

Appendix I

Investigation on the Attributes of Cloned Bovine Products

The Japanese Research Institute for Animal Science in Biochemistry and Toxicology provided an unpublished bound report “Investigation on the Attributes of Cloned Bovine Products” by the Japan Livestock Technology Association (Japan, 2002). The 489 page report, provided in the original Japanese, and was accompanied by an eight page August 2002 English-language summary.

This appendix contains a translation of the first three pages of the bound report and the eight page English summary. These are followed by tables from the original bound report. The tables present the results of a feeding study in which rats were fed diets containing freeze dried milk or freeze dried beef from ordinary cattle and clone cattle at concentrations of 0, 2.5, 5, or 10% of the diet for 28 days. General signs, body weight, food consumption, urinalysis, sensory and reflex function, spontaneous movement frequency, general function, reproductive cycle, hematology at autopsy, blood chemistry, organ weights, pathology and histopathology were compared between groups. English-language tables were provided in the original Japanese-language report with the results. These tables are included in this appendix.

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**English language translation of the first three
pages of the report “Investigation on the
Attributes of Cloned Bovine Products”**

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A project aided by the Agriculture and
Livestock Industries Corporation

PROJECT REPORT OF AN INVESTIGATION ON THE PROPERTIES
OF PRODUCTS FROM CLONED CATTLE
(An Urgent Study Project for the Utilization of Cloned Cattle)
(1999 – 2001)

September 2002

Japan Livestock Technology Association

Results of an investigation on the properties of products from cloned cattle

Rapid advances have been made in the application of cloning technology in cattle multiplication. Products from embryonic clones of cattle are already on the market as safe foods. The Ministry of Health, Labor and Welfare (MHLW) is currently gathering data on the safety of products from somatic cell cloned cattle and has released an interim report which states that so far there is no reason to anticipate safety-related problems.

Cloning technology is expected to advance further and come into wide use as a technology that can provide inexpensive meat, milk, etc to consumers. However, for this to happen, it is essential for the meat and milk of cloned cattle to become widely accepted by consumers as safe, high-quality commodities.

This Association conducted various investigations on cloned cattle, with grants from the Agriculture and Livestock Industries Corporation (ALIC), during 1999 to 2001. An investigation on the properties of products from cloned cattle, which was a part of these investigations, was commissioned to the Research Institute for Animal Science in Biochemistry and Toxicology (RIAS).

The objective of this investigation was to collect data that would confirm the safety of products from embryonic clones of cattle, which are already in use as food items, and also data that would be useful in evaluating the safety of products from somatic cell clones. For this purpose, the properties of the blood, and the composition of nutritional components such as proteins, lipids, amino acids and fatty acids of raw milk and meat were analyzed and compared among ordinary cattle, embryonic clones and somatic cell clones of Holstein and Black Japanese breeds. Digestibility studies with artificial digestive fluid and with rats, allergenicity and mutagenicity (micronucleus) tests with mice, and a 14-week feeding study with rats were also conducted and the digestibility, allergenicity, and mutagenicity of the products, and their effects on the growth, functions and morphology of the test animals were compared. The results of none of the analyses or tests showed any significant differences between products from ordinary cattle and the two types of cloned cattle. Also, no harmful effect attributable to the raw milk or meat of the two types of clones was observed.

September 10, 2002

Cloned Cattle Investigation Committee
Japan Livestock Technology Association

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Results of an investigation on the properties of products from cloned cattle

Urgent study project on the utilization of cloned cattle – List of the “Cloned Cattle Investigation Committee” members

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**English language summary of the report
“Investigation on the Attributes of Cloned
Bovine Products”**

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August 13, 2002
Livestock Technology Division,
Livestock Industry Department,
Agricultural Production Bureau,
Ministry of Agriculture,
Forestry and Fisheries

RE: Outline of Investigative Results on the Attributes of Cloned Bovine Products

An interim report of the Ministry of Health and Welfare (MHW) released in June 2000 concerning the safety of foods made from cloned cattle states, "There is no scientific basis for fearing the safety of foods", and it recommended that foods derived from BNT cloned cattle be sold with labeling to that effect (optional labeling). The interim report also stated that, "It would be desirable to obtain data on a greater number of cloned cattle that would support safety." Because somatic cloning technology is a newer technology, the Ministry of Agriculture, Forestry and Fisheries (MAFF) is requesting self-restraint on the shipment of SCNT cloned cattle. The Ministry of Health, Labour and Welfare (MHLW: a new Ministry changed from MHW) are currently conducting an investigative study on safety.

In response, the Research Institute for Animal Science in Biochemistry and Toxicology has been conducting a study on the attributes of cloned bovine products (emergency study project on cloned bovine usage). The results of this study have now been gathered so a summary is attached separately.

It is intended that the results of this study will be submitted as reference material for the "investigative research on the safety of animal foods that use cloning technology" currently being conducted at the MHLW.

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Outline of Investigation on the Attributes of Cloned Bovine Products

Commissioned by the Livestock Technology Association from FY1999, we conducted an investigation on the attributes of cloned bovine products. The following are the results of this investigation.

1. Objectives

To conduct an investigation on the blood attributes of cloned cattle (BNT cloned cattle or SCNT cloned cattle), and analyze the components of cloned bovine products (milk and beef), as well as to conduct a study on animal feeding of feed additives from cloned cattle, and obtain data comparing cloned bovine products and existing foods (products from ordinary cattle produced by artificial insemination, etc).

2. Outline of investigation

(1) Blood test

(Material and method)

Blood was sampled from ordinary cattle and cloned cattle at 3, 6, and 9 months of pregnancy and 3 and 6 weeks after birth in the case of dairy cattle (Holstein), and 3 to 4 times during a period from 21 to 28 weeks after birth in the case of beef cattle (*kuroge-wagyu*). The sampled blood was subject to hematological testing (12 items including red blood cell count, white blood cell count, and hemoglobin) and biochemical examination of blood (25 items including total protein, and total cholesterol) and compared.

(Results)

None of the animals showed abnormalities in performance status. There were also no biologically significant differences* in any of the test values between ordinary cattle and cloned cattle, for both the dairy and beef types.

- * A biologically significant difference means a difference that could possibly have an effect on factors such as health and survival evident between the study groups. There are no problems if a biologically significant difference and statistically significant difference are in accord, but even if there is a statistically significant difference between the study groups in general, and that the difference is within the range of normal values it is unlikely that health would be affected, so one could not say that a biologically significant difference exists. In the investigative report, biologically significant difference was studied in addition to statistically significant difference. The same applies hereafter.

(2) Analytical study of milk and meat components

(Material and method)

The general components (water content, protein, lipids, and sugars), amino acids (18 types), and fatty acid (21 types) content (content per 100 g) in milk and slices of meat (9 sites) sampled from ordinary cattle and cloned cattle were measured and compared.

(Results)

Although there were slight variations seen among individual cattle, no biologically significant differences were evident in the general components, amino acids, and fatty acid content between ordinary cattle and cloned cattle for both milk and different sites of meat (Table 1).

(3) Milk and meat digestion study

(Material and method)

A study of digestion of pieces of meat sampled from ordinary cattle and cloned cattle by artificial gastric juice and intestinal juice, and a study of digestion of milk and meat that had been frozen, dried, and powdered (freeze-dried food) and added to feed, using rats were conducted, and the digestion rates that were regarded as parameters of protein were compared.

(Results)

There were no biologically significant differences in the rates of digestion of the feed additives due to artificial gastric juice and intestinal juice using rats between ordinary cattle and cloned cattle (Tables 2 and 3).

(4) Allergen testing of milk and meat by mouse abdominal wall method

(Material and method)

We sensitized mice with an intraperitoneal injection of extract from freeze-dried milk and meat slices sampled from ordinary cattle and cloned cattle. Fourteen days later we retracted the abdomen and induced an allergic reaction by re-injection in the abdominal wall. Allergen activity was compared based on the extent of vascular permeability (diameter of dye leakage) seen due to the sensitization treatment.

(Results)

For both milk and meat slices there were no statistically significant differences in allergen activity between ordinary cattle and cloned cattle (Table 4).

(5) Feeding test by the supply of a combination feed of milk and meat using rats

(Material and method)

Freeze-dried milk and meat of ordinary cattle and cloned cattle were each combined with basic feed at concentrations of 2.5%, 5%, and 10% in the case of freeze-dried milk, and 1%, 2.5%, and 5% in the case of freeze-dried meat, and fed to rats (20 per group (10 males and 10 females)) for 14 weeks.

The general sign, body weight, food consumption, urinalysis (8 items), sensory and reflex function, spontaneous movement frequency, general function, reproductive cycle, hematology at autopsy (11 items), blood chemistry (23 items), autopsy and organ weights (brain, pituitary gland, cerebral gland, thyroid gland, heart, lungs, liver, pancreas, adrenal bodies, and reproductive organs) of rats given the feed were compared among a basic feed group, ordinary cattle group, and cloned cattle group.

(Results)

There were no biologically significant differences in each of the items observed and tested over time in rats at any concentration of feed additive for milk and meat between ordinary cattle and cloned cattle (Table 5).

(6) Mutagenicity by milk and meat supply using mice (micronucleus test)

(Material and method)

Feed produced in the feed test by the supply of a combination feed of milk and meat in (5) was given to mice for 14 days whereupon the incidence of bone marrow micronucleus-possessing erythrocytes appearing was tested (micronucleus) and mutagenicity (clastogenicity) was studied.

(Results)

Clastogenicity was negative and mutagenicity was not evident for milk and meat feed additives from ordinary cattle and cloned cattle (Table 6).

3. Summary

The above results revealed no biologically significant differences in component analysis testing and feed additive animal testing between products of BNT cloned cattle and SCNT cloned cattle (milk and meat), and the products of ordinary cattle.

Table 1. General components**(1) Milk**

Classification	Cattle No.	Protein (g/100 g)	Fats (g/100 g)	Sugars (g/100 g)	Ash content (g/100 g)	Water content (g/100 g)	Calcium (mg/100 g)	Cholesterol (mg/100 g)
Ordinary cattle	Min. value	3.0	2.2	4.6	0.7	88.1	100	8
	Max value	3.4	3.3	4.6	0.7	89.7	110	10
	Mean value	3.3	2.7	4.6	0.7	88.9	105	9
BNT cloned cattle	No.1	2.9	2.3	3.0	0.8	91.1	95	9
	No.2	2.9	3.6	3.5	0.7	89.3	105	9
SCNT cloned cattle	No 1	3.1	4.3	4.6	0.7	87.4	120	9
	No.2	3.3	2.6	4.4	0.7	89.1	115	11
	No.3	3.3	3.1	4.5	0.7	88.5	115	10

Note: The analytical values for each animal are the mean of the analytical values for milk sampled at two points – 3 weeks and 6 weeks after delivery.

(2) Meat

Classification	Cattle No.	Protein (g/100 g)	Fats (g/100 g)	Sugars (g/100 g)	Ash content (g/100 g)	Water content (g/100 g)	Cholesterol (mg/100 g)
Ordinary cattle	Min. value	17.8	13.8	0.4	0.9	58.0	50
	Max value	19.6	22.9	0.8	1.0	64.8	68
	Mean value	18.4	19.3	0.6	0.9	60.8	59
BNT cloned cattle		17.4	21.2	0.4	0.9	60.2	56
SCNT cloned cattle		16.8	23.8	0.5	0.9	57.9	68

Note: The analytical value for each animal is the mean value of the analytical values of 9 sites: shoulder, chuck loin, rib loin, loin end, brisket, round, silver side, rump, and tender loin.

Table 2. Rates of meat digestion by artificial digestive juices

Digestive juice	Sample	Rate of digestion after the start of incubation						
		Course	Start	0.75 hr	1.5 hr	3 hr	6 hr	12 hr
Artificial gastric juice	Ordinary beef		0	68	79	-	95	90
	Somatic cloned beef		0	59	78	-	91	90
Artificial intestinal juice	Ordinary beef		0	-	20	40	66	67
	Somatic cloned beef		0	-	28	38	67	63

Note: The digestion rate shows the protein rate of digestion.

Table 3. Digestion rates of milk and meat in rats

Sample	Test group	Number of animals	Digestion rate (mean \pm standard deviation)
Milk	Ordinary cattle	5	83.0 \pm 2.6
	BNT cloned cattle	5	82.7 \pm 2.0
	SCNT cloned cattle	5	81.3 \pm 3.4
Meat	Ordinary cattle	5	83.8 \pm 6.6
	BNT cloned cattle	5	82.3 \pm 4.7
	SCNT cloned cattle	5	84.9 \pm 3.6

Note: Milk and meat were each freeze-dried and combined in feed. The digestion rate shows the protein digestion rate.

