

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

Unit: °C

Group	Dose level	Animal No.	Day														85	
			-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	DYM01	37.1	37.4	37.7	37.3	37.0	37.5	38.0	38.2	37.1	37.5	37.8	37.9	38.1	38.0	36.9	
		DYM02	39.1	38.9	39.2	39.1	38.4	39.1	39.4	38.9	39.1	38.4	39.1	39.3	39.5	39.4	36.7	
II Escherichia coli-derived GM-CSF	15 µg/body	DYM11	39.4	39.4	39.4	38.8	39.1	39.1	39.4	39.2	38.8	39.2	39.4	39.4	39.5	39.5	37.8	
		DYM12	38.8	38.6	39.0	38.6	38.4	38.7	38.8	38.8	38.6	38.4	39.0	38.8	39.0	38.8	36.4	

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

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	DYM01	Day -1	6.01	14.1	48.6	80.9	23.5	29.0	1.1	68.2	258	14.38
			Day 14	5.59	13.2	45.9	82.0	23.6	28.7	2.7	148.9	361	18.28
			Day 28	5.95	14.2	49.2	82.7	23.8	28.8	2.1	122.7	397	14.56
			Day 42	5.89	14.1	46.7	79.3	23.9	30.2	1.8	104.2	294	12.81
			Day 56	5.85	13.9	45.8	78.3	23.7	30.3	2.0	114.9	268	10.34
			Day 70	5.72	13.7	44.9	78.5	23.9	30.5	1.5	85.6	272	13.61
			Day 84	5.72	13.6	45.3	79.2	23.7	30.0	1.8	102.6	262	11.93
		DYM02	Day -1	6.19	13.6	46.7	75.3	21.9	29.1	0.8	49.1	273	11.37
			Day 14	5.86	12.8	43.5	74.3	21.8	29.4	0.9	52.7	368	8.71
			Day 28	6.10	13.3	46.1	75.5	21.7	28.8	1.4	83.7	371	13.47
			Day 42	6.08	13.3	44.8	73.7	21.9	29.7	1.5	89.7	215	11.51
			Day 56	6.12	13.3	45.7	74.6	21.7	29.0	1.3	79.1	271	9.68
			Day 70	6.05	13.3	43.5	72.0	22.0	30.5	1.2	73.3	239	10.17
			Day 84	6.21	13.4	45.2	72.8	21.5	29.6	1.3	78.5	253	9.33
II Escherichia coli-derived GM-CSF	15 μg/body	DYM11	Day -1	5.99	13.4	47.9	80.0	22.3	27.9	0.9	53.6	327	8.90
			Day 14	5.57	12.7	44.6	80.0	22.8	28.5	0.9	51.3	557	8.04
			Day 28	5.61	13.0	45.6	81.2	23.2	28.5	1.7	93.2	488	7.90
			Day 42	5.62	13.4	44.9	79.9	23.9	29.9	1.2	64.7	463	7.38
			Day 56	6.04	14.0	49.2	81.5	23.1	28.4	1.2	70.6	460	8.64
			Day 70	5.86	13.8	46.8	79.9	23.5	29.4	1.1	64.6	492	9.66
			Day 84	5.87	13.6	46.8	79.7	23.2	29.1	1.0	61.3	432	8.29
		DYM12	Day -1	6.11	13.9	47.5	77.8	22.7	29.2	1.3	76.7	486	8.89
			Day 14	5.44	12.3	41.8	76.8	22.6	29.4	1.3	68.3	562	11.51
			Day 28	5.27	12.0	40.4	76.6	22.8	29.8	1.8	96.7	653	8.89
			Day 42	5.46	12.8	41.7	76.5	23.4	30.6	2.6	142.3	504	11.36
			Day 56	6.02	13.6	44.5	73.9	22.7	30.7	2.1	127.3	446	8.40
			Day 70	5.83	13.2	43.4	74.3	22.7	30.5	1.6	95.2	430	10.41
			Day 84	5.89	13.1	43.6	74.1	22.3	30.2	2.1	122.6	463	13.22

