

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

Mid TM5509 20 mg/kg/day	MCH	MCH	MCH	MCH	MCH	MCHC	MCHC	MCHC	MCHC	MCHC
	(pg)	(pg)	(pg)	(pg)	(pg)	(g/dL)	(g/dL)	(g/dL)	(g/dL)	(g/dL)
	-1	1	2	3	4	-1	1	2	3	4
RP4M01	24.4	23.9	24.3	24.0	23.8	30.1	30.2	29.2	30.4	30.0
RP4M02	25.3	25.1	25.4	24.9	24.7	31.9	31.9	31.9	30.6	30.7
RP4M03	24.4	24.0	23.7	23.9	23.6	31.2	30.9	30.3	31.1	31.0
RP4M04	25.7	25.6	25.7	25.7	25.5	30.1	31.1	30.8	30.7	30.2
Mean	25.0	24.7	24.8	24.6	24.4	30.8	31.0	30.6	30.7	30.5
S.D.	0.7	0.8	0.9	0.8	0.9	0.9	0.7	1.1	0.3	0.5
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

Mid TM5509 20 mg/kg/day	%Retic	%Retic	%Retic	%Retic	%Retic	#Retic	#Retic	#Retic	#Retic	#Retic
	(%)	(%)	(%)	(%)	(%)	(10 ⁹ /L)	(10 ⁹ /L)	(10 ⁹ /L)	(10 ⁹ /L)	(10 ⁹ /L)
	-1	1	2	3	4	-1	1	2	3	4
RP4M01	1.3	2.6	1.9	1.8	1.6	72.1	143.2	106.1	99.1	90.5
RP4M02	0.9	2.1	2.2	2.6	1.7	48.3	108.2	106.5	135.5	89.3
RP4M03	0.8	2.1	1.8	1.5	1.4	42.2	106.0	93.0	76.8	76.9
RP4M04	1.4	1.8	2.2	2.1	2.8	83.3	92.2	114.4	112.2	143.3
Mean	1.1	2.2	2.0	2.0	1.9	61.5	112.4	105.0	105.9	100.0
S.D.	0.3	0.3	0.2	0.5	0.6	19.4	21.7	8.9	24.6	29.5
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

Mid TM5509 20 mg/kg/day	PLT					WBC				
	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)
	-1	1	2	3	4	-1	1	2	3	4
RP4M01	394	370	429	350	385	12.50	7.68	10.28	9.72	10.93
RP4M02	304	275	301	280	291	9.70	11.90	10.49	9.72	9.45
RP4M03	383	302	399	410	359	8.11	10.81	13.13	10.19	12.19
RP4M04	402	381	410	406	404	12.93	8.74	13.66	10.57	11.08
Mean	371	332	385	362	360	10.81	9.78	11.89	10.05	10.91
S.D.	45	52	57	61	49	2.30	1.92	1.75	0.41	1.13
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

Mid TM5509 20 mg/kg/day	%Neut	%Neut	%Neut	%Neut	%Neut	%Lymph	%Lymph	%Lymph	%Lymph	%Lymph
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
	-1	1	2	3	4	-1	1	2	3	4
RP4M01	44.2	30.9	26.8	34.8	34.1	50.6	63.3	66.5	60.0	60.7
RP4M02	28.3	43.8	23.4	21.0	18.4	68.1	51.9	72.7	75.3	77.1
RP4M03	28.5	47.9	48.4	41.4	47.6	66.6	48.4	48.2	55.4	49.5
RP4M04	44.7	52.9	52.9	42.3	50.0	50.3	42.6	42.4	52.9	45.8
Mean	36.4	43.9	37.9	34.9	37.5	58.9	51.6	57.5	60.9	58.3
S.D.	9.3	9.4	14.9	9.8	14.5	9.8	8.7	14.5	10.0	14.1
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

Mid TM5509 20 mg/kg/day	%Mono					%Eos				
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
	-1	1	2	3	4	-1	1	2	3	4
RP4M01	3.4	4.0	4.8	3.4	3.5	0.9	0.9	1.0	0.8	0.8
RP4M02	2.6	3.3	2.5	2.3	3.3	0.2	0.1	0.3	0.3	0.4
RP4M03	3.8	2.8	2.5	2.4	2.2	0.3	0.4	0.3	0.4	0.2
RP4M04	3.7	3.5	3.8	3.7	3.7	0.5	0.3	0.3	0.3	0.1
Mean	3.4	3.4	3.4	3.0	3.2	0.5	0.4	0.5	0.5	0.4
S.D.	0.5	0.5	1.1	0.7	0.7	0.3	0.3	0.4	0.2	0.3
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