Table 4. Allergen study of milk and meat by mouse abdominal wall method

Sample	Test group		Number of animals	Diameter of dye leakage (mm) (mean \pm SD)
Milk	Ordinary cattle	Control group	7	7.0 \pm 3.7
		Test group	10	18.0 \pm 2.9
	BNT cloned cattle	Control group	7	4.7 \pm 3.2
		Test group	10	18.0 \pm 3.9
	SCNT cloned cattle	Control group	7	4.9 \pm 4.6
		Test group	10	17.9 \pm 4.2
Meat	Ordinary cattle	Control group	7	5.3 \pm 5.0
		Test group	10	13.0 \pm 5.9
	BNT cloned cattle	Control group	7	7.0 \pm 4.9
		Test group	10	12.5 \pm 3.5
	SCNT cloned cattle	Control group	7	5.7 \pm 4.2
		Test group	10	13.1 \pm 5.0

Note: Milk and meat were each freeze-dried and the extracts were used as samples. The test groups underwent sensitization treatment and elicitation, while the control groups underwent elicitation only.

Table 5. Feed study of milk and meat by formula feed supply using rats

(1) Changes in rat body weight by milk formula feed supply (mean \pm standard deviation)

Study group		Number of animals	Feeding period (weeks)									Amount of body weight increase in 1-14 weeks (g)	
			1	2	3	4	5	6	8	10	12		14
Male	Basal diet	10	146 \pm 6	189 \pm 20	255 \pm 34	299 \pm 45	344 \pm 59	373 \pm 58	428 \pm 56	448 \pm 58	516 \pm 47	547 \pm 77	401 \pm 76
	Ordinary cattle High concentration (10%)	10	146 \pm 6	194 \pm 11	260 \pm 13	304 \pm 17	350 \pm 19	378 \pm 22	426 \pm 36	475 \pm 43	515 \pm 43	544 \pm 48	398 \pm 48
	BNT cloned cattle High concentration (10%)	10	146 \pm 6	175 \pm 19	245 \pm 15	295 \pm 14	333 \pm 18	367 \pm 16	425 \pm 22	462 \pm 34	503 \pm 41	530 \pm 44	384 \pm 41
	SCNT cloned cattle High concentration (10%)	10	146 \pm 7	196 \pm 10	261 \pm 17	310 \pm 23	353 \pm 27	379 \pm 30	432 \pm 41	473 \pm 41	519 \pm 43	545 \pm 48	399 \pm 43
Female	Basal diet	10	117 \pm 5	150 \pm 6	184 \pm 12	208 \pm 9	229 \pm 10	242 \pm 10	267 \pm 16	283 \pm 15	304 \pm 18	310 \pm 20	193 \pm 18
	Ordinary cattle High concentration (10%)	10	118 \pm 5	152 \pm 7	181 \pm 7	209 \pm 12	234 \pm 16	247 \pm 15	273 \pm 20	298 \pm 21	316 \pm 28	329 \pm 40	211 \pm 42
	BNT cloned cattle High concentration (10%)	10	119 \pm 7	157 \pm 11	186 \pm 12	208 \pm 22	223 \pm 27	244 \pm 26	272 \pm 19	292 \pm 21	313 \pm 26	326 \pm 30	207 \pm 27
	SCNT cloned cattle High concentration (10%)	10	118 \pm 7	151 \pm 12	181 \pm 12	209 \pm 13	229 \pm 16	247 \pm 19	274 \pm 18	293 \pm 19	317 \pm 21	330 \pm 33	213 \pm 33

Note: Aside from studying a 10% milk powder concentration, 10 cattle each were also fed a low concentration (2.5%) and a medium concentration (5%), but no significant differences were noted.

(2) Changes in rat body weight by meat formula feed supply (mean \pm standard deviation)

Study group		Number of animals	Feeding period (weeks)									Amount of body weight increase in 1-14 weeks (g)	
			1	2	3	4	5	6	8	10	12		14
Male	Basal diet	10	143 \pm 5	216 \pm 12	279 \pm 14	336 \pm 16	382 \pm 18	426 \pm 22	489 \pm 31	534 \pm 37	560 \pm 42	590 \pm 50	447 \pm 51
	Ordinary cattle High concentration (5%)	10	143 \pm 5	221 \pm 9	284 \pm 17	337 \pm 24	386 \pm 30	432 \pm 36	492 \pm 44	541 \pm 55	575 \pm 62	604 \pm 65	462 \pm 65
	BNT cloned cattle High concentration (5%)	10	143 \pm 5	219 \pm 10	286 \pm 14	343 \pm 18	392 \pm 21	431 \pm 26	488 \pm 34	535 \pm 39	564 \pm 43	591 \pm 49	448 \pm 51
	SCNT cloned cattle High concentration (5%)	10	143 \pm 6	215 \pm 9	278 \pm 14	336 \pm 20	392 \pm 29	435 \pm 35	499 \pm 48	551 \pm 60	581 \pm 70	613 \pm 80	469 \pm 76
Female	Basal diet	10	120 \pm 4	167 \pm 14	198 \pm 15	228 \pm 18	253 \pm 26	272 \pm 26	290 \pm 26	313 \pm 33	330 \pm 38	338 \pm 35	218 \pm 38
	Ordinary cattle High concentration (5%)	10	120 \pm 4	169 \pm 11	200 \pm 12	230 \pm 15	254 \pm 19	274 \pm 18	297 \pm 23	316 \pm 28	331 \pm 31	341 \pm 30	221 \pm 30
	BNT cloned cattle High concentration (5%)	10	120 \pm 5	171 \pm 8	201 \pm 10	236 \pm 15	260 \pm 20	280 \pm 23	311 \pm 29	330 \pm 27	347 \pm 35	361 \pm 40	241 \pm 39
	SCNT cloned cattle High concentration (5%)	10	120 \pm 4	167 \pm 8	195 \pm 9	227 \pm 11	250 \pm 12	268 \pm 12	292 \pm 16	310 \pm 19	329 \pm 20	336 \pm 20	216 \pm 17

Note: Aside from studying a 5% meat powder concentration, 10 cattle each were also fed a low concentration (1.0%) and a medium concentration (2.5%), but no significant differences were noted.

Table 6. Mutagenicity by the supply (14 days) of milk and meat using mice (micronucleus test)

(1) Milk

Test group	Number of animals	Incidence (%) of micronucleus appearance (Min – max)		Polychromatic erythrocyte rate (%) (Min – max)		Assessment
Negative control group (basal diet)	6	0.27±0.10	(0.1 – 0.4)	49.2±6.6	(42.2 – 57.1)	
Ordinary cattle						
2.5% group	6	0.22±0.17	(0.0 – 0.4)	49.4±3.8	(43.1 – 53.1)	Negative
5% group	6	0.20±0.14	(0.0 – 0.4)	45.7±5.0	(36.8 – 50.3)	Negative
10% group	6	0.12±0.10	(0.0 – 0.2)	44.5±7.5	(35.4 – 56.9)	Negative
BNT cloned cattle						
2.5% group	6	0.30±0.14	(0.1 – 0.5)	44.0±6.7	(36.5 – 55.2)	Negative
5% group	6	0.25±0.12	(0.1 – 0.4)	47.4±8.1	(36.5 – 56.3)	Negative
10% group	6	0.17±0.08	(0.1 – 0.3)	44.7±8.4	(32.3 – 56.8)	Negative
SCNT cloned cattle						
2.5% group	6	0.22±0.13	(0.0 – 0.3)	49.7±7.4	(35.8 – 56.3)	Negative
5% group	6	0.28±0.15	(0.1 – 0.5)	49.5±7.8	(41.2 – 60.9)	Negative
10% group	6	0.25±0.05	(0.2 – 0.3)	44.0±6.2	(34.2 – 52.8)	Negative
Positive control group (Mitomycin C)	6	6.02±1.03**	(4.6 – 7.6)	34.6±5.5	(26.3 – 40.3)	Positive

(2) Meat

Test group	Number of animals	Incidence (%) of micronucleus appearance (Min – max)		Polychromatic erythrocyte rate (%) (Min – max)		Assessment
Negative control group (basal diet)	6	0.20±0.18	(0.0 – 0.5)	47.7±9.7	(30.2 – 59.7)	
Ordinary cattle						
1% group	6	0.17±0.12	(0.1 – 0.4)	50.0±9.1	(37.9 – 61.3)	Negative
2.5% group	6	0.13±0.08	(0.0 – 0.2)	47.3±13.1	(22.3 – 60.2)	Negative
5% group	6	0.12±0.15	(0.0 – 0.3)	46.8±10.5	(37.2 – 63.5)	Negative
BNT cloned cattle						
1% group	6	0.20±0.06	(0.1 – 0.3)	51.0±7.3	(41.3 – 59.3)	Negative
2.5% group	6	0.23±0.14	(0.0 – 0.4)	47.1±4.3	(40.6 – 51.1)	Negative
5% group	6	0.12±0.08	(0.1 – 0.2)	49.6±9.6	(37.9 – 61.9)	Negative
SCNT cloned cattle						
1% group	6	0.18±0.10	(0.1 – 0.3)	48.3±8.4	(35.6 – 55.1)	Negative
2.5% group	6	0.22±0.10	(0.1 – 0.4)	51.7±7.3	(44.3 – 63.9)	Negative
5% group	6	0.22±0.08	(0.1 – 0.3)	48.4±8.1	(38.4 – 58.1)	Negative
Positive control group (Mitomycin C)	6	6.95±1.56**	(4.1 – 8.4)	25.7±6.5	(19.4 – 36.4)	Positive

Note: Milk and meat were freeze-dried and powdered and combined in feed. The positive control group was administered a single dose of 2 mg/kg of mitomycin C intraperitoneally. Values were shown as mean ± standard deviation.

** denotes a significant difference at p<0.01 against the positive control group.

Results of a 28-Day Feeding Study in Rats Fed Diets Containing Freeze Dried Milk or Beef from Ordinary Cattle and Clone Cattle

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Table 1 Analyzed nutrient composition of the milk powder

Macronutrient (%)	Vitamin (mg/100g)	Mineral (mg/100g)
Crude protein 23.3	A 113IU/100g	Ca 1410
Crude fat 23.4	B ₁ 0.27	P 723
Carbohydrate 45.0	B ₂ 1.11	K 2010
Crude fiber 0.0	B ₆ 0.17	Na 195
Ash 5.4	B ₁₂ 0.0017	Mg 79.2
Water 2.9	D ₃ ND	Fe 0.326
	E 0.4	Zn 3.069
	K ₁ ND	Cu 0.064
	K ₂ 0.0070	S 220
	Niacin 0.86	Mn 0.073
	Pantotheinic acid 2.90	I 0.07
	Folic acid 0.05	Se 0.023
	Biotin 0.00919	Mo ND
	Choline 0.10 (%)	

Table 2-1 Composition of the milk powder-contained diets

(g/kg diets)

Ingredient	Basal diet	5% diet	10% diet	20% diet
Milk powder		50.000	100.000	200.000
Cornstarch	397.486	378.180	358.872	320.258
Casein (93.5% protein)	200.000	187.540	175.080	150.160
Alfa-cornstarch	132.000	125.588	119.177	106.355
Sucrose	100.000	100.000	100.000	100.000
Soybean oil	70.000	58.300	46.600	23.200
Cellulose	50.000	50.000	50.000	50.000
Mineral Mix *	35.000	35.000	35.000	35.000
Vitamin Mix *	10.000	10.000	10.000	10.000
L-Cystine	3.000	3.000	3.000	3.000
Choline Bitartrate (41.1% choline)	2.500	2.378	2.257	2.013
t-Butylhydroquinone	0.014	0.014	0.014	0.014
Caloric value (kcal)	395	396	397	398
Crude protein (%)	18.7	18.7	18.7	18.7
Crude fat (%)	7.0	7.0	7.0	7.0
Carbohydrate (%)	64.4	64.6	64.8	65.1
Crude fiber (%)	5.0	5.0	5.0	5.0

* : Ingredients of the mineral mix and vitamin mix are shown in table 2-2.

