

Table 2-2 Evaluation of Antibody Production by Recombinant Human Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF) Product in Cynomolgus Monkeys: II  
Body weight (males) -2nd course-

		Unit: kg														
Group	Dose level	Animal No.	Day													
			-1	7	14	21	28	35	42	49	56	63	70	77	84	91
I CHO cell-derived GM-CSF	15 µg/body	UJM01	4.35	4.45	4.45	4.45	4.45	4.45	4.55	4.70	4.75	4.70	4.80	4.75	4.75	4.75
		UJM02	2.90	3.00	2.95	2.95	3.00	2.95	2.90	3.00	3.00	2.95	2.95	2.90	2.95	3.00
II Escherichia coli-derived GM-CSF	15 µg/body	UJM11	3.45	3.50	3.55	3.60	3.55	3.50	3.50	3.50	3.50	3.55	3.55	3.60	3.65	3.65
		UJM12	2.80	2.75	2.75	2.80	2.85	2.85	2.85	2.85	2.95	2.95	3.00	3.00	2.95	3.00

Table 3-1 Evaluation of Antibody Production by Recombinant Human Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF) Product in Cynomolgus Monkeys: II  
Body temperature (males) -1st course-

		Unit: °C															
Group	Dose level	Animal No.	Day														
			-1	7	14	21	28	35	42	49	56	63	70	77	84	89	
																Before anesthesia	After recovery from anesthesia
I CHO cell-derived GM-CSF	15 µg/body	UJM01	37.4	37.7	38.0	38.8	38.4	38.3	38.5	38.6	38.2	38.4	38.8	37.8	37.5	38.1	36.8
		UJM02	38.9	39.2	39.2	39.4	39.5	38.9	39.4	39.5	39.5	39.5	39.4	39.1	39.3	39.1	37.0
II Escherichia coli-derived GM-CSF	15 µg/body	UJM11	39.1	39.4	39.4	39.5	39.5	39.4	39.6	39.6	39.7	39.7	39.7	39.7	39.8	39.6	37.4
		UJM12	38.6	39.1	39.1	39.1	38.5	39.2	39.3	39.3	39.1	39.1	39.5	39.4	39.3	39.4	36.6

Table 3-2 Evaluation of Antibody Production by Recombinant Human Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF) Product in Cynomolgus Monkeys: II  
Body temperature (males) -2nd course-

		Unit: °C																
Group	Dose level	Animal No.	Day													91		
			-1	7	14	21	28	35	42	49	56	63	70	77	84	Before anesthesia	After recovery from anesthesia	
I	CHO cell-derived GM-CSF	15 µg/body	UJM01	37.9	38.1	37.1	37.0	37.4	37.7	37.2	37.0	36.8	37.6	38.1	38.4	37.4	38.2	36.6
			UJM02	39.1	39.1	39.1	38.8	39.3	39.2	38.8	38.8	39.0	38.8	39.4	38.8	39.0	38.8	37.9
II	Escherichia coli-derived GM-CSF	15 µg/body	UJM11	39.4	39.6	39.3	39.4	39.7	39.6	39.7	39.4	39.8	39.3	39.5	39.6	39.5	39.3	37.7
			UJM12	38.8	39.0	39.2	38.8	38.5	38.8	39.0	38.8	39.1	38.5	39.0	39.0	38.7	38.9	38.0

Table 4-1 Evaluation of Antibody Production by Recombinant Human Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF) Product in Cynomolgus Monkeys: II  
Hematology -List of abbreviations-

Abbreviation	Expansion
RBC	Red blood cell count
HGB	Hemoglobin concentration
HCT	Hematocrit
MCV	Mean corpuscular volume
MCH	Mean corpuscular hemoglobin
MCHC	Mean corpuscular hemoglobin concentration
Retic	Reticulocytes
PLT	Platelet count
WBC	White blood cell count
Diff WBC	Differential white blood cells
Neut	Neutrophils
Lymph	Lymphocytes
Mono	Monocytes
Eos	Eosinophils
Baso	Basophils
LUC	Large unstained cells
PT	Prothrombin time
APTT	Activated partial thromboplastin time

Table 4-2 Evaluation of Antibody Production by Recombinant Human Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF) Product in Cynomolgus Monkeys: II  
Hematology (males) -1st course-