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

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	DYM01	Day -1	15.3	79.5	3.2	0.7	0.5	0.8	2.20	11.44	0.46	0.09	0.07	0.12	10.8	23.5		
			Day 14	26.6	66.9	2.8	2.2	0.6	0.9	4.86	12.23	0.52	0.41	0.11	0.16	10.7	23.4		
			Day 28	27.5	65.4	2.6	3.2	0.5	0.8	4.00	9.53	0.38	0.46	0.07	0.12	10.6	22.2		
			Day 42	18.1	75.6	2.7	2.2	0.6	0.7	2.32	9.69	0.35	0.28	0.08	0.09	11.0	23.1		
			Day 56	16.5	77.8	3.3	1.5	0.3	0.7	1.70	8.04	0.34	0.15	0.03	0.07	10.4	22.7		
			Day 70	15.1	79.7	3.3	0.8	0.5	0.7	2.05	10.85	0.44	0.11	0.07	0.09	10.7	22.5		
			Day 84	15.8	79.9	2.4	1.0	0.3	0.5	1.89	9.53	0.28	0.12	0.04	0.06	10.4	22.0		
			Day -1	17.0	78.6	2.1	1.0	0.6	0.7	1.93	8.94	0.24	0.11	0.07	0.08	9.9	23.9		
	DYM02	Day 14	33.6	61.3	2.0	2.1	0.3	0.7	2.93	5.34	0.17	0.18	0.03	0.06	9.9	22.9			
		Day 28	38.6	50.2	2.0	7.6	0.5	1.1	5.20	6.76	0.27	1.03	0.06	0.14	10.4	24.4			
		Day 42	22.6	67.3	2.2	6.6	0.3	0.9	2.61	7.75	0.26	0.76	0.04	0.11	10.2	23.6			
		Day 56	14.2	80.9	2.1	1.7	0.4	0.7	1.37	7.83	0.20	0.17	0.04	0.07	9.9	24.3			
		Day 70	17.9	76.5	2.0	2.2	0.5	1.0	1.82	7.78	0.20	0.22	0.05	0.10	9.8	24.0			
		Day 84	13.7	80.3	1.8	2.8	0.5	0.9	1.28	7.49	0.17	0.26	0.05	0.09	9.7	24.1			
		II Escherichia coli-derived GM-CSF	15 μg/body	DYM11	Day -1	19.2	74.3	3.8	1.7	0.5	0.6	1.71	6.61	0.34	0.15	0.05	0.05	9.8	22.2
					Day 14	47.9	47.3	2.9	1.5	0.3	0.3	3.85	3.80	0.23	0.12	0.02	0.02	10.0	22.4
Day 28	32.3				55.6	2.6	8.4	0.4	0.7	2.55	4.39	0.20	0.66	0.03	0.06	9.9	21.8		
Day 42	29.3				58.6	2.3	8.8	0.2	0.7	2.17	4.33	0.17	0.65	0.02	0.05	9.9	22.2		
Day 56	32.5				55.6	2.3	8.5	0.4	0.6	2.81	4.81	0.20	0.74	0.03	0.06	9.9	22.6		
Day 70	40.9				50.2	1.4	6.7	0.4	0.4	3.95	4.85	0.13	0.64	0.04	0.04	9.9	22.6		
DYM12	Day 84		22.8	65.8	2.7	7.6	0.4	0.7	1.89	5.46	0.22	0.63	0.03	0.06	9.7	22.2			
	Day -1		45.8	49.9	3.1	0.3	0.4	0.5	4.07	4.43	0.28	0.03	0.03	0.05	9.6	26.0			
	Day 14		58.1	36.3	3.3	1.5	0.2	0.5	6.69	4.17	0.39	0.18	0.02	0.06	9.5	25.2			
	Day 28		61.9	32.7	2.5	2.2	0.2	0.5	5.50	2.91	0.23	0.20	0.01	0.05	9.2	26.3			
	Day 42		60.8	34.7	2.9	0.6	0.3	0.6	6.90	3.95	0.33	0.07	0.03	0.07	9.8	26.1			
	Day 56		56.6	40.9	1.6	0.3	0.2	0.3	4.75	3.44	0.14	0.03	0.02	0.02	9.3	25.8			
DYM12	Day 70	70.1	27.6	1.7	0.2	0.2	0.2	7.29	2.87	0.17	0.02	0.03	0.02	9.3	25.7				
	Day 84	61.4	35.3	2.3	0.4	0.3	0.3	8.12	4.66	0.31	0.05	0.04	0.04	9.2	25.1				