Table 2-2 Ingredients of the mineral mix and vitamin mix for the milk powder-contained diet

(g/kg Mix)

Mineral Mix						Vitamin Mix				
Ingredients	Contents (M)	Basal diet	5% diet	10% diet	20% diet	Ingredients	Basal diet	5% diet	10% diet	20% diet
ESSENTIAL MINERALS						Vitamine A Palmitate (500,000IU/g)	0.800	0.687	0.574	0.348
Calcium Carbonate	Ca: 40.04	357.00	306.683	256.326	155.652	Thiamine HCl (B ₁)	0.600	0.590	0.570	0.550
Potassium Phosphate (monobasic)	P: 22.78	196.00	161.722	127.570	59.390	Riboflavin (B ₂)	0.800	0.540	0.490	0.380
Potassium Citrate H ₂ O	K: 28.73	124.150 *	93.211	62.174		Pyridoxine HCl (B ₆)	0.700	0.690	0.680	0.670
Sodium Chloride	K: 44.87				45.140	Vitamine B ₁₂ (0.1%)	2.500	2.400	2.300	2.200
Potassium Sulfate	Na: 39.34	74.00	66.822	59.570		Vitamine D ₃ (400,000IU/g)	0.250	0.250	0.250	0.250
Magnesium Oxide	S: 18.39	68.35 *	51.263	34.175		Vitamine B Acetate (500IU/g)	15.000	15.000	15.000	15.000
Ferric Citrate	K: 44.87				16.585	Vitamine K ₁	0.075	0.075	0.074	0.074
Zinc Carbonate	Mg: 60.32	24.00	22.118	20.282		Ritacin	3.000	3.000	3.000	3.000
Manganous Carbonate	Fe: 16.50	6.06	6.06	6.06	5.887	Calcium Pantothenate	1.600	1.500	1.300	1.000
Capric Carbonate	Zn: 52.14	1.85	1.54	1.485	1.32	Folic Acid	0.200	0.200	0.200	0.190
Potassium Iodate	Mn: 47.79	0.63	0.630	0.630	0.624	Biotin	0.020	0.020	0.019	0.018
Sodium Selenate	Cu: 57.47	0.30	0.295	0.295	0.285	Sucrose finely powdered	74.655	975.048	975.543	978.320
Ammonium Paramolybdate 4H ₂ O	I: 59.30	0.01	0.009	0.007	0.003					
	Se: 41.79	0.01025	0.00957	0.00888	0.00752					
	Mo: 54.34	0.00795	0.00795	0.00795	0.00795					
NON-ESSENTIAL MINERALS										
Sodium Metasilicate 9H ₂ O	Si: 9.88	1.45	1.45	1.45	1.45					
Chromium Potassium Sulfate 12H ₂ O	Cr: 10.42	0.275	0.275	0.275	0.275					
Lithium Chloride	Li: 16.38	0.0174	0.0174	0.0174	0.0174					
Boric Acid	B: 17.50	0.0815	0.0815	0.0815	0.0815					
Sodium Fluoride	F: 45.24	0.0635	0.0635	0.0635	0.0635					
Nickel Carbonate	Ni: 45.00	0.0318	0.0318	0.0318	0.0318					
Ammonium Vanadate	V: 43.55	0.0066	0.0066	0.0066	0.0066					

* : Composition is differ from that of the AIN standard diet.

The mineral mix and vitamin mix for each composition was designed to reflect the mineral (essential minerals) and vitamin contents of the milk powder at each additional level.

Table 3 Body weights of male rats fed the milk powder-contained diet in a 28day dose range-finding test

Conc. in diet	Number of animals	Day	(g)					Gain 0~28
			1	7	14	21	28	
0%	6		125	187	239	290	331	205
		±	3	± 6	± 7	± 10	± 13	± 12
5%	6		125	183	241	297	340	215
		±	3	± 6	± 11	± 16	± 22	± 21
10%	6		125	183	239	290	332	208
		±	3	± 7	± 12	± 18	± 20	± 17
20%	6		125	183	238	281	320	196
		±	4	± 9	± 12	± 21	± 26	± 27

Each value is expressed as mean±S.D.

Table 4 Body weights of female rats fed the milk powder-contained diet in a 28day dose range-finding test

Conc. in diet	Number of animals	Day	(g)					Gain 0~28
			1	7	14	21	28	
0%	6		116	150	177	202	224	109
		±	5	± 5	± 6	± 7	± 12	± 11
5%	6		116	153	178	203	229	113
		±	5	± 16	± 17	± 21	± 29	± 25
10%	6		115	151	177	202	226	111
		±	4	± 9	± 11	± 13	± 14	± 10
20%	6		117	153	182	207	229	112
		±	8	± 10	± 17	± 22	± 25	± 18

Each value is expressed as mean±S.D.

Table 5 Food consumption of male rats fed the milk powder-contained diet in a 28day dose range-finding test

Conc. in diet	Number of animals	Week			
		1	2	3	4
0%	6	16 ± 0	19 ± 2	20 ± 1	20 ± 1
5%	6	± 16 2	± 19 1	± 20 1	± 20 0
10%	6	± 15 2	± 19 1	± 20 2	± 20 2
20%	6	15 ± 0	18 ± 0	17 ± 3	19 ± 1

Each value is expressed as mean±S.D.

Table 6 Food consumption of female rats fed the milk powder-contained diet in a 28day dose range-finding test

Conc. in diet	Number of animals	Week			
		1	2	3	4
0%	6	11 ± 1	14 ± 0	15 ± 1	16 ± 2
5%	6	± 12 1	± 14 1	± 15 3	± 16 3
10%	6	± 11 2	± 13 2	± 14 1	± 15 2
20%	6	11 ± 2	14 ± 2	15 ± 2	15 ± 1

Each value is expressed as mean±S.D.

Table 7 Urinary findings of male rats fed the milk powder-contained diet in a 28day dose range-finding test

Conc. in diet	No. of animals	Color		Cloudy		pH								Protein					Glucose					
		PY		-	+	5.0	6.0	6.5	7.0	7.5	8.0	8.5	-	±	+	++	+++	-	±	+	++	+++		
0%	6	6		6		3	2	1					1	3	2						6			
5%	6	6		6		4	2						1	3	2						6			
10%	6	6		6		1	5						2	4							6			
20%	6	6		6		4	2						1	5							6			

Conc. in diet	No. of animals	Ketone body					Occult blood					Urobilinogen					Bilirubin							
		-	±	+	++	+++	-	±	+	++	+++	0.1	1	2	4	8	-	+	++	+++				
0%	6	4	2				6					6					6							
5%	6	4	2				6					6					6							
10%	6	3	3				6					6					6							
20%	6	4	2				6					6					6							

Color : PY(pale yellow)
 Cloudy : - (negligible), + (cloudy)
 Protein : - (negligible), ±(15~30mg/dL), + (30mg/dL), ++(100mg/dL), +++(300mg/dL)
 Glucose : - (negligible), ±(0.1g/dL), + (0.25g/dL), ++(0.5g/dL), +++(1g/dL)
 Ketone body : - (negligible), ±(5mg/dL), + (15mg/dL), ++(40mg/dL), +++(80mg/dL)
 Occult blood : - (negligible), ±(trace), + (slight), ++(moderate), +++(marked)
 Urobilinogen : Ehrlich unit/dL
 Bilirubin : - (negligible), + (slight), ++(moderate), +++(marked)

Table 8 Urinary findings of female rats fed the milk powder-contained diet in a 28day dose range-finding test

Conc. in diet	No. of animals	Color		Cloudy		pH								Protein					Glucose					
		PY		-	+	5.0	6.0	6.5	7.0	7.5	8.0	8.5	-	±	+	++	+++	-	±	+	++	+++		
0%	6	6		6		2	2	2					4	2							6			
5%	6	6		6		2	2	2					1	5							6			
10%	6	6		6		1	3	2					5	1							6			
20%	6	6		6		2	2	2					5	1							6			

Conc. in diet	No. of animals	Ketone body					Occult blood					Urobilinogen					Bilirubin							
		-	±	+	++	+++	-	±	+	++	+++	0.1	1	2	4	8	-	+	++	+++				
0%	6	6					6					6					6							
5%	6	6					3	3				6					6							
10%	6	5	1				6					6					6							
20%	6	5	1				6					6					6							

Color : PY(pale yellow)
 Cloudy : - (negligible), + (cloudy)
 Protein : - (negligible), ±(15~30mg/dL), + (30mg/dL), ++(100mg/dL), +++(300mg/dL)
 Glucose : - (negligible), ±(0.1g/dL), + (0.25g/dL), ++(0.5g/dL), +++(1g/dL)
 Ketone body : - (negligible), ±(5mg/dL), + (15mg/dL), ++(40mg/dL), +++(80mg/dL)
 Occult blood : - (negligible), ±(trace), + (slight), ++(moderate), +++(marked)
 Urobilinogen : Ehrlich unit/dL
 Bilirubin : - (negligible), + (slight), ++(moderate), +++(marked)

Table 9 Hematological findings of male rats fed the milk powder-contained diet in a 28day dose range-finding test

Conc. in diet	No. of animals	RBC (10 ⁶ /μL)	Hb (g/dL)	Ht (%)	MCV (fL)	MCH (pg)	MCHC (%)	WBC (10 ³ /μL)	Plat. (10 ⁴ /μL)	PT (sec)	APTT (sec)
0%	6	752 ± 17	14.9 ± 0.5	42.4 ± 1.0	56 ± 1	19.8 ± 0.9	35.2 ± 0.9	60 ± 17	106 ± 11	12.9 ± 0.4	20.0 ± 1.5
5%	6	734 ± 31	14.6 ± 0.8	41.6 ± 2.3	57 ± 2	19.9 ± 0.8	35.0 ± 0.9	50 ± 7	121 ± 15	12.7 ± 0.4	19.2 ± 0.8
10%	6	760 ± 37	14.8 ± 0.6	42.2 ± 1.4	56 ± 4	19.5 ± 1.1	35.0 ± 0.7	46 ± 11	122 ± 14	13.0 ± 0.3	18.8 ± 1.2
20%	6	685 ± 136	13.4 ± 3.0	38.8 ± 7.5	57 ± 2	19.4 ± 1.1	34.3 ± 1.9	48 ± 12	122 ± 19	13.0 ± 0.2	19.3 ± 1.7

Each value is expressed as mean±S.D.

Table 10 Hematological findings of female rats fed the milk powder-contained diet in the 28-day repeat dose toxicity test

Conc. in diet	No. of animals	RBC (10 ⁶ /μL)	Hb (g/dL)	Ht (%)	MCV (fL)	MCH (pg)	MCHC (%)	PT (sec)	APTT (sec)	WBC (10 ³ /μL)
0%	6	758 ± 36	14.8 ± 0.2	41.8 ± 0.8	55 ± 2	19.6 ± 0.9	35.4 ± 0.6	13.0 ± 0.3	18.3 ± 1.1	43 ± 12
5%	6	741 ± 49	14.5 ± 0.7	41.2 ± 2.1	56 ± 2	19.6 ± 0.7	35.3 ± 0.3	13.1 ± 0.4	18.6 ± 0.6	31 ± 9
10%	6	744 ± 39	14.7 ± 0.7	41.5 ± 2.2	56 ± 2	19.8 ± 0.8	35.5 ± 0.4	13.2 ± 0.3	18.6 ± 1.2	26* ± 3
20%	6	742 ± 44	14.8 ± 0.6	41.1 ± 2.1	55 ± 2	20.0 ± 0.7	36.1 ± 0.6	13.0 ± 0.7	17.5 ± 1.0	33 ± 13

Conc. in diet	No. of animals	Differential leukocyte counts (%)								Plat. (10 ³ /μL)
		Baso.	Eosin.	Neutro.			Mono.	Other		
				Stab.	Seg.	Lymph.				
0%	6	0 ± 0	1 ± 1	0 ± 0	12 ± 4	86 ± 6	2 ± 1	0 ± 0	119 ± 16	
5%	6	0 ± 0	1 ± 1	0 ± 0	14 ± 3	84 ± 4	1 ± 1	0 ± 0	120 ± 19	
10%	6	0 ± 0	1 ± 1	0 ± 0	14 ± 4	84 ± 3	1 ± 1	0 ± 0	122 ± 12	
20%	6	0 ± 0	1 ± 1	0 ± 0	11 ± 2	87 ± 4	1 ± 1	0 ± 0	132 ± 19	

Each value is expressed as mean±S.D.

* : Significantly different from control at 5% level of probability

Table 11

Blood biochemical findings of male rats fed the milk powder-contained diet
in a 28day dose range-finding test

Conc. in diet	No. of animals	LDH (IU/L)	GOT (IU/L)	GPT (IU/L)	ALP (IU/L)	γ -GTP (IU/L)	ChE (IU/L)	CK (IU/L)	T.P. (g/dL)	Alb (%)	α_1 -G (%)	α_2 -G (%)	α_3 -G (%)	β -G (%)	γ -G (%)	A/G
0%	6	293 ± 77	71 ± 2	27 ± 2	717 ± 180	0.63 ± 0.35	54 ± 5	183 ± 24	6.16 ± 0.32	49.8 ± 1.3	20.7 ± 1.1	6.1 ± 1.1	5.4 ± 0.2	14.7 ± 1.4	3.9 ± 1.0	0.97 ± 0.05
5%	6	269 ± 81	77 ± 7	31 ± 3	663 ± 106	0.42 ± 0.14	55 ± 16	194 ± 46	5.94 ± 0.13	49.9 ± 1.2	22.1 ± 1.3	5.0 ± 0.7	5.5 ± 0.3	13.9 ± 1.1	3.7 ± 1.1	1.00 ± 0.05
10%	6	301 ± 59	80 ± 9	29 ± 5	693 ± 193	0.60 ± 0.20	60 ± 25	210 ± 25	5.87* ± 0.14	50.6 ± 1.4	21.1 ± 1.6	5.2 ± 1.0	5.6 ± 0.9	14.1 ± 1.1	3.4 ± 0.8	1.03 ± 0.06
20%	6	337 ± 137	73 ± 11	27 ± 4	543 ± 172	0.61 ± 0.37	40 ± 6	207 ± 42	6.14 ± 0.12	50.8 ± 2.7	20.7 ± 2.0	5.9 ± 0.8	4.8 ± 1.2	14.0 ± 2.1	3.9 ± 0.9	1.04 ± 0.11
Conc. in diet	No. of animals	T-Chol. (mg/dL)	T.G. (mg/dL)	PL (mg/dL)	Glu. (mg/dL)	BUN (mg/dL)	UA (mg/dL)	Crea. (mg/dL)	T-Bil. (mg/dL)	Ca (mg/dL)	P (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)		
0%	6	58 ± 8	71 ± 19	93 ± 12	131 ± 14	12.7 ± 1.4	0.85 ± 0.28	0.53 ± 0.06	0.27 ± 0.04	10.3 ± 0.2	7.2 ± 0.7	144 ± 1	4.47 ± 0.21	107 ± 1		
5%	6	55 ± 11	73 ± 31	89 ± 16	127 ± 8	12.8 ± 0.9	0.83 ± 0.16	0.50 ± 0.05	0.30 ± 0.03	10.2 ± 0.1	7.7 ± 0.7	144 ± 1	4.55 ± 0.22	106 ± 1		
10%	6	43 ± 11	58 ± 25	78 ± 14	134 ± 19	12.0 ± 0.6	0.86 ± 0.13	0.55 ± 0.04	0.27 ± 0.04	10.1 ± 0.2	7.5 ± 0.5	144 ± 1	4.70 ± 0.20	108 ± 2		
20%	6	55 ± 19	78 ± 24	94 ± 20	128 ± 6	10.7* ± 1.7	0.91 ± 0.24	0.52 ± 0.05	0.25 ± 0.02	10.3 ± 0.3	7.6 ± 0.5	145 ± 1	5.06** ± 0.50	108 ± 2		

Each value is expressed as mean±S.D.

