0	938.0
2350003	1		380.0	496.0	536.0
2350005	1		1299.0	1076.0	1048.0
2350007	1		537.0	568.0	491.0
		N	4	4	4
		Mean	800.25	728.50	753.25
		SD	419.84	259.90	281.06
2350009	2		636.0	1308.0	728.0
2350011	2		226.0	607.0	763.0
2350013	2		1104.0	1004.0	1059.0
2350015	2		1066.0	816.0	630.0
		N	4	4	4
		Mean	758.00	933.75	795.00
		SD	413.32	297.56	184.78
2350017	3		831.0	777.0	711.0
2350019	3		724.0	752.0	804.0
2350021	3		1008.0	967.0	948.0
2350023	3		395.0	746.0	665.0
		N	4	4	4
		Mean	739.50	810.50	782.00
		SD	257.80	105.19	124.86
2350025	4		552.0	1559.0	494.0
2350027	4		806.0	1065.0	916.0
2350029	4		519.0	662.0	712.0
2350031	4		500.0	617.0	544.0
		N	4	4	4
		Mean	594.25	975.75	666.50
		SD	142.79	437.91	190.69

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(Dr. Alfredo Nakatata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 3E - Water consumption (g/dog/day) - Week 12 - Individual data

STUDY NO.: 235-003-009

MALES

Animal number	Group		Day of Study 78	79	80
2350002	1		1617.0	1797.0	2076.0
2350004	1		447.0	464.0	571.0
2350006	1		1638.0	838.0	977.0
2350008	1		1890.0	1537.0	1777.0
		N	4	4	4
		Mean	1398.00	1159.00	1350.25
		SD	646.02	615.36	696.51
2350010	2		1080.0	1210.0	975.0
2350012	2		718.0	1220.0	778.0
2350014	2		1120.0	1415.0	562.0
2350016	2		1240.0	1430.0	623.0
		N	4	4	4
		Mean	1039.50	1318.75	734.50
		SD	224.86	120.03	184.32
2350018	3		892.0	767.0	494.0
2350020	3		1259.0	1466.0	1305.0
2350022	3		874.0	1049.0	1104.0
2350024	3		1319.0	1513.0	1355.0
		N	4	4	4
		Mean	1086.00	1198.75	1064.50
		SD	235.80	355.44	395.50
2350026	4		966.0	835.0	956.0
2350028	4		854.0	862.0	1124.0
2350030	4		1094.0	746.0	855.0
2350032	4		1212.0	1102.0	1085.0
		N	4	4	4
		Mean	1031.50	886.25	1005.00
		SD	155.22	152.13	123.10

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A.

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 3E - Water consumption (g/dog/day) - Week 12 - Individual data

STUDY NO.: 235-003-009

FEMALES

Animal number	Group		Day of Study 78	79	80
2350001	1		1102.0	880.0	688.0
2350003	1		400.0	485.0	209.0
2350005	1		1029.0	939.0	1040.0
2350007	1		473.0	479.0	590.0
		N	4	4	4
		Mean	751.00	695.75	631.75
		SD	365.59	248.00	341.71
2350009	2		615.0	607.0	460.0
2350011	2		747.0	767.0	856.0
2350013	2		1093.0	1156.0	1130.0
2350015	2		1078.0	1026.0	721.0
		N	4	4	4
		Mean	883.25	889.00	791.75
		SD	239.75	247.97	279.05
2350017	3		1552.0	140.0	1524.0
2350019	3		487.0	642.0	539.0
2350021	3		996.0	512.0	1829.0
2350023	3		515.0	627.0	727.0
		N	4	4	4
		Mean	887.50	480.25	1154.75
		SD	500.83	234.15	619.97
2350025	4		387.0	1544.0	471.0
2350027	4		734.0	546.0	764.0
2350029	4		625.0	553.0	713.0
2350031	4		834.0	904.0	1015.0
		N	4	4	4
		Mean	645.00	886.75	740.75
		SD	192.01	468.96	223.08

029

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Roma Toxicology Centre S.p.A.
Via Pontina Km 30,400
00040 Pomezia (Roma)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 4A - Physical examination - Before treatment - Individual observation

STUDY NO.: 235-003-009

Animal number	Group/Sex	Observation
2350029	4F	Encrustation on the muzzle

021

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Roma Toxicology Centre S.p.A.
(Dr. Alfredo Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 4B - Physical examination - Week 4 - Individual observation

STUDY NO.: 235-003-009

Animal number	Group/Sex	Observation
2350018	3M	Reddened conjunctivae
2350020	3M	Reddened apparent mucosae
2350022	3M	Reddened apparent mucosae
2350005	1F	Reddened apparent mucosae
2350007	1F	Nictitating membrane apparent
2350011	2F	Reddened apparent mucosae
2350015	2F	Reddened conjuctivae
2350019	3F	Reddened apparent mucosae
2350023	3F	Reddened apparent mucosae
2350027	4F	Reddened conjuctivae
2350029	4F	Reddened apparent mucosae
2350031	4F	Reddened apparent mucosae

022

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Roma Toxicology Centre S.p.A.
(Dr. Alfredo Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 4C - Physical examination - Week 6 - Individual observation

STUDY NO.: 235-003-009

Animal number	Group/Sex	Observation
2350004	1M	Reddened apparent mucosae
2350001	1F	Reddened apparent mucosae
2350007	1F	Luxation of tail
2350009	2F	Reddened apparent mucosae
2350011	2F	Dyspnoea
2350017	3F	Dyspnoea

023

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Roma Toxicology Centre S.p.A.
(Dr. Alfredo Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 4D - Physical examination - Week 10 - Individual observation

STUDY NO.: 235-003-009

Animal number	Group/Sex	Observation
2350020	3M	Reddened apparent mucosae
2350022	3M	Reddened conjuntivae
2350028	4M	Reddened apparent mucosae
2350001	1F	Reddened apparent mucosae
2350003	1F	Subicteric oral mucosae
2350009	2F	Reddened apparent mucosae
2350011	2F	Reddened apparent mucosae - Hypertrophy nictitating gland
2350013	2F	Reddened conjunctivae (slight)
2350015	2F	Reddened apparent mucosae
2350017	3F	Reddened apparent mucosae
2350019	3F	Hypertrophy nictitating gland
2350021	3F	Reddened conjunctivae (slight)
2350023	3F	Reddened conjunctivae
2350025	4F	Reddened apparent mucosae
2350027	4F	Reddened apparent mucosae
2350029	4F	Reddened conjunctivae, corneal ulceration right eye
2350031	4F	Reddened conjunctivae

LIFE CENTRE RESEARCH
Roma Tox Centre S.p.A.
(Dr. Alfredo Nanniata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 4E - Physical examination - Week 13 - Individual observation

STUDY NO.: 235-003-009

Animal number	Group/Sex	Observation
2350004	1M	Reddened conjunctivae
2350016	2M	Reddened conjunctivae
2350022	3M	Reddened apparent mucosae
2350024	3M	Reddened conjunctivae
2350028	4M	Reddened apparent mucosae
2350001	1F	Reddened apparent mucosae
2350005	1F	Vulva swollen
2350009	2F	Reddened apparent mucosae
2350011	2F	Eye secretion, moucoid, left eye
2350017	3F	Vulva swollen
2350021	3F	Reddened conjunctivae
2350023	3F	Reddened apparent mucosae
2350025	4F	Reddened oral mucosae
2350027	4F	Reddened apparent mucosae
2350029	4F	Reddened conjunctivae

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Roma Toxicology Centre S.p.A.
(Dr. Alfredo Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 5A - Haematology - Before treatment [1] - Individual data