Group	Dose level	Animal No.	Observation time	RBC (10 <sup>6</sup> /μL)	HGB (g/dL)	HCT (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	Retic		PLT (10 <sup>3</sup> /μL)	WBC (10 <sup>3</sup> /μL)
										(%)	(10 <sup>9</sup> /L)		
I CHO cell-derived GM-CSF	15 μg/body	UJM01	Day -1	5.70	13.9	44.5	78.1	24.3	31.1	1.3	71.7	247	12.33
			Day 2	5.38	12.8	42.1	78.2	23.8	30.5	1.5	81.0	227	18.92
			Day 28	5.76	13.3	45.9	79.7	23.1	29.0	1.7	99.9	249	11.78
			Day 30	5.34	12.6	43.1	80.7	23.7	29.3	1.6	86.3	241	8.09
			Day 56	5.72	13.8	45.5	79.4	24.2	30.4	1.5	83.6	243	9.84
			Day 58	5.58	12.9	44.6	79.9	23.2	29.0	1.6	88.9	261	12.43
			Day 83	5.59	13.5	45.1	80.6	24.1	29.9	1.5	83.5	235	11.10
			Day 84	5.48	13.3	44.4	81.0	24.2	29.9	1.3	69.7	239	12.21
	UJM02	Day -1	6.03	13.9	43.4	71.9	23.0	32.0	1.2	73.7	263	9.19	
		Day 2	5.46	12.2	38.7	70.8	22.3	31.5	1.4	74.6	231	14.01	
		Day 28	5.86	12.8	43.7	74.5	21.9	29.4	1.9	110.4	258	7.51	
		Day 30	5.41	11.8	41.7	77.1	21.7	28.2	2.2	119.7	208	7.85	
		Day 56	6.09	13.4	45.6	74.9	21.9	29.3	1.1	64.7	265	8.53	
		Day 58	5.77	12.6	43.7	75.8	21.8	28.8	1.2	70.4	225	8.83	
		Day 83	6.07	13.1	44.8	73.8	21.6	29.3	1.4	82.6	206	7.75	
		Day 84	5.95	13.2	43.3	72.7	22.1	30.4	0.9	53.4	200	7.88	
II Escherichia coli-derived GM-CSF	15 μg/body	UJM11	Day -1	6.05	14.2	46.9	77.4	23.5	30.3	0.9	53.7	412	7.06
			Day 2	5.49	12.9	42.1	76.7	23.5	30.6	0.7	38.2	339	9.32
			Day 28	5.76	13.6	45.8	79.6	23.6	29.6	1.1	63.6	425	5.37
			Day 30	5.71	13.0	47.0	82.2	22.8	27.7	0.9	53.9	369	7.06
			Day 56	6.00	14.2	48.9	81.6	23.6	28.9	1.3	78.0	377	8.24
			Day 58	5.72	13.2	46.8	81.8	23.0	28.2	1.2	67.5	386	8.78
			Day 83	5.77	13.7	47.0	81.4	23.7	29.1	1.0	58.9	400	10.18
			Day 84	5.72	13.5	46.4	81.2	23.6	29.1	1.0	57.4	372	7.78
	UJM12	Day -1	5.92	13.7	42.6	72.1	23.1	32.1	1.3	79.3	403	6.38	
		Day 2	5.43	12.5	40.5	74.6	23.1	30.9	1.6	86.3	344	11.27	
		Day 28	6.01	13.5	44.4	73.8	22.5	30.5	1.6	95.0	456	6.30	
		Day 30	5.40	12.1	41.3	76.5	22.4	29.3	1.1	57.9	408	9.79	
		Day 56	5.89	13.3	45.1	76.5	22.6	29.5	1.9	109.2	400	9.07	
		Day 58	5.40	12.2	42.4	78.5	22.5	28.7	2.1	113.1	374	6.25	
		Day 83	5.66	12.8	43.8	77.4	22.7	29.3	2.0	110.6	393	10.42	
		Day 84	5.72	12.9	44.3	77.5	22.6	29.1	1.9	106.8	374	8.39	

Table 4-2 (Continued) Evaluation of Antibody Production by Recombinant Human Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF) Product in Cynomolgus Monkeys: II  
Hematology (males) -1st course-