Mid TM5509 20 mg/kg/day	%Baso	%Baso	%Baso	%Baso	%Baso	%LUC	%LUC	%LUC	%LUC	%LUC
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
	-1	1	2	3	4	-1	1	2	3	4
RP4M01	0.4	0.3	0.5	0.5	0.4	0.5	0.6	0.4	0.6	0.5
RP4M02	0.3	0.3	0.3	0.4	0.3	0.5	0.5	0.8	0.7	0.6
RP4M03	0.2	0.2	0.3	0.2	0.2	0.4	0.4	0.4	0.3	0.3
RP4M04	0.4	0.2	0.3	0.3	0.2	0.4	0.4	0.4	0.5	0.2
Mean	0.3	0.3	0.4	0.4	0.3	0.5	0.5	0.5	0.5	0.4
S.D.	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.2	0.2
N	4	4	4	4	4	4	4	4	4	4

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A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

Mid TM5509 20 mg/kg/day	#Neut	#Neut	#Neut	#Neut	#Neut	#Lymph	#Lymph	#Lymph	#Lymph	#Lymph
	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)
	-1	1	2	3	4	-1	1	2	3	4
RP4M01	5.52	2.37	2.76	3.39	3.72	6.32	4.86	6.83	5.83	6.63
RP4M02	2.75	5.22	2.45	2.04	1.74	6.60	6.18	7.63	7.32	7.28
RP4M03	2.31	5.17	6.36	4.22	5.80	5.40	5.23	6.33	5.64	6.03
RP4M04	5.78	4.63	7.23	4.47	5.54	6.51	3.73	5.79	5.59	5.07
Mean	4.09	4.35	4.70	3.53	4.20	6.21	5.00	6.65	6.10	6.25
S.D.	1.81	1.35	2.45	1.10	1.88	0.55	1.01	0.78	0.82	0.94
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

Mid TM5509 20 mg/kg/day	#Mono	#Mono	#Mono	#Mono	#Mono	#Eos	#Eos	#Eos	#Eos	#Eos
	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)
	-1	1	2	3	4	-1	1	2	3	4
RP4M01	0.43	0.31	0.50	0.33	0.38	0.12	0.07	0.10	0.07	0.09
RP4M02	0.25	0.39	0.26	0.23	0.31	0.02	0.01	0.03	0.03	0.04
RP4M03	0.31	0.31	0.32	0.24	0.27	0.03	0.04	0.04	0.04	0.02
RP4M04	0.48	0.30	0.52	0.39	0.41	0.06	0.03	0.04	0.03	0.02
Mean	0.37	0.33	0.40	0.30	0.34	0.06	0.04	0.05	0.04	0.04
S.D.	0.11	0.04	0.13	0.08	0.06	0.05	0.03	0.03	0.02	0.03
N	4	4	4	4	4	4	4	4	4	4

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A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

Mid TM5509 20 mg/kg/day	#Baso	#Baso	#Baso	#Baso	#Baso	#LUC	#LUC	#LUC	#LUC	#LUC
	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)
	-1	1	2	3	4	-1	1	2	3	4
RP4M01	0.05	0.02	0.05	0.04	0.04	0.06	0.05	0.04	0.06	0.05
RP4M02	0.03	0.03	0.04	0.04	0.03	0.05	0.06	0.09	0.07	0.05
RP4M03	0.02	0.02	0.04	0.02	0.03	0.04	0.04	0.05	0.03	0.04
RP4M04	0.05	0.02	0.04	0.04	0.02	0.05	0.04	0.05	0.05	0.03
Mean	0.04	0.02	0.04	0.04	0.03	0.05	0.05	0.06	0.05	0.04
S.D.	0.02	0.01	0.00	0.01	0.01	0.01	0.01	0.02	0.02	0.01
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

Mid TM5509 20 mg/kg/day	PT	PT	PT	PT	PT	APTT	APTT	APTT	APTT	APTT
	(s)	(s)	(s)	(s)	(s)	(s)	(s)	(s)	(s)	(s)
	-1	1	2	3	4	-1	1	2	3	4
RP4M01	9.9	9.9	9.7	10.3	10.1	21.2	21.6	21.2	21.4	21.5
RP4M02	10.5	11.4	10.9	11.1	11.0	23.7	24.5	23.7	24.1	24.5
RP4M03	10.3	10.2	10.3	10.4	10.6	25.3	24.4	25.0	25.0	24.6
RP4M04	9.6	9.9	9.4	9.9	10.0	23.6	24.0	23.4	23.4	23.8
Mean	10.1	10.4	10.1	10.4	10.4	23.5	23.6	23.3	23.5	23.6
S.D.	0.4	0.7	0.7	0.5	0.5	1.7	1.4	1.6	1.5	1.4
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