* : Significantly different from control at 5% level of probability

** : Significantly different from control at 1% level of probability

Table 12

Blood biochemical findings of female rats fed the milk powder-contained diet
in a 28day dose range-finding test

Conc. in diet	No. of animals	LDH (IU/L)	GOT (IU/L)	GPT (IU/L)	ALP (IU/L)	γ -GTP (IU/L)	ChE (IU/L)	CK (IU/L)	T.P. (g/dL)	Alb (%)	α_1 -G (%)	α_2 -G (%)	α_3 -G (%)	β -G (%)	γ -G (%)	A/G
0%	6	320 ± 87	76 ± 8	25 ± 3	441 ± 137	0.39 ± 0.16	316 ± 97	171 ± 24	6.39 ± 0.28	56.2 ± 2.2	19.6 ± 1.4	5.4 ± 0.5	2.1 ± 0.3	12.6 ± 1.8	4.2 ± 0.6	1.28 ± 0.11
5%	6	453 ± 271	82 ± 15	25 ± 4	404 ± 89	0.38 ± 0.20	412 ± 125	198 ± 64	6.38 ± 0.24	56.1 ± 2.9	17.7 ± 2.6	5.8 ± 1.0	3.0 ± 0.6	12.9 ± 0.7	4.6 ± 0.3	1.29 ± 0.15
10%	6	347 ± 57	81 ± 7	23 ± 2	451 ± 62	0.35 ± 0.19	324 ± 146	185 ± 22	6.26 ± 0.38	57.2 ± 1.6	19.6 ± 1.0	4.4 ± 0.7	2.4 ± 0.4	13.0 ± 0.5	3.5 ± 1.0	1.34 ± 0.09
20%	6	430 ± 95	85 ± 14	27 ± 5	388 ± 94	0.32 ± 0.15	378 ± 105	195 ± 24	6.48 ± 0.26	56.6 ± 1.0	18.5 ± 1.2	5.5 ± 0.5	2.6 ± 1.2	12.6 ± 1.1	4.1 ± 0.4	1.31 ± 0.05
Conc. in diet	No. of animals	T-Chol. (mg/dL)	T.G. (mg/dL)	PL (mg/dL)	Glu. (mg/dL)	BUN (mg/dL)	UA (mg/dL)	Crea. (mg/dL)	T-Bil. (mg/dL)	Ca (mg/dL)	P (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)		
0%	6	64 ± 6	30 ± 10	111 ± 12	115 ± 9	14.4 ± 2.9	0.86 ± 0.22	0.58 ± 0.06	0.25 ± 0.01	9.9 ± 0.1	6.4 ± 0.4	146 ± 1	4.53 ± 0.24	107 ± 1		
5%	6	59 ± 16	27 ± 16	107 ± 26	120 ± 14	13.8 ± 1.4	0.94 ± 0.23	0.60 ± 0.05	0.25 ± 0.03	9.6 ± 0.2	5.7 ± 0.5	146 ± 1	4.36 ± 0.21	108 ± 2		
10%	6	52 ± 10	33 ± 9	100 ± 19	123 ± 11	13.5 ± 1.5	0.98 ± 0.25	0.61 ± 0.05	0.27 ± 0.02	9.6 ± 0.2	5.7 ± 0.7	147 ± 1	4.50 ± 0.24	108 ± 2		
20%	6	55 ± 7	25 ± 20	99 ± 14	120 ± 17	16.1 ± 2.1	0.97 ± 0.23	0.66 ± 0.07	0.27 ± 0.02	9.8 ± 0.4	6.1 ± 0.8	146 ± 1	4.49 ± 0.23	107 ± 2		

Each value is expressed as mean±S.D.

Table 13-1

Absolute and relative organ weights of male rats fed milk powder-contained diet in a 28-day dose range-finding study

	Conc. in diet (%)	No. of Animals	B.W. (g)	Brain (g)	Liver (g)	Kidney (g)	Spleen (g)	Heart (g)	Lung (g)	Thymus (g)	Thyr. (mg)	Pituit. (mg)
Absolute	0	6	312 ±12	1.89 ±0.10	8.72 ±0.69	2.37 ±0.20	0.63 ±0.07	1.09 ±0.06	1.21 ±0.10	0.62 ±0.10	21.0 ±1.9	10.0 ±1.5
	5	6	320 ±20	1.93 ±0.05	8.98 ±0.61	2.49 ±0.15	0.62 ±0.14	1.15 ±0.11	1.25 ±0.13	0.67 ±0.15	21.4 ±4.4	10.6 ±1.2
	10	6	312 ±20	1.94 ±0.06	8.65 ±0.73	2.41 ±0.17	0.58 ±0.03	1.11 ±0.10	1.18 ±0.09	0.53 ±0.06	21.3 ±2.9	10.6 ±0.8
	20	6	300 ±25	1.91 ±0.02	8.88 ±1.27	2.35 ±0.19	0.64 ±0.06	1.06 ±0.06	1.19 ±0.08	0.66 ±0.09	21.7 ±3.4	10.3 ±0.5
Relative ^{a)}	0	6	312 ±12	0.61 ±0.03	2.79 ±0.17	0.76 ±0.04	0.20 ±0.02	0.35 ±0.02	0.39 ±0.03	0.20 ±0.03	6.7 ±0.7	3.2 ±0.4
	5	6	320 ±20	0.60 ±0.04	2.81 ±0.05	0.78 ±0.06	0.19 ±0.04	0.36 ±0.01	0.39 ±0.05	0.21 ±0.05	6.7 ±1.1	3.3 ±0.4
	10	6	312 ±20	0.62 ±0.06	2.77 ±0.16	0.77 ±0.06	0.18 ±0.01	0.35 ±0.03	0.38 ±0.01	0.17 ±0.01	6.9 ±1.3	3.4 ±0.3
	20	6	300 ±25	0.64 ±0.06	2.96 ±0.33	0.79 ±0.05	0.21 ±0.03	0.35 ±0.02	0.40 ±0.02	0.22 ±0.02	7.2 ±0.9	3.5 ±0.2

Each value is expressed as mean ± S.D.

a): Relative organ weight per 100g body weight

Table 13-2

Absolute and relative organ weights of male rats fed dry beef-contained diet in a 28-day dose range-finding study

	Dose (mg/kg)	No. of Animals	B.W. (g)	Adrenal (mg)	Testis (g)	Prost. (g)	Semi.v (g)	Epidid. (g)
Absolute	0	6	312 ±12	53.7 ±5.3	2.70 ±0.24	0.49 ±0.09	1.23 ±0.18	0.77 ±0.06
	5	6	320 ±20	53.1 ±5.6	2.68 ±0.13	0.50 ±0.14	1.22 ±0.12	0.75 ±0.10
	10	6	312 ±20	52.1 ±6.1	2.69 ±0.18	0.50 ±0.05	1.30 ±0.21	0.75 ±0.04
	20	6	300 ±25	53.7 ±8.5	2.61 ±0.27	0.49 ±0.10	1.36 ±0.28	0.71 ±0.05
Relative ^{a)}	0	6	312 ±12	17.2 ±1.3	0.87 ±0.08	0.16 ±0.03	0.39 ±0.07	0.25 ±0.01
	5	6	320 ±20	16.7 ±2.1	0.84 ±0.04	0.16 ±0.04	0.38 ±0.03	0.23 ±0.02
	10	6	312 ±20	16.7 ±1.8	0.87 ±0.10	0.16 ±0.02	0.42 ±0.09	0.24 ±0.03
	20	6	300 ±25	17.9 ±2.1	0.88 ±0.10	0.17 ±0.04	0.45 ±0.09	0.24 ±0.02

Each value is expressed as mean ± S.D.

a): Relative organ weight per 100g body weight

Table 14

Absolute and relative organ weights of female rats fed milk powder-contained diet in a 28-day dose range-finding study

	Conc. in diet (%)	No. of Animals	B.W. (g)	Brain (g)	Liver (g)	Kidney (g)	Spleen (g)	Heart (g)	Lung (g)	Thymus (g)	Thyr. (mg)	Pituit. (mg)	Adrenal (mg)	Ovary (mg)	Uterus (g)
Absolute	0	6	211 ±10	1.85 ±0.10	5.89 ±0.25	1.63 ±0.14	0.42 ±0.04	0.75 ±0.06	0.98 ±0.03	0.52 ±0.10	21.0 ±2.4	12.9 ±1.2	54.9 ±6.0	78.3 ±10.7	0.47 ±0.13
	5	6	217 ±28	1.83 ±0.04	6.18 ±1.17	1.57 ±0.17	0.45 ±0.08	0.77 ±0.10	1.00 ±0.07	0.49 ±0.10	20.3 ±3.8	13.3 ±2.2	60.0 ±10.8	74.3 ±7.7	0.47 ±0.16
	10	6	211 ±14	1.82 ±0.09	5.88 ±0.60	1.64 ±0.19	0.42 ±0.04	0.76 ±0.07	0.95 ±0.03	0.46 ±0.05	20.3 ±1.9	11.8 ±1.4	52.4 ±2.9	86.1 ±17.0	0.48 ±0.10
	20	6	216 ±24	1.81 ±0.05	6.09 ±0.62	1.75 ±0.13	0.42 ±0.04	0.77 ±0.08	1.01 ±0.09	0.52 ±0.09	21.3 ±2.6	12.8 ±1.4	59.0 ±4.5	79.3 ±12.6	0.46 ±0.06
Relative ^{a)}	0	6	211 ±10	0.88 ±0.06	2.79 ±0.11	0.77 ±0.05	0.20 ±0.02	0.35 ±0.02	0.47 ±0.02	0.25 ±0.05	10.0 ±1.1	6.1 ±0.6	26.1 ±3.5	37.2 ±5.4	0.22 ±0.06
	5	6	217 ±28	0.86 ±0.10	2.84 ±0.21	0.73 ±0.06	0.21 ±0.03	0.36 ±0.02	0.47 ±0.06	0.23 ±0.03	9.5 ±1.9	6.2 ±1.0	27.8 ±5.0	34.7 ±5.6	0.22 ±0.08
	10	6	211 ±14	0.86 ±0.05	2.79 ±0.15	0.78 ±0.05	0.20 ±0.02	0.36 ±0.02	0.45 ±0.01	0.22 ±0.02	9.7 ±1.1	5.6 ±0.6	24.9 ±1.4	40.8 ±7.7	0.23 ±0.04
	20	6	216 ±24	0.84 ±0.07	2.82 ±0.10	0.81 ±0.05	0.20 ±0.03	0.36 ±0.01	0.47 ±0.02	0.25 ±0.05	9.9 ±1.3	6.0 ±0.5	27.5 ±3.5	36.8 ±5.7	0.22 ±0.04

Each value is expressed as mean ± S.D.

a) : Relative organ weight per 100g body weight

Appendix 1 Individual body weights of male rats fed the milk powder-contained diet in a 28day dose range-finding test

Conc. in diet	Number of animals	Day				
		0	7	14	21	28
0%	001	125	191	243	295	337
	002	120	183	243	290	326
	003	127	184	235	279	311
	004	130	193	249	306	345
	005	124	178	232	284	323
	006	126	190	231	285	341
	Mean	125	187	239	290	331
5%	007	125	193	258	324	376
	008	119	175	230	277	312
	009	124	180	237	289	333
	010	125	186	248	304	350
	011	129	178	239	296	337
	012	127	183	232	290	330
	Mean	125	183	241	297	340
10%	013	124	182	233	286	328
	014	126	182	250	307	353
	015	123	181	235	282	324
	016	120	171	221	260	299
	017	127	192	253	309	351
	018	129	189	243	294	339
	Mean	125	183	239	290	332
20%	019	125	186	237	287	331
	020	123	187	238	288	329
	021	127	192	255	309	354
	022	118	166	218	264	299
	023	124	180	236	289	327
	024	131	187	245	251	281
	Mean	125	183	238	281	320