STUDY NO.: 235-003-009

MALES

Animal Number	Group	Day of Study	ESR mm/hour	RBC 10'6/cmm	HGB g/dl	HCT %	MCV fl	MCH pg	MCHC g/dl	PLT 10'3/cmm
2350002	1	-13	3.0	5.69	12.5	40.9	72.0	22.0	30.6	571.0
2350004	1	-13	0.0	6.75	14.4	47.6	71.0	21.3	30.3	466.0
2350006	1	-13	0.0	5.99	12.3	42.4	71.0	20.5	29.0	391.0
2350008	1	-13	5.0	5.73	12.1	41.3	72.0	21.1	29.3	321.0
		Mean:	2.00	6.040	12.83	43.05	71.50	21.23	29.80	437.25
		SD:	2.45	0.492	1.06	3.10	0.58	0.62	0.77	107.03
2350010	2	-13	0.0	5.72	11.0	38.2	67.0	19.2	28.8	529.0
2350012	2	-13	0.0	5.93	13.2	42.6	72.0	22.3	31.0	386.0
2350014	2	-13	3.0	5.13	11.6	37.1	72.0	22.6	31.3	554.0
2350016	2	-13	0.0	5.77	12.4	41.2	71.0	21.5	30.1	549.0
		Mean:	0.75	5.638	12.05	39.78	70.50	21.40	30.30	504.50
		SD:	1.50	0.350	0.96	2.56	2.38	1.54	1.12	79.73
2350018	3	-13	10.0	6.02	13.5	42.2	70.0	22.4	32.0	582.0
2350020	3	-13	5.0	5.82	12.5	40.4	69.0	21.5	30.9	373.0
2350022	3	-13	0.0	6.48	14.0	45.7	71.0	21.6	30.6	477.0
2350024	3	-13	10.0	6.12	12.9	42.0	69.0	21.1	30.7	594.0
		Mean:	6.25	6.110	13.23	42.58	69.75	21.65	31.05	506.50
		SD:	4.79	0.276	0.66	2.23	0.96	0.54	0.65	103.36
2350026	4	-13	0.0	5.64	11.9	38.4	68.0	21.1	31.0	403.0
2350028	4	-13	0.0	5.76	12.3	39.5	69.0	21.4	31.1	493.0
2350030	4	-13	0.0	5.82	12.4	41.7	72.0	21.3	29.7	463.0
2350032	4	-13	0.0	5.46	11.9	39.3	72.0	21.8	30.3	454.0
		Mean:	0.00	5.670	12.13	39.73	70.25	21.40	30.53	453.25
		SD:	0.00	0.159	0.26	1.40	2.06	0.29	0.66	37.42

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FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 5A - Haematology - Before treatment [1] - Individual data

STUDY NO.: 235-003-009

MALES

Animal Number	Group	Day of Study	WBC 10'3/cmm	NEU %	LYM %	EOS %	MON %	BAS %	RET %	PT sec	APTT sec
2350002	1	-13	16.8	61.0	33.0	6.0	0.0	0.0	NT	9.5	12.8
2350004	1	-13	8.4	49.0	47.0	4.0	0.0	0.0	NT	9.6	12.0
2350006	1	-13	8.1	64.0	31.0	5.0	0.0	0.0	NT	9.6	11.3
2350008	1	-13	21.5	79.0	20.0	1.0	0.0	0.0	NT	9.5	12.3
		Mean:	13.70	63.25	32.75	4.00	0.00	0.00	-	9.55	12.10
		SD:	6.58	12.34	11.09	2.16	0.00	0.00	-	0.06	0.63
2350010	2	-13	12.4	63.0	33.0	3.0	1.0	0.0	NT	9.4	12.7
2350012	2	-13	13.8	64.0	36.0	0.0	0.0	0.0	NT	9.8	12.5
2350014	2	-13	14.3	71.0	28.0	1.0	0.0	0.0	NT	9.6	15.2
2350016	2	-13	11.4	63.0	33.0	4.0	0.0	0.0	NT	9.5	12.9
		Mean:	12.98	65.25	32.50	2.00	0.25	0.00	-	9.58	13.33
		SD:	1.32	3.86	3.32	1.83	0.50	0.00	-	0.17	1.26
2350018	3	-13	16.8	77.0	23.0	0.0	0.0	0.0	NT	9.5	12.8
2350020	3	-13	14.1	82.0	15.0	2.0	1.0	0.0	NT	9.5	13.9
2350022	3	-13	9.6	76.0	23.0	0.0	1.0	0.0	NT	9.8	12.1
2350024	3	-13	12.2	54.0	33.0	13.0	0.0	0.0	NT	9.6	11.9
		Mean:	13.18	72.25	23.50	3.75	0.50	0.00	-	9.60	12.68
		SD:	3.04	12.45	7.37	6.24	0.58	0.00	-	0.14	0.90
2350026	4	-13	10.7	79.0	21.0	0.0	0.0	0.0	NT	9.5	14.1
2350028	4	-13	13.2	66.0	32.0	1.0	1.0	0.0	NT	9.5	12.8
2350030	4	-13	12.2	76.0	20.0	4.0	0.0	0.0	NT	9.7	12.5
2350032	4	-13	11.3	67.0	30.0	2.0	1.0	0.0	NT	9.6	12.0
		Mean:	11.85	72.00	25.75	1.75	0.50	0.00	-	9.58	12.85
		SD:	1.09	6.48	6.13	1.71	0.58	0.00	-	0.10	0.90

NT = Not taken

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Roma Toxicology Centre S.p.A.

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 5A - Haematology - Before treatment [1] - Individual data

STUDY NO.: 235-003-009

FEMALES

Animal Number	Group	Day of Study	ESR mm/hour	RBC 10'6/cmm	HGB g/dl	HCT %	MCV fl	MCH pg	MCHC g/dl	PLT 10'3/cmm
2350001	1	-13	0.0	5.73	12.4	40.8	71.0	21.6	30.4	545.0
2350003	1	-13	0.0	6.25	13.8	43.6	70.0	22.1	31.7	483.0
2350005	1	-13	0.0	5.60	11.9	40.0	71.0	21.3	29.8	412.0
2350007	1	-13	0.0	5.41	12.3	39.0	72.0	22.7	31.5	467.0
		Mean:	0.00	5.747	12.60	40.85	71.00	21.93	30.85	476.75
		SD:	0.00	0.360	0.83	1.98	0.82	0.61	0.90	54.73
2350009	2	-13	0.0	6.17	13.6	44.0	71.0	22.0	30.9	437.0
2350011	2	-13	0.0	5.42	13.2	40.2	74.0	24.4	32.8	368.0
2350013	2	-13	0.0	6.00	13.0	42.5	71.0	21.7	30.6	484.0
2350015	2	-13	0.0	5.72	12.3	40.3	70.0	21.5	30.5	552.0
		Mean:	0.00	5.827	13.03	41.75	71.50	22.40	31.20	460.25
		SD:	0.00	0.329	0.54	1.84	1.73	1.35	1.08	77.53
2350017	3	-13	3.0	5.11	10.6	35.5	69.0	20.7	29.9	429.0
2350019	3	-13	0.0	5.95	12.8	42.5	71.0	21.5	30.1	395.0
2350021	3	-13	5.0	5.13	11.7	36.5	71.0	22.8	32.1	365.0
2350023	3	-13	0.0	6.54	13.3	46.4	71.0	20.3	28.7	414.0
		Mean:	2.00	5.683	12.10	40.23	70.50	21.33	30.20	400.75
		SD:	2.45	0.693	1.20	5.15	1.00	1.10	1.41	27.60
2350025	4	-13	3.0	6.10	13.0	42.9	70.0	21.3	30.3	485.0
2350027	4	-13	0.0	7.02	15.0	49.3	70.0	21.4	30.4	429.0
2350029	4	-13	0.0	6.25	14.4	45.2	72.0	23.0	31.9	457.0
2350031	4	-13	0.0	5.80	12.7	41.0	71.0	21.9	31.0	388.0
		Mean:	0.75	6.293	13.78	44.60	70.75	21.90	30.90	439.75
		SD:	1.50	0.520	1.10	3.57	0.96	0.78	0.73	41.39

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Roma Toxicology Centre S.p.A.
(Dr. Alfredo Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 5A - Haematology - Before treatment [1] - Individual data