Group	Dose level	Animal No.	Observation time	Diff WBC (%)						Diff WBC (10 <sup>3</sup> /μL)						PT (s)	APTT (s)
				Neut	Lymph	Mono	Eos	Baso	LUC	Neut	Lymph	Mono	Eos	Baso	LUC		
I CHO cell-derived GM-CSF	15 μg/body	UJM01	Day -1	14.3	81.0	3.0	0.6	0.3	0.7	1.77	9.98	0.37	0.07	0.04	0.09	10.6	22.8
			Day 2	51.8	43.0	3.0	1.4	0.4	0.4	9.81	8.13	0.57	0.26	0.08	0.07	10.7	22.3
			Day 28	17.0	76.4	4.0	1.4	0.3	0.8	2.00	9.00	0.48	0.17	0.04	0.10	10.8	22.8
			Day 30	20.0	74.6	3.1	1.6	0.2	0.4	1.62	6.03	0.25	0.13	0.02	0.03	10.8	22.4
			Day 56	26.1	68.0	3.5	1.3	0.4	0.6	2.57	6.69	0.35	0.13	0.04	0.05	10.3	22.6
			Day 58	41.2	54.2	2.6	1.3	0.3	0.4	5.12	6.74	0.32	0.16	0.04	0.05	10.3	22.1
			Day 83	27.1	68.4	2.5	1.3	0.4	0.3	3.01	7.60	0.28	0.14	0.04	0.04	10.4	22.6
			Day 84	33.5	62.4	2.7	0.8	0.4	0.2	4.09	7.62	0.33	0.09	0.05	0.03	10.2	22.3
	UJM02	Day -1	15.2	80.2	2.3	1.0	0.5	0.9	1.40	7.37	0.21	0.09	0.04	0.08	10.4	25.3	
		Day 2	46.8	47.6	2.2	2.4	0.4	0.6	6.55	6.67	0.31	0.34	0.05	0.09	9.9	24.0	
		Day 28	16.2	77.9	2.8	2.2	0.3	0.7	1.21	5.85	0.21	0.16	0.03	0.05	10.0	23.7	
		Day 30	15.4	80.1	2.2	1.7	0.3	0.4	1.21	6.29	0.17	0.13	0.02	0.03	10.0	23.3	
		Day 56	28.9	66.1	2.1	2.0	0.4	0.6	2.47	5.64	0.18	0.17	0.03	0.05	9.9	25.3	
		Day 58	33.2	61.5	3.0	1.4	0.3	0.6	2.93	5.43	0.26	0.12	0.02	0.05	9.5	24.6	
		Day 83	22.0	71.5	2.4	3.3	0.4	0.5	1.70	5.54	0.19	0.25	0.03	0.04	9.9	24.9	
		Day 84	20.2	73.7	2.6	2.6	0.2	0.7	1.59	5.81	0.21	0.20	0.02	0.05	10.2	25.4	
II Escherichia coli-derived GM-CSF	15 μg/body	UJM11	Day -1	22.8	71.1	4.2	1.3	0.2	0.4	1.61	5.02	0.30	0.09	0.01	0.03	10.4	23.3
			Day 2	56.7	37.9	1.6	3.4	0.3	0.2	5.28	3.53	0.15	0.32	0.02	0.02	9.9	22.3
			Day 28	42.5	54.0	2.7	0.3	0.3	0.3	2.29	2.90	0.14	0.02	0.01	0.01	10.4	23.3
			Day 30	40.2	54.0	3.5	1.8	0.4	0.2	2.83	3.81	0.25	0.12	0.03	0.01	9.7	21.7
			Day 56	51.9	41.8	2.5	3.4	0.3	0.2	4.27	3.44	0.20	0.28	0.03	0.01	9.8	22.4
			Day 58	47.9	44.6	3.2	3.8	0.3	0.3	4.20	3.91	0.28	0.33	0.03	0.02	9.7	22.4
			Day 83	42.5	42.6	2.6	11.6	0.3	0.4	4.32	4.34	0.27	1.18	0.03	0.04	10.0	22.5
			Day 84	26.4	59.3	2.3	11.3	0.3	0.4	2.05	4.62	0.18	0.88	0.03	0.03	9.9	22.4
	UJM12	Day -1	44.8	51.4	2.9	0.2	0.3	0.4	2.86	3.28	0.19	0.01	0.02	0.02	9.8	25.8	
		Day 2	72.4	25.1	1.4	0.6	0.2	0.3	8.15	2.83	0.16	0.07	0.02	0.03	9.9	25.2	
		Day 28	64.9	32.9	1.7	0.1	0.1	0.2	4.09	2.07	0.11	0.01	0.00	0.01	9.9	27.2	
		Day 30	61.8	34.0	3.3	0.3	0.2	0.4	6.06	3.33	0.32	0.03	0.02	0.04	9.5	24.4	
		Day 56	63.9	32.6	2.7	0.3	0.2	0.4	5.79	2.95	0.24	0.03	0.02	0.03	9.1	25.0	
		Day 58	51.4	45.0	2.6	0.4	0.2	0.4	3.21	2.82	0.16	0.03	0.01	0.03	9.3	26.0	
		Day 83	62.5	33.6	2.8	0.4	0.1	0.5	6.51	3.50	0.30	0.05	0.01	0.05	9.3	25.5	
		Day 84	62.3	33.4	3.3	0.3	0.3	0.4	5.23	2.80	0.27	0.03	0.03	0.03	9.1	25.3	

Table 4-3 Evaluation of Antibody Production by Recombinant Human Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF) Product in Cynomolgus Monkeys: II  
Hematology (males) -2nd course-

Group	Dose level	Animal No.	Observation time	RBC ( $10^6/\mu\text{L}$ )	HGB (g/dL)	HCT (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	Retic		PLT ( $10^3/\mu\text{L}$ )	WBC ( $10^3/\mu\text{L}$ )
										(%)	( $10^9/\text{L}$ )		
I CHO cell-derived GM-CSF	15 $\mu\text{g}/\text{body}$	UJM01	Day -1	6.08	14.3	47.8	78.6	23.4	29.8	1.2	71.8	258	11.47
			Day 2	5.77	13.5	44.9	77.9	23.4	30.1	1.2	69.2	249	10.76
			Day 30	5.53	13.1	43.5	78.6	23.6	30.1	2.0	111.7	252	10.94
			Day 58	5.23	12.5	40.8	78.1	23.9	30.6	2.0	105.3	226	12.02
			Day 86	5.45	12.8	43.9	80.6	23.4	29.1	1.5	82.5	288	14.50
		UJM02	Day -1	6.48	14.0	46.3	71.4	21.5	30.1	0.7	44.1	231	10.18
			Day 2	5.84	12.8	41.6	71.4	21.9	30.6	1.2	69.8	209	14.56
			Day 30	5.76	12.8	41.3	71.8	22.2	30.9	1.2	68.6	238	8.63
			Day 58	5.81	13.1	43.2	74.3	22.5	30.2	1.2	71.5	284	10.47
			Day 86	5.89	12.8	44.0	74.7	21.7	29.0	1.2	71.6	293	11.39
II Escherichia coli-derived GM-CSF	15 $\mu\text{g}/\text{body}$	UJM11	Day -1	6.50	14.9	50.4	77.6	23.0	29.6	0.5	31.2	334	9.62
			Day 2	5.99	13.8	46.3	77.3	23.1	29.8	0.7	42.3	313	15.39
			Day 30	5.66	13.1	44.4	78.4	23.2	29.6	0.8	48.0	376	7.21
			Day 58	5.72	13.5	45.1	78.9	23.6	29.9	0.6	37.1	340	8.40
			Day 86	5.65	13.3	46.5	82.3	23.4	28.5	1.2	66.9	385	10.97
		UJM12	Day -1	6.34	14.3	46.9	73.9	22.6	30.5	0.9	57.0	356	8.41
			Day 2	6.13	13.9	45.0	73.4	22.7	30.9	0.9	53.0	368	8.59
			Day 30	5.84	13.3	44.6	76.4	22.8	29.8	1.9	112.4	401	7.61
			Day 58	5.53	12.8	45.1	81.6	23.1	28.3	2.0	109.4	380	10.16
			Day 86	5.93	13.2	46.6	78.6	22.2	28.3	1.4	85.2	441	8.99