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

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	DYM01	Day -1	29	51	1814	286	222	90	0.18	17.9	0.50	139	18	206
			Day 14	23	49	1623	332	171	77	0.13	18.6	0.57	135	36	223
			Day 28	23	48	1549	301	214	96	0.10	19.4	0.52	131	38	210
			Day 42	27	49	1592	310	254	77	0.15	16.0	0.48	140	16	217
			Day 56	28	49	1548	269	224	80	0.16	17.7	0.44	148	16	228
			Day 70	29	54	1791	268	229	102	0.12	18.1	0.51	140	28	218
			Day 84	28	50	1651	283	189	72	0.12	15.4	0.49	143	48	253
		DYM02	Day -1	34	22	1578	374	159	88	0.11	21.2	0.70	150	38	231
			Day 14	31	25	1404	457	171	97	0.09	17.4	0.69	134	23	184
			Day 28	23	22	1385	354	154	119	0.10	23.0	0.70	126	30	180
			Day 42	32	25	1413	362	163	95	0.11	19.4	0.63	142	23	197
			Day 56	38	27	1652	383	271	106	0.13	22.9	0.78	156	17	210
			Day 70	34	24	1962	359	174	56	0.14	21.3	0.75	147	25	210
			Day 84	32	24	1966	325	165	91	0.10	18.0	0.70	151	28	226
II Escherichia coli-derived GM-CSF	15 µg/body	DYM11	Day -1	28	63	1719	251	125	85	0.08	14.8	0.66	160	40	240
			Day 14	22	48	1333	365	203	82	0.10	14.8	0.72	160	31	242
			Day 28	22	65	1478	256	169	87	0.08	15.6	0.63	140	57	220
			Day 42	31	83	1420	313	91	82	0.08	15.6	0.63	133	43	217
			Day 56	25	54	1439	317	276	69	0.12	15.6	0.68	158	16	214
			Day 70	22	47	1830	305	135	68	0.10	15.0	0.65	144	35	229
			Day 84	20	45	1922	247	108	86	0.09	13.4	0.60	146	44	238
		DYM12	Day -1	24	32	1035	288	139	111	0.09	17.3	0.75	175	30	247
			Day 14	24	47	711	435	211	86	0.08	14.1	0.65	134	20	213
			Day 28	22	43	597	340	145	96	0.06	19.2	0.55	136	38	195
			Day 42	23	38	645	322	134	86	0.06	16.4	0.62	152	26	212
			Day 56	26	39	708	330	135	109	0.06	16.1	0.62	159	37	220
			Day 70	29	43	878	332	159	89	0.07	17.0	0.64	155	36	215
			Day 84	27	46	886	375	129	89	0.06	16.8	0.61	167	35	250

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

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	DYM01	Day -1	6.19	9.34	145.9	3.86	106.3	7.19	4.25	1.45	0.17
			Day 14	5.62	9.69	147.3	3.97	106.6	7.14	4.18	1.41	0.25
			Day 28	6.40	9.69	147.9	4.10	108.3	7.08	4.19	1.45	0.26
			Day 42	5.82	9.35	145.6	3.84	109.0	6.97	4.07	1.40	0.21
			Day 56	6.57	9.23	145.9	4.00	109.3	6.81	4.04	1.46	0.16
			Day 70	5.53	9.14	145.6	3.27	110.3	6.88	4.04	1.42	0.16
			Day 84	5.74	9.61	146.2	3.87	108.1	6.81	4.11	1.52	0.17
		DYM02	Day -1	5.83	9.18	148.1	3.64	108.1	7.13	3.94	1.24	0.24
			Day 14	3.43	8.85	147.8	4.05	108.6	6.86	3.72	1.18	0.17
			Day 28	4.60	8.86	146.4	3.83	110.3	6.79	3.64	1.16	0.29
			Day 42	5.60	8.96	145.5	3.49	108.1	6.74	3.57	1.13	0.40
			Day 56	6.07	8.99	149.8	3.62	107.5	6.99	3.82	1.21	0.22
			Day 70	6.07	8.92	147.4	3.76	111.2	6.80	3.72	1.21	0.33
			Day 84	5.35	8.76	147.5	3.41	105.5	6.68	3.79	1.31	0.25
II Escherichia coli-derived GM-CSF	15 µg/body	DYM11	Day -1	5.30	9.29	151.5	3.75	107.6	7.20	3.84	1.14	0.10
			Day 14	3.73	9.47	150.8	3.76	108.5	7.26	3.82	1.11	0.10
			Day 28	3.63	9.26	150.9	3.75	111.0	7.11	3.63	1.04	0.18
			Day 42	4.00	9.02	147.6	3.46	111.2	7.20	3.51	0.95	0.47
			Day 56	5.63	8.86	150.6	3.37	108.2	7.15	3.69	1.07	0.14
			Day 70	4.88	9.01	149.3	3.54	112.1	7.07	3.69	1.09	0.19
			Day 84	5.87	9.26	148.8	3.72	107.4	6.84	3.72	1.19	0.20
		DYM12	Day -1	4.55	9.60	150.8	3.79	106.4	7.52	4.07	1.18	0.07
			Day 14	1.79	9.10	151.2	4.66	109.4	6.86	3.68	1.16	0.08
			Day 28	2.35	8.91	144.1	4.62	108.8	6.51	3.29	1.02	0.14
			Day 42	5.05	9.28	150.5	3.81	110.7	7.04	3.48	0.98	0.19
			Day 56	5.33	9.00	149.9	3.82	110.8	7.31	3.71	1.03	0.09
			Day 70	4.40	9.11	149.6	3.75	113.8	7.34	3.66	0.99	0.13
			Day 84	4.43	9.16	148.8	3.93	110.2	7.10	3.62	1.04	0.15