STUDY NO.: 235-003-009

FEMALES

Animal Number	Group	Day of Study	WBC 10'3/cmm	NEU %	LYM %	EOS %	MON %	BAS %	RET %	PT sec	APTT sec
2350001	1	-13	13.1	71.0	27.0	1.0	1.0	0.0	NT	9.9	11.6
2350003	1	-13	7.4	67.0	32.0	1.0	0.0	0.0	NT	9.5	12.0
2350005	1	-13	11.4	70.0	26.0	4.0	0.0	0.0	NT	9.8	13.5
2350007	1	-13	10.4	70.0	27.0	3.0	0.0	0.0	NT	10.1	12.3
		Mean:	10.57	69.50	28.00	2.25	0.25	0.00	-	9.83	12.35
		SD:	2.39	1.73	2.71	1.50	0.50	0.00	-	0.25	0.82
2350009	2	-13	16.5	73.0	25.0	2.0	0.0	0.0	NT	10.0	13.6
2350011	2	-13	9.2	72.0	28.0	0.0	0.0	0.0	NT	9.7	13.9
2350013	2	-13	10.8	78.0	22.0	0.0	0.0	0.0	NT	10.0	12.9
2350015	2	-13	14.0	76.0	19.0	4.0	1.0	0.0	NT	10.2	13.6
		Mean:	12.63	74.75	23.50	1.50	0.25	0.00	-	9.98	13.50
		SD:	3.26	2.75	3.87	1.91	0.50	0.00	-	0.21	0.42
2350017	3	-13	9.4	69.0	29.0	2.0	0.0	0.0	NT	9.8	12.4
2350019	3	-13	11.1	77.0	23.0	0.0	0.0	0.0	NT	9.6	14.6
2350021	3	-13	11.4	78.0	19.0	3.0	0.0	0.0	NT	9.8	13.6
2350023	3	-13	11.1	79.0	20.0	1.0	0.0	0.0	NT	9.8	12.4
		Mean:	10.75	75.75	22.75	1.50	0.00	0.00	-	9.75	13.25
		SD:	0.91	4.57	4.50	1.29	0.00	0.00	-	0.10	1.06
2350025	4	-13	14.6	70.0	30.0	0.0	0.0	0.0	NT	9.7	13.2
2350027	4	-13	14.8	77.0	23.0	0.0	0.0	0.0	NT	9.7	12.6
2350029	4	-13	14.6	80.0	20.0	0.0	0.0	0.0	NT	10.0	13.5
2350031	4	-13	8.5	70.0	28.0	2.0	0.0	0.0	NT	9.8	12.7
		Mean:	13.13	74.25	25.25	0.50	0.00	0.00	-	9.80	13.00
		SD:	3.08	5.06	4.57	1.00	0.00	0.00	-	0.14	0.42

NT = Not taken

LIFE SCIENCE RESEARCH

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 5B - Haematology - Before treatment [2] - Individual data

STUDY NO.: 235-003-009

MALES

Animal Number	Group	Day of Study	ESR mm/hour	RBC 10'6/cmm	HGB g/dl	HCT %	MCV fl	MCH pg	MCHC g/dl	PLT 10'3/cmm
2350002	1	-5	0.0	5.63	12.9	40.4	72.0	22.9	31.9	463.0
2350004	1	-5	0.0	6.52	14.2	45.8	70.0	21.8	31.0	434.0
2350006	1	-5	0.0	6.33	13.6	44.8	71.0	21.5	30.4	501.0
2350008	1	-5	0.0	6.10	13.4	43.7	72.0	22.0	30.7	343.0
		Mean:	0.00	6.145	13.53	43.67	71.25	22.05	31.00	435.25
		SD:	0.00	0.384	0.54	2.35	0.96	0.60	0.65	67.34
2350010	2	-5	0.0	5.72	11.4	38.8	68.0	19.9	29.4	567.0
2350012	2	-5	0.0	6.08	13.6	43.8	72.0	22.4	31.1	494.0
2350014	2	-5	0.0	5.77	12.8	41.0	71.0	22.2	31.2	583.0
2350016	2	-5	0.0	5.55	12.1	39.2	71.0	21.8	30.9	482.0
		Mean:	0.00	5.780	12.48	40.70	70.50	21.58	30.65	531.50
		SD:	0.00	0.221	0.94	2.28	1.73	1.14	0.84	50.89
2350018	3	-5	0.0	5.61	12.8	39.1	70.0	22.8	32.7	534.0
2350020	3	-5	0.0	6.01	13.4	41.6	69.0	22.3	32.2	367.0
2350022	3	-5	0.0	6.32	13.7	44.2	70.0	21.7	31.0	466.0
2350024	3	-5	0.0	6.67	13.9	46.6	70.0	20.8	29.8	553.0
		Mean:	0.00	6.153	13.45	42.88	69.75	21.90	31.43	480.00
		SD:	0.00	0.451	0.48	3.24	0.50	0.86	1.30	84.08
2350026	4	-5	0.0	6.56	13.7	45.2	69.0	20.9	30.3	438.0
2350028	4	-5	0.0	5.83	12.7	40.4	69.0	21.8	31.4	516.0
2350030	4	-5	0.0	6.34	13.3	45.4	72.0	21.0	29.3	460.0
2350032	4	-5	0.0	5.43	12.6	39.0	72.0	23.2	32.3	470.0
		Mean:	0.00	6.040	13.08	42.50	70.50	21.73	30.83	471.00
		SD:	0.00	0.509	0.52	3.28	1.73	1.06	1.30	32.84

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Roma Toxicology Centre S.p.A

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 5B - Haematology - Before treatment [2] - Individual data

STUDY NO.: 235-003-009

MALES

Animal Number	Group	Day of Study	WBC 10'3/cmm	NEU %	LYM %	EOS %	MON %	BAS %	RET %	PT sec	APTT sec
2350002	1	-5	12.9	53.0	37.0	10.0	0.0	0.0	NT	9.6	11.6
2350004	1	-5	10.5	48.0	45.0	6.0	1.0	0.0	NT	10.4	11.6
2350006	1	-5	11.3	75.0	24.0	1.0	0.0	0.0	NT	9.6	11.7
2350008	1	-5	9.7	65.0	34.0	1.0	0.0	0.0	NT	9.6	12.1
		Mean:	11.10	60.25	35.00	4.50	0.25	0.00	-	9.80	11.75
		SD:	1.37	12.15	8.68	4.36	0.50	0.00	-	0.40	0.24
2350010	2	-5	11.6	75.0	21.0	4.0	0.0	0.0	NT	9.5	11.9
2350012	2	-5	9.5	49.0	47.0	4.0	0.0	0.0	NT	10.0	12.3
2350014	2	-5	9.9	58.0	39.0	3.0	0.0	0.0	NT	9.9	13.3
2350016	2	-5	9.1	52.0	41.0	7.0	0.0	0.0	NT	9.6	13.2
		Mean:	10.03	58.50	37.00	4.50	0.00	0.00	-	9.75	12.68
		SD:	1.10	11.62	11.20	1.73	0.00	0.00	-	0.24	0.68
2350018	3	-5	11.6	69.0	31.0	0.0	0.0	0.0	NT	9.6	13.0
2350020	3	-5	7.9	61.0	32.0	6.0	1.0	0.0	NT	10.0	12.1
2350022	3	-5	8.6	80.0	20.0	0.0	0.0	0.0	NT	9.8	13.1
2350024	3	-5	12.7	57.0	32.0	10.0	1.0	0.0	NT	9.7	11.9
		Mean:	10.20	66.75	28.75	4.00	0.50	0.00	-	9.78	12.53
		SD:	2.31	10.14	5.85	4.90	0.58	0.00	-	0.17	0.61
2350026	4	-5	7.7	63.0	37.0	0.0	0.0	0.0	NT	9.6	11.7
2350028	4	-5	9.0	58.0	40.0	1.0	1.0	0.0	NT	9.9	11.5
2350030	4	-5	10.8	56.0	34.0	9.0	1.0	0.0	NT	9.9	13.9
2350032	4	-5	8.8	60.0	35.0	5.0	0.0	0.0	NT	10.0	11.9
		Mean:	9.08	59.25	36.50	3.75	0.50	0.00	-	9.85	12.25
		SD:	1.28	2.99	2.65	4.11	0.58	0.00	-	0.17	1.11

NT = Not taken

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A.