Table 4-3 (Continued) Evaluation of Antibody Production by Recombinant Human Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF) Product in Cynomolgus Monkeys: II  
Hematology (males) -2nd course-

Group	Dose level	Animal No.	Observation time	Diff WBC (%)						Diff WBC ( $10^3/\mu\text{L}$ )						PT (s)	APTT (s)
				Neut	Lymph	Mono	Eos	Baso	LUC	Neut	Lymph	Mono	Eos	Baso	LUC		
I CHO cell-derived GM-CSF	15 $\mu\text{g}/\text{body}$	UJM01	Day -1	22.3	72.0	3.8	0.9	0.4	0.5	2.56	8.26	0.44	0.10	0.05	0.06	10.6	22.4
			Day 2	25.9	68.3	3.9	1.1	0.2	0.6	2.78	7.35	0.42	0.12	0.02	0.06	10.7	22.8
			Day 30	46.2	49.2	3.0	0.9	0.3	0.6	5.05	5.38	0.32	0.09	0.03	0.06	10.4	22.6
			Day 58	27.4	67.8	3.3	0.8	0.4	0.4	3.29	8.15	0.39	0.09	0.04	0.05	10.5	23.2
			Day 86	47.6	47.8	2.9	0.8	0.4	0.5	6.90	6.93	0.43	0.12	0.05	0.08	10.1	21.7
		UJM02	Day -1	20.2	75.3	2.8	0.7	0.3	0.6	2.06	7.66	0.29	0.07	0.03	0.07	10.2	24.1
			Day 2	43.9	50.4	2.4	2.3	0.3	0.7	6.40	7.33	0.36	0.33	0.04	0.10	10.0	24.4
			Day 30	45.0	49.6	2.2	2.6	0.1	0.4	3.88	4.29	0.19	0.23	0.01	0.03	10.4	24.7
			Day 58	33.2	60.6	1.9	3.5	0.2	0.6	3.47	6.35	0.20	0.37	0.02	0.06	10.2	24.3
			Day 86	43.5	48.8	2.2	4.6	0.2	0.6	4.96	5.56	0.25	0.53	0.03	0.07	10.3	24.5
II Escherichia coli-derived GM-CSF	15 $\mu\text{g}/\text{body}$	UJM11	Day -1	28.8	66.3	3.0	1.2	0.2	0.4	2.77	6.38	0.29	0.11	0.02	0.04	10.1	22.3
			Day 2	63.3	30.9	1.8	3.5	0.2	0.3	9.74	4.76	0.28	0.54	0.03	0.04	9.9	22.3
			Day 30	55.5	40.3	2.4	1.2	0.3	0.3	4.00	2.90	0.17	0.09	0.02	0.02	10.2	22.6
			Day 58	46.3	48.7	2.0	2.2	0.3	0.4	3.89	4.09	0.17	0.19	0.02	0.04	10.2	22.0
			Day 86	56.3	38.9	2.1	2.1	0.2	0.3	6.18	4.27	0.24	0.23	0.02	0.03	9.9	22.4
		UJM12	Day -1	54.8	41.1	3.3	0.2	0.1	0.4	4.61	3.45	0.28	0.02	0.01	0.04	9.4	25.2
			Day 2	61.1	35.0	3.1	0.3	0.2	0.3	5.25	3.01	0.26	0.03	0.02	0.03	9.7	25.7
			Day 30	56.6	37.7	4.8	0.1	0.2	0.5	4.31	2.87	0.37	0.01	0.01	0.04	9.8	26.1
			Day 58	64.5	31.8	2.6	0.4	0.2	0.6	6.55	3.23	0.26	0.04	0.02	0.06	9.1	24.9
			Day 86	60.2	35.9	2.8	0.4	0.2	0.6	5.41	3.23	0.25	0.03	0.01	0.05	9.5	24.5

Table 5-1 Evaluation of Antibody Production by Recombinant Human Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF) Product in Cynomolgus Monkeys: II  
Clinical chemistry -List of abbreviations-