Appendix 2 Individual body weights of female rats fed the milk powder-contained diet in a 28day dose range-finding test

Conc. in diet	Number of animals	Day				
		0	7	14	21	28
0%	501	114	154	179	205	231
	502	116	153	186	210	243
	503	112	144	168	194	216
	504	120	153	178	197	217
	505	110	143	173	195	211
	506	122	154	178	208	228
	Mean	116	150	177	202	224
5%	507	125	184	209	240	281
	508	112	144	169	198	221
	509	111	141	161	180	200
	510	118	151	174	190	208
	511	115	147	172	201	239
	512	116	151	181	208	225
	Mean	116	153	178	203	229
10%	513	110	139	161	188	212
	514	112	144	169	187	215
	515	116	153	185	213	232
	516	119	164	190	220	248
	517	121	156	184	207	232
	518	114	151	175	199	219
	Mean	115	151	177	202	226
20%	519	115	140	160	185	205
	520	110	152	183	205	225
	521	133	167	211	247	278
	522	119	161	189	211	228
	523	114	150	178	203	220
	524	112	148	173	192	216
	Mean	117	153	182	207	229

Appendix 3 Individual food consumption of male rats fed the milk powder-contained diet in a 28day dose range-finding test

Conc. in diet	Cage number	(g/day/rat)			
		Week 1	2	3	4
0%	1	16	21	20	20
	2	16	19	20	19
	3	16	17	19	21
	Mean	16	19	20	20
5%	4	17	20	21	20
	5	16	19	20	20
	6	14	19	20	20
	Mean	16	19	20	20
10%	7	15	19	20	20
	8	14	18	18	18
	9	17	20	21	21
	Mean	15	19	20	20
20%	10	15	18	19	19
	11	15	18	19	20
	12	15	18	14	19
	Mean	15	18	17	19

Appendix 4 Individual food consumption of female rats fed the milk powder-contained diet in a 28day dose range-finding test

Conc. in diet	Cage number	(g/day/rat)			
		Week 1	2	3	4
0%	13	12	14	16	17
	14	11	14	15	16
	15	11	14	14	14
	Mean	11	14	15	16
5%	16	13	15	19	19
	17	11	13	13	13
	18	11	15	14	16
	Mean	12	14	15	16
10%	19	10	12	13	13
	20	13	15	15	16
	21	11	13	14	15
	Mean	11	13	14	15
20%	22	10	13	14	14
	23	13	16	17	16
	24	11	12	13	14
	Mean	11	14	15	15

Appendix 5

Individual urinary findings of male rats fed the milk powder-contained diet
in a 28day dose range-finding test

Conc. in diet	Animal number	Color	Cloudy	pH	Protein	Glucose	Ketone body	Occult blood	Urobilinogen	Bilirubin
0%	001	PY	-	6.0	+	-	-	-	0.1	-
	002	PY	-	6.0	+	-	-	-	0.1	-
	003	PY	-	6.0	±	-	-	-	0.1	-
	004	PY	-	6.5	-	-	-	-	0.1	-
	005	PY	-	7.0	±	-	±	-	0.1	-
	008	PY	-	6.5	±	-	±	-	0.1	-
5%	007	PY	-	6.0	±	-	-	-	0.1	-
	008	PY	-	6.5	±	-	±	-	0.1	-
	009	PY	-	6.0	+	-	-	-	0.1	-
	010	PY	-	6.5	+	-	±	-	0.1	-
	011	PY	-	6.0	±	-	-	-	0.1	-
	012	PY	-	6.0	-	-	-	-	0.1	-
10%	013	PY	-	6.5	±	-	-	-	0.1	-
	014	PY	-	6.5	±	-	-	-	0.1	-
	015	PY	-	6.0	±	-	±	-	0.1	-
	016	PY	-	6.5	±	-	-	-	0.1	-
	017	PY	-	6.5	-	-	±	-	0.1	-
	018	PY	-	6.5	-	-	±	-	0.1	-
20%	019	PY	-	6.0	±	-	-	-	0.1	-
	020	PY	-	6.5	±	-	±	-	0.1	-
	021	PY	-	6.0	±	-	-	-	0.1	-
	022	PY	-	6.0	-	-	-	-	0.1	-
	023	PY	-	6.0	±	-	±	-	0.1	-
	024	PY	-	6.5	±	-	-	-	0.1	-

Color : PY (pale yellow)

Cloudy : - (negligible)

Protein : - (negligible), ±(15~30mg/dL), + (30mg/dL)

Glucose : - (negligible)

Ketone body : - (negligible), ±(5mg/dL)

Occult blood : - (negligible)

Urobilinogen : Ehrlich unit/dL

Bilirubin : - (negligible)

Appendix 6

Individual urinary findings of female rats fed the milk powder-contained diet
in a 28day dose range-finding test

Conc. in diet	Animal number	Color	Cloudy	pH	Protein	Glucose	Ketone body	Occult blood	Urobilinogen	Bilirubin
0%	501	PY	-	7.0	-	-	-	-	0.1	-
	502	PY	-	6.5	±	-	-	-	0.1	-
	503	PY	-	6.0	-	-	-	-	0.1	-
	504	PY	-	7.0	-	-	-	-	0.1	-
	505	PY	-	6.5	-	-	-	-	0.1	-
	508	PY	-	6.0	±	-	-	-	0.1	-
5%	507	PY	-	6.5	±	-	-	-	0.1	-
	508	PY	-	6.0	-	-	-	±	0.1	-
	509	PY	-	6.5	±	-	-	±	0.1	-
	510	PY	-	7.0	±	-	-	±	0.1	-
	511	PY	-	6.0	±	-	-	-	0.1	-
	512	PY	-	7.0	±	-	-	-	0.1	-
10%	513	PY	-	6.0	-	-	-	-	0.1	-
	514	PY	-	7.0	-	-	-	-	0.1	-
	515	PY	-	7.0	-	-	-	-	0.1	-
	516	PY	-	6.5	±	-	±	-	0.1	-
	517	PY	-	6.5	-	-	-	-	0.1	-
	518	PY	-	6.5	-	-	-	-	0.1	-
20%	519	PY	-	7.0	-	-	-	-	0.1	-
	520	PY	-	7.0	-	-	-	-	0.1	-
	521	PY	-	6.5	-	-	-	-	0.1	-
	522	PY	-	6.5	-	-	-	-	0.1	-
	523	PY	-	6.0	±	-	-	-	0.1	-
	524	PY	-	6.0	-	-	±	-	0.1	-

Color : PY (pale yellow)

Cloudy : - (negligible)

Protein : - (negligible), ±(15~30mg/dL)

Glucose : - (negligible)

Ketone body : - (negligible), ±(5mg/dL)

Occult blood : - (negligible), ±(trace)

Urobilinogen : Ehrlich unit/dL

Bilirubin : - (negligible)

Appendix 7

Individual hematological findings of male rats fed the milk powder-contained diet in a 28day dose range finding test

Conc. in diet	Animal number	RBC (10 ⁶ /μL)	Hb (g/dL)	Ht (%)	MCV (fL)	MCH (pg)	MCHC (%)	WBC (10 ³ /μL)	Plat. (10 ⁴ /μL)	PT (sec)	APTT (sec)
0%	001	770	14.8	42.2	55	19.2	35.1	67	110	13.2	20.1
	002	764	15.5	43.7	57	20.3	35.5	61	95	12.9	22.4
	003	735	14.7	41.2	56	20.0	35.7	49	94	13.4	20.6
	004	754	14.2	41.4	55	18.8	34.3	56	124	12.3	18.2
	005	728	15.4	42.2	58	21.2	36.5	39	110	12.6	19.9
	006	762	14.8	43.5	57	19.4	34.0	90	102	12.8	18.6
	Mean	752	14.9	42.4	56	19.8	35.2	60	106	12.9	20.0
5%	007	714	13.8	39.7	56	19.3	34.8	53	148	12.5	19.1
	008	718	14.9	41.0	57	20.8	36.3	50	105	12.5	20.3
	009	739	14.2	42.1	57	19.2	33.7	61	120	12.6	18.6
	010	701	13.7	38.5	55	19.5	35.6	49	120	12.4	20.1
	011	739	15.5	44.4	60	21.0	34.9	38	124	13.4	18.2
	012	790	15.3	43.8	55	19.4	34.9	48	110	12.9	19.0
	Mean	734	14.6	41.6	57	19.9	35.0	50	121	12.7	19.2
10%	013	716	14.2	40.3	56	19.8	35.2	52	115	12.8	20.3
	014	781	15.5	42.9	55	19.8	36.1	52	118	12.7	19.1
	015	743	15.4	43.8	59	20.7	35.2	60	120	13.5	18.7
	016	822	14.2	40.6	49	17.3	35.0	28	150	12.9	18.6
	017	753	14.8	42.6	57	19.7	34.7	46	118	13.0	16.8
	018	747	14.7	43.2	58	19.7	34.0	39	110	12.8	19.5
	Mean	760	14.8	42.2	56	19.5	35.0	46	122	13.0	18.8
20%	019	749	14.7	41.3	55	19.6	35.6	52	129	12.8	20.7
	020	719	14.8	42.3	59	20.6	35.0	45	115	13.0	21.2
	021	718	14.6	42.0	58	20.3	34.8	30	129	13.1	18.4
	022	780	14.8	42.0	54	19.0	35.2	40	132	12.7	18.3
	023	734	14.4	41.6	57	19.6	34.6	57	142	13.2	20.3
	024	411	7.2	23.6	57	17.5	30.5	61	87	13.1	16.8
	Mean	685	13.4	38.8	57	19.4	34.3	48	122	13.0	19.3

Appendix 8-1

Individual hematological findings of female rats fed the milk powder-contained diet in a 28day dose range-finding test

Conc. in diet	Animal number	RBC (10 ⁶ /μL)	Hb (g/dL)	Ht (%)	MCV (fL)	MCH (pg)	MCHC (%)	PT (sec)	APTT (sec)	WBC (10 ³ /μL)
0%	501	769	14.9	41.8	54	19.4	35.6	13.3	18.3	64
	502	714	14.9	41.1	58	20.9	36.3	13.0	18.8	34
	503	797	14.7	42.3	53	18.4	34.8	12.5	19.8	39
	504	735	14.8	41.3	56	20.1	35.8	13.0	16.5	30
	505	800	15.0	43.2	54	18.8	34.7	13.2	18.3	47
	506	731	14.5	41.1	56	19.8	35.3	12.9	18.0	42
	Mean	758	14.8	41.8	55	19.6	35.4	13.0	18.3	43
5%	507	667	13.6	38.5	58	20.4	35.3	12.6	17.6	42
	508	806	15.4	43.8	54	19.1	35.2	12.8	19.3	39
	509	761	14.1	39.8	52	18.5	35.4	13.3	18.9	17
	510	748	15.1	42.2	56	20.2	35.8	12.6	18.0	30
	511	704	14.0	39.9	57	19.9	35.1	13.5	18.5	26
	512	762	15.0	42.8	56	19.7	35.0	13.5	19.0	31
	Mean	741	14.5	41.2	56	19.6	35.3	13.1	18.6	31
10%	513	795	14.9	42.3	53	18.7	35.2	12.6	18.8	27
	514	785	15.3	44.0	56	19.5	34.8	13.2	20.2	28
	515	718	14.1	39.6	56	19.8	35.6	13.5	18.4	22
	516	744	15.8	44.1	59	21.2	35.8	13.4	17.4	22
	517	699	13.9	39.2	56	19.9	35.5	13.0	17.1	27
	518	730	14.3	39.9	55	19.6	35.8	13.2	19.6	27
	Mean	744	14.7	41.5	56	19.8	35.5	13.2	18.6	26
20%	519	756	15.3	43.3	57	20.2	35.3	13.4	18.3	27
	520	687	14.4	38.7	56	21.0	37.2	12.9	18.7	37
	521	725	14.5	40.5	56	20.0	35.8	14.1	17.4	25
	522	806	15.1	42.1	52	18.7	35.9	12.6	16.4	22
	523	708	14.1	38.8	55	19.9	36.3	12.8	18.0	30
	524	772	15.6	43.1	56	20.2	36.2	11.9	16.4	57
	Mean	742	14.8	41.1	55	20.0	36.1	13.0	17.5	33

Appendix 8-2

Individual hematological findings of female rats fed the milk powder-contained diet in the 28-day repeat dose toxicity test

Conc. in diet	Animal number	Differential leukocyte counts (%)							Plat. (10 ⁴ /μL)
		Baso.	Eosin.	Neutro.		Lymph.	Mono.	Other	
				Stab.	Seg.				
0%	501	0	1	0	14	82	3	0	102
	502	0	0	0	9	89	2	0	96
	503	0	0	1	6	93	0	0	131
	504	0	0	0	14	86	0	0	129
	505	0	0	0	10	87	3	0	131
	506	0	3	0	18	76	3	0	127
	Mean	0	1	0	12	86	2	0	119
5%	507	0	0	0	12	86	2	0	90
	508	0	1	1	16	81	1	0	139
	509	0	3	0	18	78	1	0	120
	510	0	2	0	10	88	0	0	106
	511	0	1	0	14	83	2	0	127
	512	0	1	0	11	87	1	0	138
	Mean	0	1	0	14	84	1	0	120
10%	513	0	0	0	18	80	2	0	130
	514	0	1	0	10	89	0	0	128
	515	0	2	0	9	86	3	0	99
	516	0	2	0	13	84	1	0	122
	517	0	0	0	19	81	0	0	124
	518	0	2	0	12	85	1	0	131
	Mean	0	1	0	14	84	1	0	122
20%	519	0	0	0	10	90	0	0	120
	520	0	1	0	9	90	0	0	119
	521	0	2	0	15	80	3	0	147
	522	0	2	0	9	88	1	0	158
	523	0	0	0	10	90	0	0	108
	524	0	1	0	12	86	1	0	138
	Mean	0	1	0	11	87	1	0	132