Mid TM5509 20 mg/kg/day	Fib	Fib	Fib	Fib	Fib
	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)
	-1	1	2	3	4
RP4M01	210.5	267.8	236.1	215.6	225.3
RP4M02	156.2	202.4	188.9	185.4	183.2
RP4M03	184.6	236.1	213.3	213.3	211.4
RP4M04	208.3	225.4	220.4	213.3	218.2
Mean	189.9	232.9	214.7	206.9	209.5
S.D.	25.3	27.2	19.6	14.4	18.4
N	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

Mid-High TM5509 80 mg/kg/day	RBC	RBC	RBC	RBC	RBC	HGB	HGB	HGB	HGB	HGB
	(10 ⁶ /μL)	(10 ⁶ /μL)	(10 ⁶ /μL)	(10 ⁶ /μL)	(10 ⁶ /μL)	(g/dL)	(g/dL)	(g/dL)	(g/dL)	(g/dL)
	-1	1	2	3	4	-1	1	2	3	4
RP5M01	5.69	5.14	4.92	4.99	5.20	13.3	12.2	11.8	12.0	12.5
RP5M02	7.03	6.16	5.94	5.91	5.74	14.2	12.7	12.1	12.1	11.8
RP5M03	5.74	5.08	4.98	5.11	5.04	14.7	13.1	12.8	13.1	13.1
RP5M04	6.05	5.65	5.61	5.70	5.74	13.8	13.1	12.6	13.1	13.1
Mean	6.13	5.51	5.36	5.43	5.43	14.0	12.8	12.3	12.6	12.6
S.D.	0.62	0.50	0.50	0.45	0.36	0.6	0.4	0.5	0.6	0.6
N	4	4	4	4	4	4	4	4	4	4

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A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

Mid-High TM5509 80 mg/kg/day	HCT	HCT	HCT	HCT	HCT	MCV	MCV	MCV	MCV	MCV
	(%)	(%)	(%)	(%)	(%)	(fL)	(fL)	(fL)	(fL)	(fL)
	-1	1	2	3	4	-1	1	2	3	4
RP5M01	42.5	38.4	37.5	39.1	41.2	74.7	74.7	76.1	78.3	79.3
RP5M02	51.2	44.7	42.9	44.3	40.9	72.9	72.6	72.2	74.9	71.3
RP5M03	48.8	42.2	41.5	43.1	42.0	85.0	83.1	83.4	84.4	83.3
RP5M04	44.2	41.3	42.2	43.5	43.2	73.0	73.1	75.2	76.3	75.3
Mean	46.7	41.7	41.0	42.5	41.8	76.4	75.9	76.7	78.5	77.3
S.D.	4.0	2.6	2.4	2.3	1.0	5.8	4.9	4.8	4.2	5.2
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

Mid-High TM5509 80 mg/kg/day	MCH					MCHC				
	(pg)	(pg)	(pg)	(pg)	(pg)	(g/dL)	(g/dL)	(g/dL)	(g/dL)	(g/dL)
	-1	1	2	3	4	-1	1	2	3	4
RP5M01	23.4	23.7	24.0	24.1	24.0	31.3	31.7	31.5	30.8	30.3
RP5M02	20.2	20.7	20.3	20.5	20.6	27.8	28.5	28.2	27.4	28.8
RP5M03	25.6	25.8	25.8	25.7	25.9	30.1	31.0	30.9	30.5	31.1
RP5M04	22.8	23.2	22.5	23.0	22.9	31.3	31.7	29.9	30.1	30.4
Mean	23.0	23.4	23.2	23.3	23.4	30.1	30.7	30.1	29.7	30.2
S.D.	2.2	2.1	2.3	2.2	2.2	1.7	1.5	1.4	1.6	1.0
N	4	4	4	4	4	4	4	4	4	4

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A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

Mid-High TM5509 80 mg/kg/day	%Retic	%Retic	%Retic	%Retic	%Retic	#Retic	#Retic	#Retic	#Retic	#Retic
	(%)	(%)	(%)	(%)	(%)	(10 ⁹ /L)	(10 ⁹ /L)	(10 ⁹ /L)	(10 ⁹ /L)	(10 ⁹ /L)
	-1	1	2	3	4	-1	1	2	3	4
RP5M01	0.8	2.5	2.2	2.2	1.9	45.8	130.5	105.9	110.3	101.3
RP5M02	0.9	2.1	1.0	1.6	0.9	59.9	129.3	58.6	92.1	53.9
RP5M03	1.1	2.0	2.4	2.4	2.1	61.5	100.0	121.0	123.8	107.5
RP5M04	1.8	2.2	2.5	2.2	2.0	107.6	121.8	142.5	125.5	116.6
Mean	1.2	2.2	2.0	2.1	1.7	68.7	120.4	107.0	112.9	94.8
S.D.	0.5	0.2	0.7	0.3	0.6	26.9	14.1	35.6	15.5	28.0
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