Abbreviation	Expansion
AST	Aspartate aminotransferase
ALT	Alanine aminotransferase
ALP	Alkaline phosphatase
LD	Lactate dehydrogenase
CK	Creatine kinase
GLU	Glucose
BIL	Total bilirubin
UN	Urea nitrogen
CRE	Creatinine
CHO	Total cholesterol
TG	Triglycerides
PL	Phospholipids
IP	Inorganic phosphorus
CA	Calcium
NA	Sodium
K	Potassium
CL	Chloride
TP	Total protein
ALB	Albumin
A/G	Albumin/globulin ratio
CRP	C-reactive protein

Table 5-2 Evaluation of Antibody Production by Recombinant Human Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF) Product in Cynomolgus Monkeys: II  
Clinical chemistry (males) -1st course-

Group	Dose level	Animal No.	Observation time	AST (U/L)	ALT (U/L)	ALP (U/L)	LD (U/L)	CK (U/L)	GLU (mg/dL)	BIL (mg/dL)	UN (mg/dL)	CRE (mg/dL)	CHO (mg/dL)	TG (mg/dL)	PL (mg/dL)
I CHO cell-derived GM-CSF	15 µg/body	UJM01	Day -1	29	52	1704	290	194	63	0.15	23.0	0.61	116	43	195
			Day 2	29	59	1646	295	181	58	0.11	18.3	0.62	109	48	185
			Day 28	26	53	1645	271	191	73	0.15	21.2	0.61	131	30	210
			Day 30	28	55	1593	312	177	64	0.13	16.9	0.62	124	41	197
			Day 56	29	56	1678	281	191	68	0.12	20.7	0.58	136	38	214
			Day 58	30	57	1668	279	162	71	0.11	17.3	0.61	125	48	198
			Day 83	28	55	1397	260	160	56	0.09	25.2	0.65	117	88	204
			Day 84	31	63	1428	275	159	76	0.08	22.9	0.65	119	97	226
	UJM02	Day -1	33	29	1220	326	195	76	0.11	18.7	0.80	150	29	187	
		Day 2	51	35	1143	450	228	74	0.12	17.1	0.82	128	39	192	
		Day 28	30	24	1462	344	162	104	0.10	20.5	0.79	140	28	182	
		Day 30	38	25	1370	408	159	78	0.11	20.5	0.79	130	29	175	
		Day 56	34	26	1616	368	201	87	0.10	21.0	0.85	159	26	213	
		Day 58	44	29	1632	430	190	73	0.08	17.9	0.84	143	36	208	
		Day 83	35	31	1558	388	199	87	0.08	22.0	0.88	140	29	189	
		Day 84	35	30	1538	438	180	95	0.08	21.6	0.88	145	41	187	
II Escherichia coli-derived GM-CSF	15 µg/body	UJM11	Day -1	29	45	2501	260	212	71	0.12	15.9	0.70	161	29	221
			Day 2	81	89	2456	483	502	86	0.14	15.3	0.67	136	50	214
			Day 28	32	71	2596	334	198	58	0.28	14.8	0.80	172	22	251
			Day 30	38	77	1961	448	140	79	0.10	14.8	0.70	139	46	220
			Day 56	26	66	2513	331	201	56	0.16	19.3	0.74	162	20	240
			Day 58	36	72	2208	431	316	73	0.11	15.8	0.73	153	20	205
			Day 83	33	72	2451	325	129	83	0.09	16.7	0.71	149	41	224
			Day 84	24	73	2340	308	113	82	0.07	16.2	0.73	138	70	240
	UJM12	Day -1	22	32	992	234	131	93	0.08	16.4	0.66	149	44	207	
		Day 2	178	95	987	951	3023	102	0.09	10.7	0.66	133	21	195	
		Day 28	45	63	1187	410	234	62	0.15	19.1	0.82	160	14	227	
		Day 30	41	58	923	452	117	101	0.07	17.8	0.70	129	29	207	
		Day 56	32	50	916	304	197	97	0.06	17.6	0.68	162	64	234	
		Day 58	30	46	912	324	150	88	0.06	12.6	0.70	147	50	198	
		Day 83	26	37	751	315	137	80	0.05	18.3	0.68	149	60	235	
		Day 84	30	41	803	309	167	87	0.06	15.9	0.72	150	87	226	

Table 5-2 (Continued) Evaluation of Antibody Production by Recombinant Human Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF) Product in Cynomolgus Monkeys: II  
Clinical chemistry (males) -1st course-