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 5B - Haematology - Before treatment [2] - Individual data

STUDY NO.: 235-003-009

FEMALES

Animal Number	Group	Day of Study	ESR mm/hour	RBC 10'6/cmm	HGB g/dl	HCT %	MCV fl	MCH pg	MCHC g/dl	PLT 10'3/cmm
2350001	1	-5	0.0	5.66	12.6	40.3	71.0	22.3	31.3	552.0
2350003	1	-5	0.0	6.35	13.6	44.7	70.0	21.4	30.4	446.0
2350005	1	-5	0.0	6.01	14.1	42.8	71.0	23.5	32.9	434.0
2350007	1	-5	0.0	6.08	13.2	43.8	72.0	21.7	30.1	491.0
		Mean:	0.00	6.025	13.38	42.90	71.00	22.23	31.18	480.75
		SD:	0.00	0.284	0.63	1.90	0.82	0.93	1.26	53.46
2350009	2	-5	0.0	6.01	14.0	42.9	71.0	23.3	32.6	429.0
2350011	2	-5	0.0	6.01	13.7	44.2	74.0	22.8	31.0	403.0
2350013	2	-5	0.0	5.67	11.7	39.4	69.0	20.6	29.7	436.0
2350015	2	-5	0.0	5.72	12.1	40.2	70.0	21.2	30.1	533.0
		Mean:	0.00	5.852	12.88	41.68	71.00	21.98	30.85	450.25
		SD:	0.00	0.183	1.14	2.25	2.16	1.28	1.29	56.96
2350017	3	-5	0.0	5.26	11.5	36.6	70.0	21.9	31.4	430.0
2350019	3	-5	0.0	6.49	13.4	46.4	71.0	20.6	28.9	381.0
2350021	3	-5	0.0	5.41	12.3	38.7	72.0	22.7	31.8	323.0
2350023	3	-5	0.0	6.94	14.5	49.1	71.0	20.9	29.5	394.0
		Mean:	0.00	6.025	12.93	42.70	71.00	21.53	30.40	382.00
		SD:	0.00	0.820	1.31	6.00	0.82	0.96	1.42	44.46
2350025	4	-5	0.0	6.16	13.6	43.2	70.0	22.1	31.5	383.0
2350027	4	-5	0.0	6.96	15.4	48.7	70.0	22.1	31.6	419.0
2350029	4	-5	0.0	6.86	15.8	49.3	72.0	23.0	32.0	503.0
2350031	4	-5	0.0	5.97	13.3	41.9	70.0	22.3	31.7	351.0
		Mean:	0.00	6.487	14.52	45.78	70.50	22.38	31.70	414.00
		SD:	0.00	0.496	1.26	3.77	1.00	0.43	0.22	65.51

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A.

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 5B - Haematology - Before treatment [2] - Individual data

STUDY NO.: 235-003-009

FEMALES

Animal Number	Group	Day of Study	WBC 10'3/cmm	NEU %	LYM %	EOS %	MON %	BAS %	RET %	PT sec	APTT sec
2350001	1	-5	11.5	78.0	19.0	3.0	0.0	0.0	NT	9.8	11.4
2350003	1	-5	9.4	58.0	40.0	2.0	0.0	0.0	NT	10.4	11.5
2350005	1	-5	12.2	59.0	38.0	3.0	0.0	0.0	NT	9.7	13.0
2350007	1	-5	10.4	66.0	33.0	1.0	0.0	0.0	NT	10.3	12.6
		Mean:	10.88	65.25	32.50	2.25	0.00	0.00	-	10.05	12.13
		SD:	1.23	9.22	9.47	0.96	0.00	0.00	-	0.35	0.80
2350009	2	-5	9.5	64.0	36.0	0.0	0.0	0.0	NT	9.9	13.0
2350011	2	-5	6.3	53.0	45.0	1.0	1.0	0.0	NT	9.9	12.2
2350013	2	-5	7.8	53.0	45.0	2.0	0.0	0.0	NT	9.8	12.7
2350015	2	-5	9.2	77.0	21.0	2.0	0.0	0.0	NT	10.1	13.5
		Mean:	8.20	61.75	36.75	1.25	0.25	0.00	-	9.93	12.85
		SD:	1.47	11.41	11.32	0.96	0.50	0.00	-	0.13	0.54
2350017	3	-5	8.4	57.0	42.0	0.0	1.0	0.0	NT	9.9	12.2
2350019	3	-5	6.9	73.0	25.0	1.0	1.0	0.0	NT	10.1	12.5
2350021	3	-5	7.3	54.0	42.0	4.0	0.0	0.0	NT	9.9	12.9
2350023	3	-5	7.6	78.0	21.0	1.0	0.0	0.0	NT	10.1	12.2
		Mean:	7.55	65.50	32.50	1.50	0.50	0.00	-	10.00	12.45
		SD:	0.64	11.79	11.09	1.73	0.58	0.00	-	0.12	0.33
2350025	4	-5	12.7	60.0	38.0	2.0	0.0	0.0	NT	10.1	12.9
2350027	4	-5	10.4	64.0	32.0	4.0	0.0	0.0	NT	9.9	11.6
2350029	4	-5	10.4	77.0	22.0	1.0	0.0	0.0	NT	10.0	13.1
2350031	4	-5	8.2	58.0	41.0	1.0	0.0	0.0	NT	10.1	13.2
		Mean:	10.43	64.75	33.25	2.00	0.00	0.00	-	10.03	12.70
		SD:	1.84	8.54	8.38	1.41	0.00	0.00	-	0.10	0.74

NT = Not taken

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A.

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 5C - Haematology - Week 6 of treatment - Individual data

STUDY NO.: 235-003-009

MALES

Animal Number	Group	Day of Study	ESR mm/hour	RBC 10'6/cmm	HGB g/dl	HCT %	MCV fl	MCH pg	MCHC g/dl	PLT 10'3/cmm
2350002	1	42	0.0	6.72	14.4	49.0	73.0	21.4	29.4	326.0
2350004	1	42	0.0	7.25	16.1	52.2	72.0	22.2	30.8	296.0
2350006	1	42	0.0	6.52	14.7	47.4	73.0	22.5	31.0	266.0
2350008	1	42	0.0	6.70	14.7	49.4	74.0	21.9	29.8	157.0
		Mean:	0.00	6.798	14.98	49.50	73.00	22.00	30.25	261.25
		SD:	0.00	0.315	0.76	2.00	0.82	0.47	0.77	73.69
2350010	2	42	0.0	6.27	12.7	44.1	70.0	20.3	28.8	333.0
2350012	2	42	0.0	6.24	13.4	45.2	72.0	21.5	29.6	332.0
2350014	2	42	0.0	6.30	13.9	45.3	72.0	22.1	30.7	387.0
2350016	2	42	0.0	6.25	12.7	44.2	71.0	20.3	28.7	378.0
		Mean:	0.00	6.265	13.18	44.70	71.25	21.05	29.45	357.50
		SD:	0.00	0.026	0.59	0.64	0.96	0.90	0.93	29.10
2350018	3	42	0.0	6.40	14.3	45.4	71.0	22.3	31.5	318.0
2350020	3	42	0.0	6.57	14.1	45.6	69.0	21.5	30.9	154.0
2350022	3	42	0.0	6.98	15.7	49.6	71.0	22.5	31.7	347.0
2350024	3	42	0.0	6.76	15.1	48.6	72.0	22.3	31.1	394.0
		Mean:	0.00	6.678	14.80	47.30	70.75	22.15	31.30	303.25
		SD:	0.00	0.250	0.74	2.12	1.26	0.44	0.37	104.31
2350026	4	42	0.0	6.86	15.1	48.1	70.0	22.0	31.4	290.0
2350028	4	42	0.0	6.97	15.4	49.1	70.0	22.1	31.4	333.0
2350030	4	42	0.0	6.98	15.3	50.7	73.0	21.9	30.2	337.0
2350032	4	42	0.0	6.58	15.0	48.4	74.0	22.8	31.0	312.0
		Mean:	0.00	6.847	15.20	49.08	71.75	22.20	31.00	318.00
		SD:	0.00	0.186	0.18	1.16	2.06	0.41	0.57	21.65

LIFE SCIENCE RESEARCH
Rome Toxicology Centre S.p.A.