Table 1 Analyzed nutrient composition of the dried beef

Macronutrient (%)	Vitamin (mg/100g)	Mineral (mg/100g)
Crude protein 42.8	A ND	Ca 17.1
Crude fat 50.0	B ₁ 0.23	P 386
Carbohydrate 4.3	B ₂ 0.50	K 1120
Crude fiber 0.0	B ₆ 0.54	Na 767
Ash 2.0	B ₁₂ 0.0031	Mg 47.3
Water 0.9	D ₃ ND	Fe 6.26
	E 0.2	Zn 9.99
	K ₁ ND	Cu 0.14
	K ₂ 0.010	S 370
	Niacin 12.1	Mn 0.03
	Pantotheinic acid 2.55	I ND
	Folic acid 0.019	Se 0.03
	Biotin 0.0042	Mo ND
	Choline 0.13 (%)	

Table 2-1 Composition of the dried beef-contained diets

Ingredient	(g/kg diets)				
	Basal diet I	5% diet	10% diet	Basal diet II	20% diet
Dried beef		50.000	100.000		200.000
Cornstarch	397.486	396.019	394.552	374.965	369.097
Casein (93.5% protein)	200.000	177.112	154.225	200.000	108.449
Alfa-cornstarch	132.000	131.513	131.027	124.521	122.573
Sucrose	100.000	100.000	100.000	100.000	100.000
Soybean oil	70.000	45.000	20.000	100.000	
Cellulose	50.000	50.000	50.000	50.000	50.000
Mineral Mix *	35.000	35.000	35.000	35.000	35.000
Vitamin Mix *	10.000	10.000	10.000	10.000	10.000
L-Cystine	3.000	3.000	3.000	3.000	3.000
Choline Bitartrate (41.1% choline)	2.500	2.342	2.184	2.500	1.867
t-Butylhydroquinone	0.014	0.014	0.014	0.014	0.014
Caloric value (kcal)	397	398	399	411	415
Crude protein (%)	18.7	18.7	18.7	18.7	18.7
Crude fat (%)	7.0	7.0	7.0	10.0	10.0
Carbohydrate (%)	64.7	65.0	65.2	61.5	62.5
Crude fiber (%)	5.0	5.0	5.0	5.0	5.0

*: Ingredients of the mineral mix and vitamin mix are shown in table 2-2.

Table 2-2 Ingredients of the mineral mix and vitamin mix for the dried beef-contained diet

Mineral Mix							Vitamin Mix				
Ingredients	Contents (%)	Basal diet I	5% diet	10% diet	Basal diet II	20% diet	Ingredients	Basal diet I/II	5% diet	10% diet	20% diet
ESSENTIAL MINERALS							Vitamine A Palmitate (500,000IU/g)	0.800	0.800	0.800	0.800
Calcium Carbonate	Ca: 40.04	357.00	356.357	355.786	357.00	354.572	Thiamine HCl (B ₁)	0.600	0.590	0.580	0.550
Potassium Phosphate (monobasic)	P: 22.78	196.00	192.359	188.843	196.00	181.688	Riboflavin (B ₂)	0.600	0.580	0.550	0.500
Potassium Citrate H ₂ O	K: 28.73	57.29*	51.612	45.832	122.844*		Pyridoxine HCl (B ₆)	0.700	0.670	0.650	0.590
Sodium Chloride	Na: 39.34	74.00	45.584	17.242	114.00*		Vitamine B ₁₂ (0.1%)	2.500	2.300	2.200	1.900
Potassium Sulfate	S: 18.39	57.47*	28.735		115.00*		Vitamine D ₃ (400,000IU/g)	0.250	0.250	0.250	0.250
Magnesium Oxide	Mg: 44.87	24.00	22.871	21.788	24.00	19.529	Vitamine E Acetate (500IU/g)	15.000	15.000	15.000	15.000
Ferric Citrate	Fe: 16.50	6.08	5.541	5.021	6.08	3.809	Vitamine K ₁	0.075	0.075	0.074	0.073
Zinc Carbonate	Zn: 52.14	1.65	1.375	1.100	1.65	0.550	Niacin	3.000	3.000	3.000	3.000
Manganous Carbonate	Mn: 47.79	0.63	0.630	0.630	0.63	0.620	Calcium Pantothenate	1.600	1.500	1.300	1.100
Cupric Carbonate	Cu: 57.47	0.30	0.295	0.295	0.30	0.285	Folic Acid	0.200	0.200	0.200	0.200
Potassium Iodate	I: 59.30	0.01	0.01	0.01	0.01	0.01	Biotin	0.020	0.020	0.019	0.018
Sodium Selenate	Se: 41.79	0.01025	0.00957	0.00820	0.01025	0.00615	Sucrose finely powdered	974.655	975.015	975.376	976.018
Ammonium Paramolybdate 4H ₂ O	Mo: 54.34	0.00795	0.00795	0.00795	0.00795	0.00795					
NON-ESSENTIAL MINERALS											
Sodium Metaalicate 9H ₂ O	Si: 9.88	1.45	1.45	1.45	1.45	1.45					
Chromium Potassium Sulfate 12H ₂ O	Cr: 10.42	0.275	0.275	0.275	0.275	0.275					
Lithium Chloride	Li: 16.38	0.0174	0.0174	0.0174	0.0174	0.0174					
Boric Acid	B: 17.50	0.0815	0.0815	0.0815	0.0815	0.0815					
Sodium Fluoride	F: 45.24	0.0635	0.0635	0.0635	0.0635	0.0635					
Nickel Carbonate	Ni: 45.00	0.0318	0.0318	0.0318	0.0318	0.0318					
Ammonium Vanadate	V: 43.55	0.0066	0.0066	0.0066	0.0066	0.0066					
Sucrose finely powdered		223.648	292.688	381.511	160.562	436.999					

*: Composition is differ from that of the AIN standard diet. The mineral mix and vitamin mix for each composition was designed to reflect the mineral (essential minerals) and vitamin contents of the dried beef at each additional level.

Table 3 Body weights of male rats fed the dry beef-contained diet in a 28day dose range-finding test

Conc. in diet	Number of animals	Day					Gain 0~28
		1	7	14	21	28	
0% ^{a)}	6	121	176	236	291	335	214
		± 4	± 6	± 8	± 7	± 11	± 14
5%	6	122	181	239	296	340	218
		± 6	± 8	± 14	± 24	± 31	± 28
10%	6	121	172	226	280	308	188
		± 6	± 7	± 12	± 20	± 23	± 20
0% ^{b)}	6	122	180	240	286	319	198
		± 5	± 8	± 12	± 23	± 40	± 37
20%	6	121	164 *	208 *	246 *	271 *	150 *
		± 5	± 12	± 22	± 30	± 34	± 30

Each value is expressed as mean±S.D.

a):Control I b):Control II

*:Significantly different from control II at 5% level of probability

Table 4 Body weights of female rats fed the dry beef-contained diet in a 28day dose range-finding test

Conc. in diet	Number of animals	Day					Gain 0~28
		1	7	14	21	28	
0% ^{a)}	6	116	146	174	198	218	102
		± 5	± 6	± 10	± 12	± 16	± 16
5%	6	115	149	171	201	223	107
		± 7	± 15	± 15	± 15	± 17	± 11
10%	6	115	145	175	195	210	94
		± 5	± 7	± 9	± 14	± 18	± 15
0% ^{b)}	6	116	148	180	207	231	115
		± 7	± 11	± 12	± 13	± 18	± 13
20%	6	116	145	174	197	217	101
		± 6	± 11	± 17	± 17	± 20	± 18

Each value is expressed as mean±S.D.

a):Control I b):Control II

Table 5 Food consumption of male rats fed the dry beef-contained diet in a 28day dose range-finding test

Conc. in diet	Number of animals	(g/day/rat)			
		Week 1	2	3	4
0% ^{a)}	6	18	21	22	22
		± 1	± 1	± 2	± 1
5%	6	18	19	21	21
		± 2	± 2	± 3	± 3
10%	6	17	19	20	18
		± 1	± 1	± 2	± 1
0% ^{b)}	6	17	19	20	17
		± 1	± 2	± 2	± 0
20%	6	16	18	17	15
		± 1	± 3	± 3	± 5

Each value is expressed as mean±S.D.
a):Control I b):Control II

Table 6 Food consumption of female rats fed the dry beef-contained diet in a 28day dose range-finding test

Conc. in diet	Number of animals	(g/day/rat)			
		Week 1	2	3	4
0% ^{a)}	6	13	14	15	15
		± 1	± 2	± 1	± 2
5%	6	13	13	15	15
		± 2	± 3	± 1	± 1
10%	6	14	14	14	13
		± 1	± 2	± 3	± 1
0% ^{b)}	6	14	14	15	15
		± 1	± 1	± 0	± 2
20%	6	13	14	13	14
		± 1	± 1	± 1	± 1

Each value is expressed as mean±S.D.
a):Control I b):Control II

Table
Conc. diet
0'
5'
10%

0'
20%
Conc. diet
0%
5%
10%

0%
20%
Color:
Cloud:
Protei:
Glucos:
Keton:
Occult:
Urobil:
Bilirub:
a): Co

Table
Conc diet
0
5
10

0
20
Conc diet
0
5
10'

0
20'
Color:
Cloud:
Prote:
Glucos:
Keton:
Occul:
Urobi:
Biliru:
a): Co

Table 7 Urinary findings of male rats fed the dry beef-contained diet in a 28day dose range-finding test

Conc. in diet	No. of animals	Color		Cloudy		pH						Protein					Glucose					
		PY		-	+	5.0	6.0	6.5	7.0	7.5	8.0	8.5	-	±	+	++	+++	-	±	+	++	+++
0% ^{a)}	6	6		6		5	1					2	4				6					
5%	6	6		6		6						3	3				6					
10%	6	6		6		4	1	1				1	4	1			6					
0% ^{b)}	6	6		6		6						1	4	1			6					
20%	6	6		6		5	1					3	2	1			6					

Conc. in diet	No. of animals	Ketone body					Occult blood					Urobilinogen				Bilirubin					
		-	±	+	++	+++	-	±	+	++	+++	0.1	1	2	4	8	-	+	++	+++	
0% ^{a)}	6	4	2				6					6					6				
5%	6	5	1				6					6					6				
10%	6	5	1				4	2				6					6				
0% ^{b)}	6	6					6					6					6				
20%	6	6					5	1				6					6				

Color: PY(pale yellow)
 Cloudy: - (negligible), + (cloudy)
 Protein: - (negligible), ±(15~30mg/dL), + (30mg/dL), ++(100mg/dL), +++(300mg/dL)
 Glucose: - (negligible), ±(0.1g/dL), + (0.25g/dL), ++(0.5g/dL), +++(1g/dL)
 Ketone body: - (negligible), ±(5mg/dL), + (15mg/dL), ++(40mg/dL), +++(80mg/dL)
 Occult blood: - (negligible), ±(trace), + (slight), ++(moderate), +++(marked)
 Urobilinogen: Ehrlich unit/dL
 Bilirubin: - (negligible), + (slight), ++(moderate), +++(marked)
 a): Control I, b): Control II

Table 8 Urinary findings of female rats fed the dry beef-contained diet in a 28day dose range-finding test

Conc. in diet	No. of animals	Color		Cloudy		pH						Protein					Glucose					
		PY		-	+	5.0	6.0	6.5	7.0	7.5	8.0	8.5	-	±	+	++	+++	-	±	+	++	+++
0% ^{a)}	6	6		6		5	1					2	4				6					
5%	6	6		6		3	2	1				5	1				6					
10%	6	6		6		3	2	1				3	2	1			6					
0% ^{b)}	6	6		6		4	1	1				2	4				6					
20%	6	6		6		4	1	1				4	2				6					

Conc. in diet	No. of animals	Ketone body					Occult blood					Urobilinogen				Bilirubin					
		-	±	+	++	+++	-	±	+	++	+++	0.1	1	2	4	8	-	+	++	+++	
0% ^{a)}	6	6					6					6					6				
5%	6	6					3	2	1			6					6				
10%	6	6					6					6					6				
0% ^{b)}	6	6					5	1				6					6				
20%	6	6					6					6					6				