Group	Dose level	Animal No.	Observation time	IP (mg/dL)	CA (mg/dL)	NA (mEq/L)	K (mEq/L)	CL (mEq/L)	TP (g/dL)	ALB (g/dL)	A/G	CRP (mg/dL)
I CHO cell-derived GM-CSF	15 µg/body	UJM01	Day -1	5.87	9.81	145.7	3.90	109.1	7.00	4.29	1.58	0.18
			Day 2	5.24	9.43	147.5	3.70	112.6	6.52	4.17	1.77	0.20
			Day 28	5.52	9.47	147.3	3.42	110.5	6.74	4.09	1.54	0.19
			Day 30	5.15	9.39	145.9	3.68	110.7	6.60	4.02	1.56	0.18
			Day 56	5.72	9.30	148.0	3.60	107.5	6.83	4.19	1.59	0.20
			Day 58	4.66	9.24	148.5	2.98	111.5	6.53	4.03	1.61	0.17
			Day 83	4.97	9.30	147.5	4.01	109.7	6.96	4.16	1.49	0.16
			Day 84	5.58	9.33	148.5	3.89	109.2	7.16	4.27	1.48	0.19
	UJM02	Day -1	5.78	9.11	148.7	3.92	109.7	7.00	3.86	1.23	0.11	
		Day 2	4.39	9.05	150.0	4.41	116.0	6.28	3.59	1.33	0.42	
		Day 28	4.91	8.66	147.4	3.24	110.3	6.96	3.67	1.12	0.16	
		Day 30	4.64	8.99	150.6	4.04	111.7	6.65	3.62	1.19	0.15	
		Day 56	5.55	9.10	149.9	3.54	106.2	7.05	3.91	1.25	0.30	
		Day 58	4.39	9.30	151.1	3.64	110.2	6.89	3.77	1.21	0.85	
		Day 83	4.83	8.98	149.8	4.05	108.0	6.68	3.81	1.33	0.23	
		Day 84	4.78	8.80	147.8	3.58	109.8	6.92	3.87	1.27	0.18	
II Escherichia coli-derived GM-CSF	15 µg/body	UJM11	Day -1	5.12	9.10	149.5	3.75	111.1	6.76	3.63	1.16	0.08
			Day 2	4.20	8.94	149.0	3.96	115.9	6.47	3.42	1.12	0.87
			Day 28	6.07	8.90	148.0	3.44	108.6	6.97	3.66	1.11	0.47
			Day 30	4.36	9.46	150.1	4.28	111.0	6.84	3.56	1.09	0.12
			Day 56	5.73	9.07	151.3	3.75	108.6	7.23	3.71	1.05	0.21
			Day 58	5.41	8.90	153.2	3.86	110.9	6.86	3.57	1.09	0.26
			Day 83	4.52	9.05	151.8	3.75	109.7	6.89	3.70	1.16	0.48
			Day 84	4.38	9.04	150.6	3.70	109.5	7.08	3.73	1.11	0.24
	UJM12	Day -1	4.94	9.26	149.2	4.03	113.5	6.92	3.90	1.29	0.09	
		Day 2	4.56	9.44	150.8	4.20	112.8	6.54	3.76	1.35	0.95	
		Day 28	5.98	8.35	146.2	3.43	108.4	7.01	3.75	1.15	0.43	
		Day 30	2.88	8.88	147.0	4.27	110.0	6.52	3.39	1.08	0.18	
		Day 56	4.09	9.21	152.4	3.96	111.4	7.15	3.74	1.10	0.16	
		Day 58	4.69	9.15	156.7	4.53	113.7	6.84	3.65	1.14	0.14	
		Day 83	3.52	9.35	153.4	4.13	112.1	6.83	3.69	1.18	0.23	
		Day 84	3.81	8.94	152.8	3.66	109.7	7.03	3.72	1.12	0.20	

Table 5-3 Evaluation of Antibody Production by Recombinant Human Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF) Product in Cynomolgus Monkeys: II  
Clinical chemistry (males) -2nd course-

Group	Dose level	Animal No.	Observation time	AST (U/L)	ALT (U/L)	ALP (U/L)	LD (U/L)	CK (U/L)	GLU (mg/dL)	BIL (mg/dL)	UN (mg/dL)	CRE (mg/dL)	CHO (mg/dL)	TG (mg/dL)	PL (mg/dL)
I CHO cell-derived GM-CSF	15 µg/body	UJM01	Day -1	29	72	1458	254	182	65	0.14	24.0	0.64	128	28	195
			Day 2	27	88	1473	256	165	59	0.13	22.5	0.62	122	29	191
			Day 30	32	77	1066	277	229	56	0.13	23.3	0.68	116	26	182
			Day 58	29	55	898	245	237	57	0.13	29.8	0.65	99	52	170
			Day 86	37	170	1131	295	153	66	0.07	21.9	0.67	126	90	241
		UJM02	Day -1	31	32	1106	281	228	104	0.08	21.2	0.81	162	39	204
			Day 2	44	35	1143	373	233	84	0.09	22.2	0.78	145	25	190
			Day 30	33	33	1044	361	220	74	0.11	21.9	0.86	139	24	197
			Day 58	30	29	897	381	305	76	0.07	22.5	0.81	136	29	200
			Day 86	31	29	1057	333	191	78	0.06	21.7	0.78	126	36	210
II Escherichia coli-derived GM-CSF	15 µg/body	UJM11	Day -1	28	82	2514	230	179	91	0.08	16.9	0.71	147	58	234
			Day 2	51	90	2573	350	322	82	0.10	17.6	0.73	142	47	221
			Day 30	41	67	1798	342	120	67	0.17	18.7	0.75	142	14	210
			Day 58	34	88	1898	294	136	93	0.09	19.1	0.75	144	71	237
			Day 86	49	91	1778	424	203	83	0.08	16.5	0.73	137	63	231
		UJM12	Day -1	20	44	713	243	164	92	0.06	17.7	0.71	151	39	226
			Day 2	33	51	738	322	175	88	0.07	15.0	0.64	152	26	217
			Day 30	29	45	735	293	150	77	0.07	14.2	0.67	173	26	236
			Day 58	40	48	798	375	177	80	0.05	15.1	0.64	176	51	276
			Day 86	34	41	993	349	180	89	0.05	14.4	0.67	169	43	256