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 5C - Haematology - Week 6 of treatment - Individual data

STUDY NO.: 235-003-009

MALES

Animal Number	Group	Day of Study	WBC 10'3/cmm	NEU %	LYM %	EOS %	MON %	BAS %	RET %	PT sec	APTT sec
2350002	1	42	9.8	66.0	30.0	4.0	0.0	0.0	NT	10.2	12.1
2350004	1	42	8.4	47.0	49.0	0.0	4.0	0.0	NT	9.5	12.5
2350006	1	42	7.2	74.0	21.0	5.0	0.0	0.0	NT	9.8	12.4
2350008	1	42	13.2	69.0	29.0	2.0	0.0	0.0	NT	9.4	12.4
		Mean:	9.65	64.00	32.25	2.75	1.00	0.00	-	9.73	12.35
		SD:	2.59	11.80	11.87	2.22	2.00	0.00	-	0.36	0.17
2350010	2	42	11.1	73.0	23.0	4.0	0.0	0.0	NT	9.9	12.9
2350012	2	42	10.1	46.0	51.0	1.0	2.0	0.0	NT	9.2	12.8
2350014	2	42	9.8	59.0	39.0	2.0	0.0	0.0	NT	9.3	14.0
2350016	2	42	9.7	49.0	46.0	4.0	1.0	0.0	NT	9.7	14.3
		Mean:	10.18	56.75	39.75	2.75	0.75	0.00	-	9.53	13.50
		SD:	0.64	12.18	12.20	1.50	0.96	0.00	-	0.33	0.76
2350018	3	42	15.6	61.0	37.0	2.0	0.0	0.0	NT	9.3	12.7
2350020	3	42	9.7	66.0	34.0	0.0	0.0	0.0	NT	9.6	12.9
2350022	3	42	7.8	74.0	26.0	0.0	0.0	0.0	NT	9.8	12.2
2350024	3	42	11.4	54.0	31.0	14.0	1.0	0.0	NT	9.7	13.8
		Mean:	11.13	63.75	32.00	4.00	0.25	0.00	-	9.60	12.90
		SD:	3.33	8.42	4.69	6.73	0.50	0.00	-	0.22	0.67
2350026	4	42	9.1	57.0	38.0	4.0	1.0	0.0	NT	9.5	12.6
2350028	4	42	10.2	75.0	22.0	2.0	1.0	0.0	NT	9.4	12.2
2350030	4	42	11.3	63.0	27.0	9.0	1.0	0.0	NT	10.0	13.5
2350032	4	42	9.0	53.0	42.0	5.0	0.0	0.0	NT	9.7	13.5
		Mean:	9.90	62.00	32.25	5.00	0.75	0.00	-	9.65	12.95
		SD:	1.08	9.59	9.32	2.94	0.50	0.00	-	0.26	0.66

NT = Not taken

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A.

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 5C - Haematology - Week 6 of treatment - Individual data

STUDY NO.: 235-003-009

FEMALES

Animal Number	Group	Day of Study	ESR mm/hour	RBC 10'6/cmm	HGB g/dl	HCT %	MCV fl	MCH pg	MCHC g/dl	PLT 10'3/cmm
2350001	1	42	0.0	7.51	17.0	55.2	74.0	22.6	30.8	304.0
2350003	1	42	0.0	7.10	15.2	51.1	72.0	21.4	29.7	297.0
2350005	1	42	0.0	6.52	14.8	46.7	72.0	22.7	31.7	284.0
2350007	1	42	0.0	6.40	14.7	46.1	72.0	23.0	31.9	295.0
		Mean:	0.00	6.883	15.43	49.78	72.50	22.43	31.03	295.00
		SD:	0.00	0.518	1.07	4.25	1.00	0.70	1.00	8.29
2350009	2	42	0.0	7.01	16.0	50.2	72.0	22.8	31.9	322.0
2350011	2	42	0.0	6.38	15.1	48.8	76.0	23.7	30.9	247.0
2350013	2	42	0.0	6.40	13.6	45.0	70.0	21.3	30.2	312.0
2350015	2	42	0.0	6.34	14.2	45.1	71.0	22.4	31.5	310.0
		Mean:	0.00	6.533	14.73	47.28	72.25	22.55	31.13	297.75
		SD:	0.00	0.319	1.05	2.63	2.63	0.99	0.74	34.24
2350017	3	42	0.0	6.32	12.7	45.0	71.0	20.1	28.2	291.0
2350019	3	42	0.0	7.65	17.4	55.3	72.0	22.7	31.5	277.0
2350021	3	42	0.0	6.41	14.8	46.7	73.0	23.1	31.7	203.0
2350023	3	42	0.0	7.82	16.2	55.6	71.0	20.7	29.1	298.0
		Mean:	0.00	7.050	15.28	50.65	71.75	21.65	30.13	267.25
		SD:	0.00	0.795	2.02	5.59	0.96	1.47	1.74	43.71
2350025	4	42	0.0	7.39	16.1	52.9	72.0	21.8	30.4	200.0
2350027	4	42	0.0	8.52	17.3	60.2	71.0	20.3	28.7	300.0
2350029	4	42	0.0	7.32	17.3	53.9	74.0	23.6	32.1	394.0
2350031	4	42	0.0	6.93	14.8	49.4	71.0	21.4	30.0	292.0
		Mean:	0.00	7.540	16.38	54.10	72.00	21.77	30.30	296.50
		SD:	0.00	0.684	1.19	4.50	1.41	1.37	1.40	79.27

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A.
(Dr. Alfredo Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 5C - Haematology - Week 6 of treatment - Individual data

STUDY NO.: 235-003-009

FEMALES

Animal Number	Group	Day of Study	WBC 10'3/cmm	NEU %	LYM %	EOS %	MON %	BAS %	RET %	PT sec	APTT sec
2350001	1	42	9.3	58.0	34.0	6.0	2.0	0.0	NT	9.7	11.7
2350003	1	42	6.9	57.0	35.0	7.0	1.0	0.0	NT	9.4	12.4
2350005	1	42	10.9	64.0	33.0	2.0	1.0	0.0	NT	10.6	13.6
2350007	1	42	10.7	63.0	26.0	9.0	2.0	0.0	NT	9.9	13.5
		Mean:	9.45	60.50	32.00	6.00	1.50	0.00	-	9.90	12.80
		SD:	1.84	3.51	4.08	2.94	0.58	0.00	-	0.51	0.91
2350009	2	42	8.6	62.0	37.0	1.0	0.0	0.0	NT	9.2	13.1
2350011	2	42	7.7	60.0	37.0	0.0	3.0	0.0	NT	9.3	12.6
2350013	2	42	7.8	72.0	25.0	2.0	1.0	0.0	NT	9.1	13.3
2350015	2	42	20.8	87.0	13.0	0.0	0.0	0.0	NT	9.7	13.4
		Mean:	11.23	70.25	28.00	0.75	1.00	0.00	-	9.32	13.10
		SD:	6.40	12.34	11.49	0.96	1.41	0.00	-	0.26	0.36
2350017	3	42	10.0	69.0	30.0	0.0	1.0	0.0	NT	10.1	13.1
2350019	3	42	9.2	69.0	27.0	3.0	1.0	0.0	NT	9.7	13.1
2350021	3	42	8.7	62.0	32.0	5.0	1.0	0.0	NT	9.2	13.3
2350023	3	42	8.3	82.0	17.0	1.0	0.0	0.0	NT	10.1	12.3
		Mean:	9.05	70.50	26.50	2.25	0.75	0.00	-	9.78	12.95
		SD:	0.73	8.35	6.66	2.22	0.50	0.00	-	0.43	0.44
2350025	4	42	11.5	45.0	53.0	1.0	1.0	0.0	NT	9.6	13.1
2350027	4	42	9.6	69.0	28.0	3.0	0.0	0.0	NT	9.4	12.2
2350029	4	42	10.1	66.0	32.0	2.0	0.0	0.0	NT	9.3	13.6
2350031	4	42	8.3	67.0	31.0	1.0	1.0	0.0	NT	9.6	13.3
		Mean:	9.88	61.75	36.00	1.75	0.50	0.00	-	9.48	13.05
		SD:	1.32	11.24	11.46	0.96	0.58	0.00	-	0.15	0.60

NT = Not taken

LIFE SCIENCE RESEARCH

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 5D - Haematology - Week 13 of treatment - Individual data