Color: PY(pale yellow)
 Cloudy: - (negligible), + (cloudy)
 Protein: - (negligible), ±(15~30mg/dL), + (30mg/dL), ++(100mg/dL), +++(300mg/dL)
 Glucose: - (negligible), ±(0.1g/dL), + (0.25g/dL), ++(0.5g/dL), +++(1g/dL)
 Ketone body: - (negligible), ±(5mg/dL), + (15mg/dL), ++(40mg/dL), +++(80mg/dL)
 Occult blood: - (negligible), ±(trace), + (slight), ++(moderate), +++(marked)
 Urobilinogen: Ehrlich unit/dL
 Bilirubin: - (negligible), + (slight), ++(moderate), +++(marked)
 a): Control I, b): Control II

Table 9

Hematological findings of male rats fed the dry beef-contained diet in the 28-day repeat dose toxicity test

Conc. in diet	No. of animals	RBC (10 ⁶ /μL)	Hb (g/dL)	Ht (%)	MCV (fL)	MCH (pg)	MCHC (%)	PT (sec)	APTT (sec)	WBC (10 ³ /μL)
0% ^{a)}	6	737 ± 24	14.0 ± 0.7	40.7 ± 1.9	55 ± 4	19.0 ± 1.2	34.4 ± 0.7	12.8 ± 0.3	19.4 ± 1.7	60 ± 7
5%	6	773 ± 20	14.6 ± 0.6	42.5 ± 1.1	55 ± 2	18.8 ± 0.7	34.2 ± 0.6	13.3 ± 0.4	18.8 ± 1.1	62 ± 22
10%	6	731 ± 65	14.2 ± 1.3	40.9 ± 3.4	56 ± 2	19.4 ± 0.8	34.6 ± 1.2	13.6 ± 0.8	19.1 ± 1.4	46 ± 5
0% ^{b)}	6	756 ± 48	14.6 ± 0.9	42.8 ± 2.5	57 ± 4	19.3 ± 1.6	34.0 ± 0.4	13.4 ± 1.0	19.7 ± 2.9	51 ± 17
20%	6	822 ± 64	14.3 ± 2.1	41.4 ± 4.5	51 # ± 4	17.3 ± 2.0	34.4 ± 1.7	13.6 ± 0.3	18.2 ± 1.1	38 ± 10
		Differential leukocyte counts (%)								Plat. (10 ³ /μL)
Conc. in diet	No. of animals	Baso.	Eosin.	Neutro.					Other	Plat. (10 ³ /μL)
				Stab.	Seg.	Lymph.	Mono.			
0% ^{a)}	6	0 ± 0	1 ± 1	0 ± 0	14 ± 5	83 ± 6	2 ± 1	0 ± 0	132 ± 9	
5%	6	0 ± 0	1 ± 1	0 ± 0	14 ± 4	84 ± 4	1 ± 1	0 ± 0	119 ± 16	
10%	6	0 ± 0	1 ± 2	0 ± 0	12 ± 4	86 ± 5	2 ± 1	0 ± 0	143 ± 47	
0% ^{b)}	6	0 ± 0	0 ± 1	0 ± 0	15 ± 4	83 ± 5	1 ± 1	0 ± 0	124 ± 18	
20%	6	0 ± 0	1 ± 1	0 ± 0	12 ± 3	86 ± 4	1 ± 1	0 ± 0	134 ± 50	

Each value is expressed as mean ± S.D.

a) : Control I, b) : Control II

: Significantly different from control II at 5% level of probability

Table 10

Hematological findings of female rats fed the dry beef-contained diet in a 28day dose range-finding test

Conc. in diet	No. of animals	RBC (10 ⁶ /μL)	Hb (g/dL)	Ht (%)	MCV (fL)	MCH (pg)	MCHC (%)	WBC (10 ³ /μL)	Plat. (10 ³ /μL)	PT (sec)	APTT (sec)
0% ^{a)}	6	762 ± 28	15.0 ± 0.3	42.0 ± 1.2	55 ± 2	19.7 ± 0.6	35.8 ± 0.6	37 ± 6	104 ± 7	12.8 ± 0.3	18.1 ± 1.4
5%	6	767 ± 21	14.8 ± 0.4	42.2 ± 0.6	55 ± 2	19.4 ± 0.7	35.2 ± 0.7	46 ± 30	120 ± 13	12.9 ± 0.3	17.7 ± 1.4
10%	6	787 ± 38	15.3 ± 0.4	43.1 ± 0.8	55 ± 2	19.5 ± 0.8	35.5 ± 0.7	29 ± 6	126 ± 10	13.0 ± 0.4	18.0 ± 0.5
0% ^{b)}	6	748 ± 23	15.3 ± 0.4	43.0 ± 0.9	58 ± 1	20.4 ± 0.5	35.6 ± 0.7	34 ± 9	114 ± 15	13.2 ± 0.6	18.1 ± 1.6
20%	6	765 ± 28	14.2 ± 1.2	40.8# ± 2.2	53## ± 2	18.6## ± 1.2	34.9 ± 1.6	33 ± 10	124 ± 17	12.9 ± 0.3	18.3 ± 0.5

Each value is expressed as mean ± S.D.

a) : Control I, b) : Control II

* : Significantly different from control I at 5% level of probability

** : Significantly different from control I at 1% level of probability

: Significantly different from control II at 5% level of probability

: Significantly different from control II at 1% level of probability

Table 11

Conc. in diet

0%^{a)}

5%

10%

0%^{b)}

20%

Conc. in diet

0%^{a)}

5%

10%

0%^{b)}

20%

Each val.

a) : Contr

* : Signi

** : Signi

: Signi

: Signi

Table

Conc diet

0%

5%

10%

0%

20%

Conc diet

0

5

10%

0

20%

Each

a) : C

* : S

** : S

: S

: S

Table 11

Blood biochemical findings of male rats fed the dry beef-contained diet in a 28day dose range-finding test

Conc. in diet	No. of animals	LDH (U/L)	GOT (U/L)	GPT (U/L)	ALP (U/L)	γ -GTP (U/L)	ChE (U/L)	CK (U/L)	T.P. (g/dL)	Alb (%)	α_1 -G (%)	α_2 -G (%)	α_3 -G (%)	β -G (%)	γ -G (%)	A/G
0% ^{a)}	6	323 ± 119	82 ± 8	30 ± 3	666 ± 164	0.56 ± 0.26	50 ± 10	223 ± 34	5.84 ± 0.22	50.7 ± 2.1	22.8 ± 1.6	5.5 ± 0.9	2.9 ± 0.5	14.3 ± 1.0	3.9 ± 0.9	1.03 ± 0.09
5%	6	238 ± 84	75 ± 8	28 ± 2	736 ± 136	0.47 ± 0.12	49 ± 5	220 ± 87	5.88 ± 0.32	52.6 ± 1.6	21.9 ± 0.9	6.0 ± 1.0	2.8 ± 0.5	13.5 ± 1.0	3.2 ± 0.7	1.11 ± 0.07
10%	6	344 ± 98	74 ± 12	32 ± 3	799 ± 164	0.20** ± 0.11	41 ± 7	288 ± 42	5.83 ± 0.19	52.2 ± 6.0	23.2 ± 2.9	5.2 ± 1.3	2.7 ± 0.7	13.4 ± 3.8	3.3 ± 1.4	1.12 ± 0.25
0% ^{b)}	6	403 ± 57	82 ± 6	28 ± 3	710 ± 306	0.41 ± 0.25	51 ± 10	249 ± 43	5.89 ± 0.12	50.3 ± 1.7	24.0 ± 5.5	4.9 ± 1.2	3.4 ± 0.8	12.9 ± 3.0	4.5 ± 0.5	1.01 ± 0.07
20%	6	339 ± 170	96 ± 18	32 ± 5	1086 ± 187	0.55 ± 0.42	41 ± 4	228 ± 69	5.66# ± 0.14	51.5 ± 2.6	21.0 ± 2.1	5.6 ± 1.2	3.7 ± 1.1	13.9 ± 1.4	4.3 ± 1.0	1.07 ± 0.11
Conc. in diet	No. of animals	T-Chol. (mg/dL)	T.G. (mg/dL)	PL (mg/dL)	Glu. (mg/dL)	BUN (mg/dL)	UA (mg/dL)	Crea. (mg/dL)	T-Bil. (mg/dL)	Ca (mg/dL)	P (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)		
0% ^{a)}	6	52 ± 12	55 ± 28	84 ± 18	115 ± 11	12.8 ± 2.0	0.96 ± 0.21	0.49 ± 0.05	0.28 ± 0.02	9.9 ± 0.3	7.6 ± 0.5	144 ± 1	4.22 ± 0.19	105 ± 1		
5%	6	47 ± 14	60 ± 18	85 ± 15	136* ± 15	10.6 ± 2.5	1.07 ± 0.31	0.53 ± 0.07	0.25 ± 0.04	9.9 ± 0.5	8.3 ± 0.7	144 ± 1	4.53 ± 0.39	105 ± 1		
10%	6	42 ± 4	41 ± 17	75 ± 8	126 ± 10	11.3 ± 2.3	1.26 ± 0.15	0.53 ± 0.09	0.27 ± 0.03	9.6 ± 0.1	8.1 ± 0.4	145 ± 1	4.65 ± 0.67	107 ± 1		
0% ^{b)}	6	43 ± 8	34 ± 14	71 ± 12	120 ± 6	11.1 ± 2.1	0.94 ± 0.10	0.47 ± 0.03	0.28 ± 0.03	9.7 ± 0.4	8.2 ± 0.6	146 ± 1	4.59 ± 0.36	106 ± 2		
20%	6	39 ± 6	31 ± 10	75 ± 7	129 ± 15	12.8 ± 1.6	1.37 ± 0.30	0.52 ± 0.07	0.28 ± 0.03	9.4 ± 0.3	7.3 ± 0.6	144 ± 1	4.25 ± 0.65	104 ± 3		

Each value is expressed as mean±S.D.

a): Control I, b): Control II

*: Significantly different from control I at 5% level of probability

**: Significantly different from control I at 1% level of probability

: Significantly different from control II at 5% level of probability

Table 12

Blood biochemical findings of female rats fed the dry beef-contained diet in a 28day dose range-finding test

Conc. in diet	No. of animals	LDH (U/L)	GOT (U/L)	GPT (U/L)	ALP (U/L)	γ -GTP (U/L)	ChE (U/L)	CK (U/L)	T.P. (g/dL)	Alb (%)	α_1 -G (%)	α_2 -G (%)	α_3 -G (%)	β -G (%)	γ -G (%)	A/G
0% ^{a)}	6	378 ± 106	84 ± 5	26 ± 5	415 ± 55	0.49 ± 0.19	257 ± 86	221 ± 73	6.33 ± 0.32	57.4 ± 1.3	18.5 ± 1.9	5.9 ± 0.8	2.7 ± 0.3	12.6 ± 0.7	3.1 ± 0.4	1.35 ± 0.07
5%	6	474 ± 115	78 ± 11	25 ± 2	416 ± 70	0.44 ± 0.25	319 ± 104	205 ± 46	6.34 ± 0.44	56.5 ± 2.2	19.1 ± 1.7	5.9 ± 0.4	2.5 ± 0.6	12.3 ± 0.9	3.7 ± 0.3	1.30 ± 0.12
10%	6	551 ± 134	87 ± 11	24 ± 2	498 ± 153	0.54 ± 0.32	349 ± 79	219 ± 34	6.19 ± 0.25	58.0 ± 2.5	17.8 ± 2.3	4.1* ± 1.3	2.8 ± 1.0	13.1 ± 0.9	4.2** ± 0.6	1.39 ± 0.14
0% ^{b)}	6	609 ± 200	81 ± 6	26 ± 2	413 ± 42	0.44 ± 0.21	253 ± 72	196 ± 32	6.40 ± 0.39	59.7 ± 2.0	18.6 ± 0.6	4.0 ± 0.7	2.1 ± 0.9	12.3 ± 1.0	3.3 ± 1.3	1.49 ± 0.12
20%	6	495 ± 229	78 ± 4	26 ± 2	462 ± 55	0.23# ± 0.08	371# ± 67	228 ± 88	6.37 ± 0.42	56.8 ± 2.9	18.8 ± 1.3	5.8## ± 1.0	2.3 ± 0.7	12.8 ± 0.8	8.6 ± 1.6	1.32 ± 0.15
Conc. in diet	No. of animals	T-Chol. (mg/dL)	T.G. (mg/dL)	PL (mg/dL)	Glu. (mg/dL)	BUN (mg/dL)	UA (mg/dL)	Crea. (mg/dL)	T-Bil. (mg/dL)	Ca (mg/dL)	P (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)		
0% ^{a)}	6	54 ± 12	20 ± 6	99 ± 15	117 ± 12	16.5 ± 2.7	0.89 ± 0.22	0.64 ± 0.09	0.25 ± 0.03	9.7 ± 0.4	6.7 ± 0.9	143 ± 1	4.11 ± 0.32	106 ± 2		
5%	6	51 ± 9	20 ± 12	93 ± 16	122 ± 11	14.7 ± 3.6	1.20 ± 0.29	0.63 ± 0.10	0.27 ± 0.03	9.8 ± 0.2	6.8 ± 1.0	144 ± 1	4.14 ± 0.37	107 ± 1		
10%	6	52 ± 12	13 ± 5	95 ± 16	107 ± 7	15.1 ± 3.0	1.13 ± 0.11	0.68 ± 0.07	0.27 ± 0.03	9.6 ± 0.2	6.6 ± 0.6	145 ± 1	4.28 ± 0.22	110* ± 2		
0% ^{b)}	6	51 ± 8	14 ± 4	91 ± 10	122 ± 15	14.2 ± 2.2	0.92 ± 0.16	0.60 ± 0.05	0.26 ± 0.03	9.8 ± 0.3	6.4 ± 0.7	145 ± 1	4.27 ± 0.27	108 ± 2		
20%	6	45 ± 8	20 ± 13	90 ± 16	127 ± 6	17.8 ± 5.2	1.18 ± 0.29	0.68# ± 0.06	0.27 ± 0.02	9.8 ± 0.3	6.7 ± 0.6	145 ± 2	4.46 ± 0.87	108 ± 2		