Table 5-3 (Continued) Evaluation of Antibody Production by Recombinant Human Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF) Product in Cynomolgus Monkeys: II  
Clinical chemistry (males) -2nd course-

Group	Dose level	Animal No.	Observation time	IP (mg/dL)	CA (mg/dL)	NA (mEq/L)	K (mEq/L)	CL (mEq/L)	TP (g/dL)	ALB (g/dL)	A/G	CRP (mg/dL)
I CHO cell-derived GM-CSF	15 µg/body	UJM01	Day -1	5.44	9.36	147.2	3.74	110.7	6.85	4.19	1.58	0.16
			Day 2	5.57	9.29	147.5	3.72	108.7	6.68	4.03	1.52	0.18
			Day 30	5.37	9.62	153.1	4.23	113.7	6.96	4.29	1.61	0.20
			Day 58	4.28	9.43	136.1	4.07	97.7	6.74	4.22	1.67	0.13
			Day 86	4.74	9.73	149.8	3.71	114.3	7.23	4.29	1.46	0.22
		UJM02	Day -1	4.43	9.56	146.4	3.84	108.1	6.61	3.72	1.29	0.19
			Day 2	5.12	9.50	151.7	4.11	108.6	6.56	3.62	1.23	0.39
			Day 30	3.76	9.05	149.6	4.12	109.6	6.60	3.77	1.33	0.19
			Day 58	3.85	9.36	149.6	4.54	111.4	6.73	3.62	1.16	0.28
			Day 86	3.28	9.08	149.9	4.20	111.7	6.97	3.86	1.24	0.38
II Escherichia coli-derived GM-CSF	15 µg/body	UJM11	Day -1	4.76	9.06	147.5	3.33	108.5	6.81	3.79	1.25	0.12
			Day 2	4.18	9.07	152.8	3.75	109.3	6.70	3.62	1.18	0.58
			Day 30	4.87	8.75	152.8	3.85	110.2	6.39	3.56	1.26	0.26
			Day 58	3.97	9.06	150.8	3.77	108.3	6.83	3.68	1.17	0.22
			Day 86	4.38	9.03	153.2	4.12	113.8	7.04	3.86	1.21	0.34
		UJM12	Day -1	3.76	9.00	149.9	3.68	109.5	6.76	3.95	1.41	0.08
			Day 2	5.38	9.67	155.4	4.96	114.5	6.87	3.88	1.30	0.19
			Day 30	5.10	9.62	155.0	4.39	110.8	6.97	3.97	1.32	0.13
			Day 58	4.40	9.56	158.8	4.46	112.4	6.98	3.71	1.13	0.51
			Day 86	4.84	9.23	153.5	4.13	112.4	7.09	3.76	1.13	0.26

Table 6-1 Evaluation of Antibody Production by Recombinant Human Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF) Product in Cynomolgus Monkeys: II  
Volume of bronchoalveolar lavage fluid (BALF) collected (males) -1st course-

Unit: mL

Group	Dose level	Animal No.	Day 89						Total
			Time of BALF collection						
			1st	2nd	3rd	4th	5th	6th	
I CHO cell-derived GM-CSF	15 µg/body	UJM01	3.6	5.0	5.0	5.0	4.6	4.6	27.8
		UJM02	3.8	4.4	4.4	5.4	4.6	4.8	27.4
II Escherichia coli-derived GM-CSF	15 µg/body	UJM11	2.4	3.2	4.0	4.4	4.6	4.0	22.6
		UJM12	3.2	3.2	3.8	4.2	4.0	4.0	22.4

Table 6-2 Evaluation of Antibody Production by Recombinant Human Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF) Product in Cynomolgus Monkeys: II  
Volume of bronchoalveolar lavage fluid (BALF) collected (males) -2nd course-

Unit: mL

Group	Dose level	Animal No.	Day 91						Total
			Time of BALF collection						
			1st	2nd	3rd	4th	5th	6th	
I CHO cell-derived GM-CSF	15 µg/body	UJM01	2.3	4.3	4.4	4.8	5.0	5.2	26.0
		UJM02	3.0	4.0	4.7	4.4	4.6	4.4	25.1
II Escherichia coli-derived GM-CSF	15 µg/body	UJM11	2.7	3.8	4.2	4.4	4.8	5.4	25.3
		UJM12	2.4	3.5	4.0	4.2	4.6	4.9	23.6

Table 7 Evaluation of Antibody Production by Recombinant Human Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF) Product in Cynomolgus Monkeys: II  
Gross pathology (males)

Day 92

Organ and tissue	Findings	Group Animal No.	I CHO cell-derived GM-CSF 15 µg/body		II Escherichia coli-derived GM-CSF 15 µg/body	
			UJM01	UJM02	UJM11	UJM12
Lung	Focus, yellowish brown, left and right anterior lobes, right: 8·3 mm, left: 5·2 mm		-	P	-	-

-: None/Negative      P: Present

Table 8 Evaluation of Antibody Production by Recombinant Human Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF) Product in Cynomolgus Monkeys: II  
Histopathology (males)