STUDY NO.: 235-003-009

MALES

Animal Number	Group	Day of Study	ESR mm/hour	RBC 10'6/cmm	HGB g/dl	HCT %	MCV fl	MCH pg	MCHC g/dl	PLT 10'3/cmm
2350002	1	86	0.0	6.75	14.7	47.1	70.0	21.8	31.2	301.0
2350004	1	86	0.0	7.51	17.3	51.5	69.0	23.0	33.6	263.0
2350006	1	86	0.0	6.80	15.1	48.2	71.0	22.2	31.3	244.0
2350008	1	86	0.0	6.85	15.8	48.8	71.0	23.1	32.4	182.0
		Mean:	0.00	6.978	15.73	48.90	70.25	22.52	32.13	247.50
		SD:	0.00	0.357	1.14	1.87	0.96	0.63	1.12	49.68
2350010	2	86	0.0	6.78	14.2	45.3	67.0	20.9	31.3	NT
2350012	2	86	0.0	6.43	15.1	45.1	70.0	23.5	33.5	300.0
2350014	2	86	0.0	6.39	14.6	44.5	70.0	22.8	32.8	332.0
2350016	2	86	0.0	6.14	13.7	42.1	69.0	22.3	32.5	337.0
		Mean:	0.00	6.435	14.40	44.25	69.00	22.38	32.53	323.00
		SD:	0.00	0.263	0.59	1.47	1.41	1.10	0.92	20.07
2350018	3	86	0.0	8.13	17.8	56.3	69.0	21.9	31.6	343.0
2350020	3	86	0.0	5.81	13.1	38.6	66.0	22.5	33.9	146.0
2350022	3	86	0.0	7.63	17.6	52.9	69.0	23.1	33.3	297.0
2350024	3	86	0.0	7.00	15.5	48.8	70.0	22.1	31.8	317.0
		Mean:	0.00	7.143	16.00	49.15	68.50	22.40	32.65	275.75
		SD:	0.00	1.001	2.20	7.67	1.73	0.53	1.13	88.53
2350026	4	86	0.0	6.55	14.5	44.5	68.0	22.1	32.6	260.0
2350028	4	86	0.0	7.44	16.3	50.4	68.0	21.9	32.3	287.0
2350030	4	86	0.0	6.99	15.4	49.5	71.0	22.0	31.1	296.0
2350032	4	86	0.0	6.67	15.9	46.9	70.0	23.8	33.9	337.0
		Mean:	0.00	6.913	15.53	47.83	69.25	22.45	32.48	295.00
		SD:	0.00	0.398	0.78	2.67	1.50	0.90	1.15	31.91

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A.

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 5D - Haematology - Week 13 of treatment - Individual data

STUDY NO.: 235-003-009

MALES

Animal Number	Group	Day of Study	WBC 10'3/cmm	NEU %	LYM %	EOS %	MON %	BAS %	RET %	PT sec	APTT sec	
2350002	1	86	9.6	67.0	31.0	2.0	0.0	0.0	NT	9.4	12.7	
2350004	1	86	10.9	55.0	40.0	4.0	1.0	0.0	NT	9.4	12.1	
2350006	1	86	8.2	51.0	44.0	4.0	1.0	0.0	NT	9.9	11.4	
2350008	1	86	8.6	65.0	27.0	5.0	3.0	0.0	NT	10.0	12.1	
		Mean:	9.33	59.50	35.50	3.75	1.25	0.00	-	9.68	12.08	
		SD:	1.20	7.72	7.85	1.26	1.26	0.00	-	0.32	0.53	
2350010	2	86	9.6	51.0	45.0	4.0	0.0	0.0	0	NT	9.4	11.8
2350012	2	86	10.2	46.0	52.0	2.0	0.0	0.0	0	NT	9.4	12.4
2350014	2	86	13.4	67.0	32.0	1.0	0.0	0.0	0	NT	9.4	14.2
2350016	2	86	10.8	63.0	33.0	4.0	0.0	0.0	0	NT	10.5	13.3
		Mean:	11.00	56.75	40.50	2.75	0.00	0.00	-	9.68	12.93	
		SD:	1.67	9.88	9.68	1.50	0.00	0.00	-	0.55	1.05	
2350018	3	86	13.2	60.0	37.0	2.0	1.0	0.0	NT	10.1	12.0	
2350020	3	86	10.2	60.0	37.0	3.0	0.0	0.0	NT	9.3	13.6	
2350022	3	86	11.8	86.0	13.0	0.0	1.0	0.0	NT	9.1	12.0	
2350024	3	86	12.6	46.0	33.0	21.0	0.0	0.0	NT	9.1	13.2	
		Mean:	11.95	63.00	30.00	6.50	0.50	0.00	-	9.40	12.70	
		SD:	1.30	16.69	11.49	9.75	0.58	0.00	-	0.48	0.82	
2350026	4	86	11.9	75.0	18.0	7.0	0.0	0.0	NT	9.1	14.0	
2350028	4	86	10.1	68.0	29.0	2.0	1.0	0.0	NT	10.3	12.1	
2350030	4	86	14.6	68.0	30.0	2.0	0.0	0.0	NT	9.6	13.1	
2350032	4	86	11.8	63.0	32.0	4.0	1.0	0.0	NT	10.0	12.1	
		Mean:	12.10	68.50	27.25	3.75	0.50	0.00	-	9.75	12.83	
		SD:	1.86	4.93	6.29	2.36	0.58	0.00	-	0.52	0.91	

NT = Not taken

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A.

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 5D - Haematology - Week 13 of treatment - Individual data

STUDY NO.: 235-003-009

FEMALES

Animal Number	Group	Day of Study	ESR mm/hour	RBC 10'6/cmm	HGB g/dl	HCT %	MCV fl	MCH pg	MCHC g/dl	PLT 10'3/cmm
2350001	1	86	0.0	7.32	17.0	52.1	71.0	23.2	32.6	237.0
2350003	1	86	0.0	6.29	14.2	44.0	70.0	22.6	32.3	294.0
2350005	1	86	0.0	6.30	14.4	43.4	69.0	22.9	33.2	274.0
2350007	1	86	0.0	6.84	16.0	48.0	70.0	23.4	33.3	291.0
		Mean:	0.00	6.688	15.40	46.88	70.00	23.03	32.85	274.00
		SD:	0.00	0.494	1.34	4.04	0.82	0.35	0.48	26.19
2350009	2	86	0.0	7.01	16.0	48.9	70.0	22.8	32.7	302.0
2350011	2	86	0.0	6.54	16.1	47.7	73.0	24.6	33.8	236.0
2350013	2	86	0.0	6.93	15.9	46.6	67.0	22.9	34.1	278.0
2350015	2	86	0.0	6.81	15.5	47.0	69.0	22.8	33.0	337.0
		Mean:	0.00	6.822	15.88	47.55	69.75	23.28	33.40	288.25
		SD:	0.00	0.206	0.26	1.01	2.50	0.88	0.66	42.43
2350017	3	86	0.0	6.88	15.3	47.0	68.0	22.2	32.6	301.0
2350019	3	86	0.0	7.35	16.2	51.7	70.0	22.0	31.3	248.0
2350021	3	86	0.0	6.90	16.2	48.6	70.0	23.5	33.3	235.0
2350023	3	86	0.0	7.31	17.0	51.0	70.0	23.3	33.3	303.0
		Mean:	0.00	7.110	16.18	49.58	69.50	22.75	32.63	271.75
		SD:	0.00	0.255	0.69	2.17	1.00	0.76	0.94	35.34
2350025	4	86	0.0	6.81	15.5	47.3	69.0	22.8	32.8	226.0
2350027	4	86	0.0	7.12	16.5	49.0	69.0	23.2	33.7	246.0
2350029	4	86	0.0	7.38	17.8	52.8	72.0	24.1	33.7	342.0
2350031	4	86	0.0	6.81	15.2	47.4	70.0	22.3	32.1	294.0
		Mean:	0.00	7.030	16.25	49.13	70.00	23.10	33.08	277.00
		SD:	0.00	0.275	1.17	2.57	1.41	0.76	0.78	51.88

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A.