Mid-High TM5509 80 mg/kg/day	PLT	PLT	PLT	PLT	PLT	WBC	WBC	WBC	WBC	WBC
	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)
	-1	1	2	3	4	-1	1	2	3	4
RP5M01	450	456	506	476	522	9.71	7.25	7.23	5.81	6.76
RP5M02	460	450	506	507	436	10.92	8.70	8.96	11.78	8.96
RP5M03	434	438	442	399	421	13.74	6.60	11.40	9.32	7.38
RP5M04	697	425	443	430	452	10.69	8.41	9.43	8.43	10.53
Mean	510	442	474	453	458	11.27	7.74	9.26	8.84	8.41
S.D.	125	14	37	48	45	1.73	0.98	1.71	2.46	1.69
N	4	4	4	4	4	4	4	4	4	4

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A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

Mid-High TM5509 80 mg/kg/day	%Neut					%Lymph				
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
	-1	1	2	3	4	-1	1	2	3	4
RP5M01	31.4	48.1	43.1	31.1	31.5	60.0	46.0	49.7	57.8	59.9
RP5M02	22.2	46.8	32.3	52.8	37.3	73.3	49.5	63.0	44.7	58.9
RP5M03	32.2	43.1	53.8	56.5	47.4	64.5	54.3	43.8	42.0	50.4
RP5M04	23.6	29.5	23.2	24.4	23.2	71.4	66.2	71.4	71.9	71.8
Mean	27.4	41.9	38.1	41.2	34.9	67.3	54.0	57.0	54.1	60.3
S.D.	5.2	8.5	13.3	15.8	10.2	6.2	8.8	12.5	13.7	8.8
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

Mid-High TM5509 80 mg/kg/day	%Mono	%Mono	%Mono	%Mono	%Mono	%Eos	%Eos	%Eos	%Eos	%Eos
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
	-1	1	2	3	4	-1	1	2	3	4
RP5M01	5.1	4.1	4.1	4.2	3.6	2.2	1.0	1.9	5.0	3.7
RP5M02	2.8	2.8	2.9	1.4	2.5	0.6	0.3	0.5	0.4	0.4
RP5M03	1.8	2.0	1.7	1.0	1.4	0.3	0.1	0.1	0.1	0.3
RP5M04	2.7	2.8	3.0	2.3	3.2	1.5	0.8	1.5	0.6	1.0
Mean	3.1	2.9	2.9	2.2	2.7	1.2	0.6	1.0	1.5	1.4
S.D.	1.4	0.9	1.0	1.4	1.0	0.9	0.4	0.8	2.3	1.6
N	4	4	4	4	4	4	4	4	4	4

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A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

Mid-High TM5509 80 mg/kg/day	%Baso	%Baso	%Baso	%Baso	%Baso	%LUC	%LUC	%LUC	%LUC	%LUC
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
	-1	1	2	3	4	-1	1	2	3	4
RP5M01	0.4	0.2	0.3	0.3	0.4	1.0	0.5	0.9	1.6	1.0
RP5M02	0.4	0.4	0.5	0.3	0.3	0.6	0.3	0.8	0.4	0.6
RP5M03	0.6	0.3	0.3	0.2	0.2	0.6	0.2	0.2	0.2	0.3
RP5M04	0.4	0.2	0.4	0.3	0.3	0.4	0.4	0.4	0.5	0.6
Mean	0.5	0.3	0.4	0.3	0.3	0.7	0.4	0.6	0.7	0.6
S.D.	0.1	0.1	0.1	0.0	0.1	0.3	0.1	0.3	0.6	0.3
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

Mid-High TM5509 80 mg/kg/day	#Neut	#Neut	#Neut	#Neut	#Neut	#Lymph	#Lymph	#Lymph	#Lymph	#Lymph
	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)
	-1	1	2	3	4	-1	1	2	3	4
RP5M01	3.05	3.49	3.12	1.81	2.13	5.82	3.34	3.60	3.36	4.05
RP5M02	2.43	4.07	2.89	6.22	3.34	8.01	4.31	5.65	5.27	5.28
RP5M03	4.43	2.84	6.13	5.26	3.50	8.86	3.58	5.00	3.91	3.72
RP5M04	2.53	2.48	2.19	2.06	2.45	7.64	5.57	6.73	6.06	7.56
Mean	3.11	3.22	3.58	3.84	2.86	7.58	4.20	5.25	4.65	5.15
S.D.	0.92	0.70	1.74	2.23	0.67	1.28	1.00	1.31	1.24	1.74
N	4	4	4	4	4	4	4	4	4	4