Day 92						
Organ and tissue	Findings	Group Animal No.	I CHO cell-derived GM-CSF 15 µg/body		II Escherichia coli-derived GM-CSF 15 µg/body	
			UJM01	UJM02	UJM11	UJM12
Lung with bronchus (left of the anterior) (left of the middle) (left of the posterior) (right of the anterior) (right of the middle) (right of the posterior)	Aggregation, alveolar macrophage, multifocal		±	±	-	-
	Granuloma, bronchioloalveolar (accompanied by foreign body)		-	+	-	-
	Aggregation, alveolar macrophage, multifocal		±	-	-	-
	Aggregation, alveolar macrophage, multifocal		±	-	-	-
	Granuloma, bronchioloalveolar (accompanied by foreign body)		-	±	-	-
	Aggregation, alveolar macrophage, multifocal		±	±	-	-
	Granuloma, bronchioloalveolar (accompanied by alveolar dilatation and foreign body)		-	+	-	-
	Aggregation, alveolar macrophage, multifocal		±	-	-	-
	Cell infiltration, mononuclear cell, subpleura		-	-	+	-
	Aggregation, alveolar macrophage, multifocal		±	-	-	-
Trachea	Bronchopneumonia (accompanied by alveolar dilatation and edema)		-	++	-	-
	Granuloma, bronchioloalveolar		-	+	-	-
	Pathological change		-	-	-	-
Hilar lymph node	Pathological change		-	-	-	-
Mediastinal lymph node	Pathological change		-	-	-	-

-: None/Negative    ±: Slight    +: Moderate    ++: Severe    +++: Very severe    P: Present

Table 9-1 Evaluation of Antibody Production by Recombinant Human Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF) Product in Cynomolgus Monkeys: II  
Bone marrow examinations -List of abbreviations-

Abbreviation	Expansion
NBMC	Nucleated bone marrow cell counts
PEBL	Proerythroblasts
BAS E	Basophilic erythroblasts
POL E	Polychromatic erythroblasts
ORT E	Orthochromatic erythroblasts
MIT E	Mitotic erythroid cells
MBL	Myeloblasts
PRO	Promyelocytes
N MY	Neutrophilic myelocytes
N META	Neutrophilic metamyelocytes
N BAND	Neutrophilic band cells
N SEG	Neutrophilic segmented cells
EOS	Eosinophils
BASO	Basophils
MIT M	Mitotic myeloid cells
MONO	Monocytes
LYMPH	Lymphocytes
PLASM	Plasma cells
MEGK	Megakaryocytes
RETICU	Reticulum cells
MACRO	Macrophages
MAST	Mast cells
M/E	Myeloid/Erythroid ratio

Table 9-2 Evaluation of Antibody Production by Recombinant Human Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF) Product in Cynomolgus Monkeys: II  
Bone marrow examinations (males)

Day 92

Group	Dose level	Animal No.	NBMC (10 <sup>4</sup> /μL)	Erythroid cells (%)						Myeloid cells (%)									
				PEBL	BAS E	POL E	ORT E	MIT E	Total	MBL	PRO	NMY	NMETA	NBAND	NSEG	EOS	BASO	MITM	Total
I CHO cell-derived GM-CSF	15 μg/body	UJM01	162	0.0	3.2	24.8	1.4	1.4	30.8	0.6	2.0	4.8	5.6	13.8	18.2	2.6	0.2	0.6	48.4
		UJM02	144	0.0	5.6	30.8	3.4	0.8	40.6	0.0	2.4	7.4	4.2	8.6	13.8	3.6	0.4	0.4	40.8
II Escherichia coli-derived GM-CSF	15 μg/body	UJM11	162	0.4	4.4	30.8	2.4	0.6	38.6	0.0	3.8	7.2	5.4	8.8	9.0	1.2	0.4	0.2	36.0
		UJM12	165	0.4	4.0	43.8	1.2	1.4	50.8	0.0	1.4	4.0	5.2	11.0	13.4	1.2	0.6	0.4	37.2

Table 9-2 (Continued-1) Evaluation of Antibody Production by Recombinant Human Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF) Product in Cynomolgus Monkeys: II  
Bone marrow examinations (males)

		Day 92										Erythroid cells ( $10^4/\mu\text{L}$ )					
Group	Dose level	Animal No.	MONO (%)	LYMPH (%)	PLASM (%)	MEGK (%)	RETICU (%)	MACRO (%)	MAST (%)	OTHERS (%)	M/E	PEBL	BAS E	POL E	ORT E	MIT E	Total
I CHO cell-derived GM-CSF	15 $\mu\text{g}/\text{body}$	UJM01	2.4	17.0	0.6	0.2	0.0	0.6	0.0	0.0	1.57	0.0	5.2	40.2	2.3	2.3	49.9
		UJM02	4.4	13.6	0.4	0.2	0.0	0.0	0.0	0.0	1.00	0.0	8.1	44.4	4.9	1.2	58.5
II Escherichia coli-derived GM-CSF	15 $\mu\text{g}/\text{body}$	UJM11	3.4	19.8	1.0	0.2	0.0	0.8	0.2	0.0	0.93	0.6	7.1	49.9	3.9	1.0	62.5
		UJM12	2.0	8.4	0.6	0.2	0.0	0.8	0.0	0.0	0.73	0.7	6.6	72.3	2.0	2.3	83.8