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 5D - Haematology - Week 13 of treatment - Individual data

STUDY NO.: 235-003-009

FEMALES

Animal Number	Group	Day of Study	WBC 10'3/cmm	NEU %	LYM %	EOS %	MON %	BAS %	RET %	PT sec	APTT sec
2350001	1	86	9.9	66.0	30.0	4.0	0.0	0.0	NT	9.8	11.8
2350003	1	86	7.6	56.0	36.0	8.0	0.0	0.0	NT	9.3	12.4
2350005	1	86	14.1	72.0	28.0	0.0	0.0	0.0	NT	9.3	13.3
2350007	1	86	13.3	54.0	36.0	10.0	0.0	0.0	NT	9.3	12.9
		Mean:	11.23	62.00	32.50	5.50	0.00	0.00	-	9.43	12.60
		SD:	3.03	8.49	4.12	4.43	0.00	0.00	-	0.25	0.65
2350009	2	86	10.2	55.0	43.0	2.0	0.0	0.0	NT	9.1	12.6
2350011	2	86	7.8	61.0	35.0	2.0	2.0	0.0	NT	9.1	12.8
2350013	2	86	9.0	56.0	42.0	2.0	0.0	0.0	NT	9.5	13.3
2350015	2	86	14.5	62.0	33.0	4.0	1.0	0.0	NT	9.4	13.4
		Mean:	10.38	58.50	38.25	2.50	0.75	0.00	-	9.28	13.03
		SD:	2.92	3.51	4.99	1.00	0.96	0.00	-	0.21	0.39
2350017	3	86	10.0	73.0	27.0	0.0	0.0	0.0	NT	9.3	12.3
2350019	3	86	8.7	69.0	30.0	1.0	0.0	0.0	NT	9.6	12.8
2350021	3	86	9.9	60.0	40.0	0.0	0.0	0.0	NT	9.8	12.6
2350023	3	86	9.2	65.0	35.0	0.0	0.0	0.0	NT	9.0	11.9
		Mean:	9.45	66.75	33.00	0.25	0.00	0.00	-	9.43	12.40
		SD:	0.61	5.56	5.72	0.50	0.00	0.00	-	0.35	0.39
2350025	4	86	13.4	56.0	42.0	2.0	0.0	0.0	NT	9.7	12.6
2350027	4	86	10.7	57.0	36.0	7.0	0.0	0.0	NT	9.5	12.2
2350029	4	86	8.7	58.0	39.0	3.0	0.0	0.0	NT	9.3	12.6
2350031	4	86	9.3	62.0	36.0	1.0	1.0	0.0	NT	9.7	12.7
		Mean:	10.52	58.25	38.25	3.25	0.25	0.00	-	9.55	12.53
		SD:	2.09	2.63	2.87	2.63	0.50	0.00	-	0.19	0.22

NT = Not taken

LIFE SCIENCE RESEARCH
Rome Toxicology Centre S.p.A.

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 5E - Haematology - Bone marrow smear evaluation - Individual data

STUDY NO.: 235-003-009

MALES

Animal Number	Group	Myeloid cells %	Erythroid cells %	Ratio M/E
2350002	1	63	37	1.70
2350004	1	61	39	1.56
2350006	1	66	34	1.94
2350008	1	63	37	1.70
2350010	2	64	36	1.78
2350012	2	65	35	1.86
2350014	2	60	40	1.50
2350016	2	64	36	1.78
2350018	3	65	35	1.86
2350020	3	64	36	1.78
2350022	3	66	34	1.94
2350024	3	70	30	2.33
2350026	4	65	35	1.86
2350028	4	67	33	2.03
2350030	4	66	34	1.94
2350032	4	64	36	1.78

LIFE SCIENCE RESEARCH
Roma Technology Centre S.p.A.
(Dr. Alfredo Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 5E - Haematology - Bone marrow smear evaluation - Individual data

STUDY NO.: 235-003-009

FEMALES

Animal Number	Group	Myeloid cells %	Erythroid cells %	Ratio M/E
2350001	1	63	37	1.70
2350003	1	60	40	1.50
2350005	1	64	36	1.78
2350007	1	61	39	1.56
2350009	2	65	35	1.86
2350011	2	64	36	1.78
2350013	2	66	34	1.94
2350015	2	71	29	2.45
2350017	3	67	33	2.03
2350019	3	63	37	1.70
2350021	3	65	35	1.86
2350023	3	62	38	1.63
2350025	4	65	35	1.86
2350027	4	62	38	1.63
2350029	4	68	32	2.12
2350031	4	67	33	2.03

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A.
(Dr. Alfredo Nardini)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 6A - Clinical chemistry - Before treatment [1] - Individual data

STUDY NO.: 235-003-009

MALES

Animal Number	Group	Day of Study	AP U/l	ALT U/l	AST U/l	UREA mg/dl	GLU mg/dl	BILT mg/dl	CHOL mg/dl	CREA mg/dl
2350002	1	-13	180.9	23.8	10.3	43.0	95.0	0.110	155.6	0.80
2350004	1	-13	189.7	15.0	6.5	23.9	94.5	0.110	214.2	0.76
2350006	1	-13	163.1	16.8	10.1	23.0	93.3	0.070	143.8	0.65
2350008	1	-13	233.2	16.8	14.8	24.6	101.1	0.110	169.5	0.68
		Mean:	191.70	18.12	10.42	28.62	95.97	0.1000	170.78	0.723
		SD:	29.78	3.89	3.41	9.57	3.51	0.0200	30.80	0.069
2350010	2	-13	180.1	18.2	6.8	25.9	107.6	0.080	153.5	0.75
2350012	2	-13	189.5	18.9	12.1	22.7	110.1	0.100	186.5	0.71
2350014	2	-13	291.5	19.4	16.7	35.9	89.4	0.100	145.8	0.87
2350016	2	-13	184.5	11.8	10.4	28.2	94.5	0.100	158.6	0.68
		Mean:	211.41	17.07	11.50	28.18	100.42	0.0950	161.11	0.753
		SD:	53.55	3.58	4.11	5.61	10.02	0.0100	17.75	0.083
2350018	3	-13	257.3	16.0	10.8	25.1	108.5	0.090	154.2	0.64
2350020	3	-13	240.9	15.0	10.4	21.1	100.2	0.090	217.2	0.75
2350022	3	-13	203.7	18.2	10.5	25.6	101.3	0.100	161.7	0.80
2350024	3	-13	257.9	15.1	9.3	27.0	105.2	0.100	203.3	0.79
		Mean:	239.97	16.08	10.25	24.71	103.81	0.0950	184.11	0.745
		SD:	25.42	1.46	0.63	2.53	3.76	0.0058	30.89	0.073
2350026	4	-13	130.9	13.1	8.7	29.8	87.4	0.110	168.6	0.83
2350028	4	-13	205.0	17.7	11.1	36.0	109.3	0.060	181.4	0.82
2350030	4	-13	358.5	26.3	10.0	20.5	90.8	0.100	174.5	0.72
2350032	4	-13	449.5	23.9	12.9	22.0	105.7	0.110	150.1	0.82
		Mean:	285.95	20.26	10.69	27.09	98.32	0.0950	168.65	0.798
		SD:	144.46	6.01	1.79	7.21	10.85	0.0238	13.42	0.052

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.r.l.

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 6A - Clinical chemistry - Before treatment [1] - Individual data

STUDY NO.: 235-003-009

MALES

Animal Number	Group	Day of Study	PROT g/dl	ALB %	A1G %	A2G %	BETA %	GAM %	AGR
2350002	1	-13	5.8	55.2	5.7	7.0	12.3	19.9	1.23
2350004	1	-13	6.0	59.3	4.8	7.0	10.6	18.3	1.46
2350006	1	-13	5.4	59.9	6.0	6.1	11.3	16.7	1.49
2350008	1	-13	5.4	63.9	5.2	5.5	11.2	14.2	1.77
		Mean:	5.62	59.58	5.43	6.40	11.35	17.27	1.488
		SD:	0.31	3.56	0.53	0.73	0.70	2.43	0.221
2350010	2	-13	5.3	59.2	5.6	7.2	10.9	17.1	1.45
2350012	2	-13	5.7	62.5	4.7	5.6	13.9	13.2	1.67
2350014	2	-13	5.7	59.3	5.1	5.5	14.5	15.6	1.46
2350016	2	-13	6.0	56.6	5.0	6.0	17.3	15.1	1.31
		Mean:	5.69	59.40	5.10	6.08	14.15	15.25	1.473
		SD:	0.30	2.42	0.37	0.78	2.62	1.61	0.148
2350018	3	-13	6.3	54.1	5.1	7.4	13.1	20.3	1.18
2350020	3	-13	5.5	58.2	5.3	8.2	11.6	16.7	1.39
2350022	3	-13	5.6	61.9	4.7	6.7	9.3	17.4	1.63
2350024	3	-13	6.3	55.0	5.3	7.0	12.8	19.8	1.22
		Mean:	5.90	57.30	5.10	7.33	11.70	18.55	1.355
		SD:	0.41	3.54	0.28	0.65	1.73	1.77	0.205
2350026	4	-13	5.6	61.1	4.5	7.1	10.0	17.3	1.57
2350028	4	-13	5.7	60.4	5.3	7.7	9.9	16.7	1.53
2350030	4	-13	5.6	61.0	5.4	6.9	9.9	16.8	1.57
2350032	4	-13	5.7	58.3	5.3	7.0	12.1	17.3	1.40
		Mean:	5.64	60.20	5.13	7.18	10.48	17.02	1.518
		SD:	0.07	1.30	0.42	0.36	1.08	0.32	0.081

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LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A.

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 6A - Clinical chemistry - Before treatment [1] - Individual data

STUDY NO.: 235-003-009

MALES

Animal Number	Group	Day of Study	Cl^- mmol/l	Na^+ mmol/l	K^+ mmol/l	Ca^{++} mmol/l
2350002	1	-13	95.0	144.20	5.12	2.70
2350004	1	-13	95.9	143.50	5.14	2.75
2350006	1	-13	95.7	146.10	4.58	2.71
2350008	1	-13	97.5	146.20	4.12	2.58
		Mean:	96.02	145.000	4.740	2.685
		SD:	1.05	1.359	0.488	0.073
2350010	2	-13	93.5	143.10	4.93	2.77
2350012	2	-13	96.4	143.90	4.95	2.78
2350014	2	-13	98.2	146.70	4.94	2.78
2350016	2	-13	97.2	145.70	5.00	2.77
		Mean:	96.32	144.850	4.955	2.775
		SD:	1.99	1.644	0.031	0.006
2350018	3	-13	92.0	142.00	4.80	2.67
2350020	3	-13	100.4	144.90	5.38	2.74
2350022	3	-13	97.2	143.40	4.62	2.54
2350024	3	-13	96.5	143.20	5.28	2.68
		Mean:	96.53	143.375	5.020	2.658
		SD:	3.46	1.189	0.368	0.084
2350026	4	-13	100.0	143.20	4.87	2.60
2350028	4	-13	96.8	144.00	4.51	2.64
2350030	4	-13	97.5	142.90	4.87	2.53
2350032	4	-13	100.2	144.10	4.92	2.53
		Mean:	98.61	143.550	4.793	2.575
		SD:	1.71	0.591	0.190	0.054

LIFE SCIENCE RESEARCH
Roma Toxicology Centre S.p.A.
(Dr. Alfredo Nunziata)

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 6A - Clinical chemistry - Before treatment [1] - Individual data

STUDY NO.: 235-003-009

FEMALES

Animal Number	Group	Day of Study	AP U/l	ALT U/l	AST U/l	UREA mg/dl	GLU mg/dl	BILT mg/dl	CHOL mg/dl	CREA mg/dl
2350001	1	-13	207.0	19.7	8.5	31.6	86.5	0.110	211.5	0.72
2350003	1	-13	261.2	12.9	10.1	30.6	95.8	0.070	198.6	0.82
2350005	1	-13	225.4	22.8	11.6	28.2	104.4	0.100	159.0	0.77
2350007	1	-13	146.8	11.4	10.3	32.4	93.4	0.050	157.1	0.81
		Mean:	210.10	16.68	10.14	30.70	95.04	0.0825	181.56	0.780
		SD:	47.81	5.46	1.27	1.83	7.42	0.0275	27.66	0.045
2350009	2	-13	158.9	18.3	12.0	27.9	100.3	0.080	120.0	0.63
2350011	2	-13	178.7	16.5	9.9	28.8	83.6	0.080	119.1	0.52
2350013	2	-13	161.6	17.1	14.9	32.1	96.8	0.010	140.6	0.57
2350015	2	-13	241.8	17.8	12.6	25.4	88.9	0.100	149.3	0.55
		Mean:	185.24	17.44	12.35	28.54	92.41	0.0675	132.26	0.568
		SD:	38.69	0.78	2.09	2.79	7.56	0.0395	15.06	0.046
2350017	3	-13	349.0	19.0	12.1	23.5	93.4	0.080	153.5	0.52
2350019	3	-13	180.5	17.8	8.1	32.0	96.8	0.090	144.6	0.66
2350021	3	-13	191.8	23.2	8.8	35.1	100.9	0.080	154.3	0.54
2350023	3	-13	116.8	19.2	11.1	30.6	102.1	0.080	150.0	0.65
		Mean:	209.53	19.82	10.04	30.32	98.30	0.0825	150.63	0.593
		SD:	98.66	2.33	1.88	4.92	3.97	0.0050	4.40	0.073
2350025	4	-13	186.8	20.5	10.8	28.9	85.6	0.090	164.1	0.59
2350027	4	-13	194.8	13.8	9.5	25.6	97.8	0.090	154.2	0.65
2350029	4	-13	192.9	19.9	10.6	36.1	92.8	0.100	153.5	0.66
2350031	4	-13	147.0	17.4	12.5	31.7	93.8	0.060	155.8	0.55
		Mean:	180.38	17.89	10.84	30.55	92.49	0.0850	156.89	0.613
		SD:	22.49	3.04	1.25	4.45	5.11	0.0173	4.93	0.052

LIFE SCIENCES RESEARCH
Roma Toxicology Centre S.p.A.
Dr Alfredo Nunziati

FDP: 13 WEEK INTRAVENOUS TOXICITY STUDY IN DOGS

APPENDIX 6A - Clinical chemistry - Before treatment [1] - Individual data

STUDY NO.: 235-003-009

FEMALES

Animal Number	Group	Day of Study	PROT g/dl	ALB %	A1G %	A2G %	BETA %	GAM %	AGR
2350001	1	-13	5.7	61.6	4.8	7.1	10.2	16.2	1.61
2350003	1	-13	5.9	59.0	5.0	7.5	10.7	17.9	1.44
2350005	1	-13	5.7	60.3	5.6	5.1	11.2	17.7	1.52
2350007	1	-13	5.5	62.6	5.1	5.8	9.5	17.0	1.67
		Mean:	5.68	60.88	5.13	6.38	10.40	17.20	1.560
		SD:	0.15	1.56	0.34	1.12	0.73	0.77	0.101
2350009	2	-13	5.7	61.9	4.7	6.2	8.1	19.2	1.62
2350011	2	-13	5.5	61.5	5.8	5.0	10.0	17.7	1.59
2350013	2	-13	5.2	63.7	5.1	6.4	12.5	12.4	1.75
2350015	2	-13	5.4	60.4	5.3	6.0	10.0	18.3	1.53
		Mean:	5.47	61.88	5.23	5.90	10.15	16.90	1.623
		SD:	0.22	1.37	0.46	0.62	1.80	3.06	0.093
2350017	3	-13	5.5	60.9	5.3	6.4	9.8	17.5	1.56
2350019	3	-13	5.9	58.0	4.9	5.8	11.1	20.2	1.38
2350021	3	-13	5.8	58.4	4.9	6.3	11.1	19.3	1.40
2350023	3	-13	5.8	64.8	4.5	5.4	9.2	16.1	1.84
		Mean:	5.74	60.53	4.90	5.98	10.30	18.27	1.545
		SD:	0.18	3.13	0.33	0.46	0.96	1.83	0.213
2350025	4	-13	6.1	57.2	5.2	7.2	10.4	20.0	1.34
2350027	4	-13	6.2	58.4	5.0	5.1	9.8	21.7	1.40
2350029	4	-13	5.9	63.2	4.5	6.3	9.0	16.9	1.72
2350031	4	-13	5.3	63.4	4.8	6.6	8.6	16.7	1.73
		Mean:	5.89	60.55	4.88	6.30	9.45	18.83	1.548
		SD:	0.39	3.21	0.30	0.88	0.81	2.44	0.206

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