Each value is expressed as mean±S.D.

a): Control I, b): Control II

*: Significantly different from control I at 5% level of probability

**: Significantly different from control I at 1% level of probability

: Significantly different from control II at 5% level of probability

: Significantly different from control II at 1% level of probability

Table 13-1 Absolute and relative organ weights of male rats fed dry beef-contained diet in a 28-day dose range-finding study

	Conc. in diet(%)	No. of Animals	B.W. (g)	Brain (g)	Liver (g)	Kidney (g)	Spleen (g)	Heart (g)	Lung (g)	Thymus (g)	Thyr. (mg)	Pitui. (mg)
Absolute	0 ^a	6	314 ±9	1.85 ±0.08	8.94 ±0.43	2.33 ±0.15	0.60 ±0.06	1.11 ±0.03	1.32 ±0.07	0.57 ±0.07	25.5 ±4.2	10.4 ±1.2
	5	6	318 ±30	1.92 ±0.08	8.97 ±1.21	2.56 ±0.11	0.56 ±0.10	1.10 ±0.12	1.28 ±0.04	0.67 ±0.15	19.3 ** ±2.4	10.0 ±1.4
	10	6	288 ±22	1.94 ±0.09	7.57 ±0.60	2.27 ±0.22	0.56 ±0.08	1.00 ±0.10	1.21 ±0.10	0.52 ±0.10	20.5 * ±1.9	10.1 ±1.0
	0 ^b	6	299 ±36	1.94 ±0.08	8.51 ±1.55	2.39 ±0.24	0.56 ±0.13	1.06 ±0.14	1.21 ±0.10	0.49 ±0.09	23.2 ±3.0	10.9 ±1.4
	20	6	257 ±29	1.90 ±0.08	6.32 # ±0.76	2.07 # ±0.12	0.50 ±0.08	0.96 ±0.14	1.13 ±0.06	0.47 ±0.06	21.4 ±2.3	9.6 ±1.0
	Relative ^c	0 ^a	6	314 ±9	0.59 ±0.03	2.84 ±0.12	0.74 ±0.03	0.19 ±0.01	0.35 ±0.01	0.42 ±0.02	0.18 ±0.02	8.2 ±1.5
5		6	318 ±30	0.61 ±0.05	2.82 ±0.20	0.81 ±0.05	0.18 ±0.01	0.35 ±0.02	0.40 ±0.03	0.21 ±0.04	6.1 * ±0.8	3.2 ±0.2
10		6	288 ±22	0.68 ±0.06	2.63 ±0.08	0.79 ±0.06	0.19 ±0.03	0.35 ±0.02	0.42 ±0.03	0.18 ±0.03	7.2 ±0.8	3.5 ±0.3
0 ^b		6	299 ±36	0.65 ±0.06	2.83 ±0.20	0.80 ±0.04	0.19 ±0.02	0.35 ±0.01	0.41 ±0.03	0.16 ±0.02	8.0 ±1.8	3.7 ±0.2
20		6	257 ±29	0.75 # ±0.08	2.47 # ±0.29	0.81 ±0.05	0.19 ±0.02	0.37 ±0.04	0.44 ±0.04	0.18 ±0.02	8.4 ±1.0	3.7 ±0.2

Each value is expressed as mean ± S.D.
a) : Control I ; b) : Control II
c) : Relative organ weight per 100g body weight
* : Significantly different from control I at 5% level of probability
** : Significantly different from control I at 1% level of probability
: Significantly different from control II at 5% level of probability

Table 13-2 Absolute and relative organ weights of male rats fed dry beef-contained diet in a 28-day dose range-finding study

	Conc. in diet(%)	No. of Animals	B.W. (g)	Adrenal (mg)	Testis (g)	Prost. (g)	Semi.v (g)	Epidid. (g)
Absolute	0 ^a	6	314 ±9	53.5 ±5.1	2.65 ±0.15	0.46 ±0.07	1.46 ±0.17	0.72 ±0.05
	5	6	318 ±30	51.0 ±7.2	2.64 ±0.15	0.43 ±0.07	1.33 ±0.17	0.68 ±0.02
	10	6	288 ±22	52.3 ±5.2	2.74 ±0.19	0.42 ±0.05	1.25 ±0.16	0.69 ±0.07
	0 ^b	6	299 ±36	51.2 ±6.5	2.65 ±0.17	0.49 ±0.11	1.40 ±0.25	0.71 ±0.06
	20	6	257 ±29	43.7 # ±4.4	2.58 ±0.17	0.30 ## ±0.04	1.09 # ±0.11	0.63 # ±0.03
	Relative ^c	0 ^a	6	314 ±9	17.0 ±1.3	0.84 ±0.04	0.15 ±0.02	0.46 ±0.04
5		6	318 ±30	16.1 ±2.0	0.84 ±0.09	0.14 ±0.02	0.42 ±0.05	0.22 ±0.02
10		6	288 ±22	18.3 ±2.5	0.95 ±0.08	0.15 ±0.02	0.44 ±0.06	0.24 ±0.01
0 ^b		6	299 ±36	17.2 ±1.5	0.89 ±0.09	0.16 ±0.03	0.47 ±0.06	0.24 ±0.03
20		6	257 ±29	17.1 ±2.0	1.02 ±0.11	0.12 ## ±0.02	0.42 ±0.03	0.25 ±0.03

Each value is expressed as mean ± S.D.
a) : Control I ; b) : Control II
c) : Relative organ weight per 100g body weight
: Significantly different from control II at 5% level of probability
: Significantly different from control II at 1% level of probability

Table 14

Co
d

Absoluta

Relative ^c

Each value is
a) : Control
b) : Relative o
: Significantly

Absolute and relative organ weights of female rats fed dry beef-contaminated diet in a 28-day dose range-finding study

	Conc. in diet (%)	No. of Animals	B.W. (g)	Brain (g)	Liver (g)	Kidney (g)	Spleen (g)	Heart (g)	Lung (g)	Thymus (g)	Thyr. (mg)	Pitui. (mg)	Adrenal (mg)	Ovary (mg)	Uterus (g)
absolute	0 ^a	6	204 ±14	1.78 ±0.08	6.09 ±0.75	1.75 ±0.14	0.43 ±0.08	0.74 ±0.07	0.97 ±0.05	0.49 ±0.11	20.5 ±2.2	13.1 ±2.2	55.8 ±6.3	67.4 ±5.8	0.47 ±0.11
	5	6	208 ±16	1.80 ±0.07	6.16 ±0.88	1.67 ±0.18	0.45 ±0.08	0.77 ±0.10	1.03 ±0.06	0.46 ±0.06	20.5 ±3.5	13.3 ±2.0	52.5 ±9.4	73.8 ±14.9	0.48 ±0.14
	10	6	198 ±15	1.83 ±0.07	5.40 ±0.56	1.65 ±0.19	0.43 ±0.06	0.71 ±0.03	0.98 ±0.05	0.45 ±0.05	20.6 ±1.6	13.2 ±1.3	56.9 ±7.5	76.6 ±13.2	0.46 ±0.11
	0 ^b	6	215 ±17	1.83 ±0.06	6.31 ±0.81	1.74 ±0.20	0.42 ±0.05	0.76 ±0.08	1.00 ±0.09	0.52 ±0.08	21.4 ±2.2	13.5 ±2.7	62.5 ±8.4	73.9 ±7.4	0.54 ±0.19
	20	6	203 ±19	1.81 ±0.03	5.39 ±0.74	1.63 ±0.11	0.43 ±0.14	0.75 ±0.09	0.99 ±0.10	0.49 ±0.10	20.1 ±2.0	12.9 ±1.8	53.8 ±8.6	69.0 ±10.4	0.45 ±0.12
	relative ^c	0 ^a	6	204 ±14	0.88 ±0.07	2.98 ±0.19	0.86 ±0.07	0.21 ±0.03	0.36 ±0.03	0.48 ±0.04	0.24 ±0.05	10.1 ±1.4	6.4 ±0.9	27.4 ±2.2	33.1 ±2.7
5		6	208 ±16	0.87 ±0.04	2.96 ±0.26	0.80 ±0.04	0.22 ±0.03	0.37 ±0.02	0.50 ±0.04	0.22 ±0.04	10.0 ±1.9	6.4 ±0.6	25.2 ±3.3	35.5 ±6.5	0.23 ±0.07
10		6	198 ±15	0.93 ±0.09	2.72 ±0.13	0.83 ±0.05	0.22 ±0.02	0.36 ±0.02	0.50 ±0.02	0.23 ±0.02	10.5 ±1.1	6.7 ±0.5	28.8 ±2.9	38.8 ±6.7	0.23 ±0.05
0 ^b		6	215 ±17	0.86 ±0.04	2.93 ±0.17	0.81 ±0.05	0.20 ±0.03	0.36 ±0.03	0.47 ±0.03	0.25 ±0.04	10.1 ±1.8	6.3 ±0.8	29.1 ±3.2	34.4 ±1.9	0.25 ±0.08
20		6	203 ±19	0.90 ±0.08	2.65 # ±0.18	0.81 ±0.06	0.21 ±0.06	0.37 ±0.02	0.49 ±0.03	0.24 ±0.05	10.0 ±0.8	6.4 ±0.5	26.6 ±4.0	34.0 ±3.1	0.22 ±0.06

Each value is expressed as mean ± S.D.

a): Control I; b): Control II

c): Relative organ weight per 100g body weight

Significantly different from control II at 5% level of probability

Appendix 2 Individual body weights of female rats fed the dry beef-contained diet in a 28day dose range-finding test

Conc. in diet	Animal number	(g)				
		Day 0	7	14	21	28
0% ^{a)}	501	111	143	167	187	203
	502	112	143	172	197	223
	503	121	144	169	197	210
	504	114	155	185	215	242
	505	122	151	187	210	229
	506	116	141	161	183	201
	Mean	116	146	174	198	218
5%	507	104	132	154	181	196
	508	120	151	166	216	235
	509	113	145	168	196	220
	510	113	140	162	188	212
	511	124	176	196	219	245
	512	118	148	178	206	227
	Mean	115	149	171	201	223
10%	513	112	142	165	180	186
	514	109	139	162	179	188
	515	122	150	180	191	214
	516	114	137	177	206	217
	517	116	149	180	200	221
	518	119	154	185	214	231
	Mean	115	145	175	195	210
0% ^{b)}	519	105	134	164	193	210
	520	120	159	194	218	248
	521	111	136	168	189	206
	522	124	160	187	217	240
	523	116	151	182	208	235
	524	118	150	187	219	246
	Mean	116	148	180	207	231
20%	525	113	145	179	208	229
	526	125	150	182	210	224
	527	118	140	166	191	202
	528	109	143	172	198	216
	529	111	131	146	165	187
	530	120	163	196	210	244
	Mean	116	145	174	197	217

a):Control I b):Control II

Appendix 1 Individual body weights of male rats fed the dry beef-contained diet in a 28day dose range-finding test

Conc. in diet	Animal number	(g)				
		Day 0	7	14	21	28
0% ^{a)}	001	117	172	233	285	334
	002	121	176	228	285	328
	003	125	184	249	298	341
	004	122	171	231	287	330
	005	115	170	234	300	352
	006	126	180	241	290	322
	Mean	121	176	236	291	335
5%	007	122	177	228	274	308
	008	113	173	223	275	317
	009	129	196	264	336	385
	010	125	184	242	301	349
	011	122	179	241	309	365
	012	118	179	235	281	314
	Mean	122	181	239	296	340
10%	013	117	166	215	257	285
	014	124	174	221	274	311
	015	111	163	213	259	296
	016	129	182	241	300	336
	017	121	171	232	299	286
	018	122	176	236	292	335
	Mean	121	172	226	280	308
0% ^{b)}	019	116	166	227	285	321
	020	121	182	238	293	330
	021	125	190	258	323	375
	022	116	185	247	254	252
	023	124	178	228	271	306
	024	127	180	239	291	330
	Mean	122	180	240	286	319
20%	025	123	176	225	256	258
	026	121	158	194	221	241
	027	125	166	211	259	295
	028	128	180	242	296	329
	029	116	152	191	225	252
	030	114	152	187	221	249
	Mean	121	164	208	246	271

a):Control I b):Control II

Appendix 4 Individual food consumption of female rats fed the dry beef-contained diet in a 28day dose range-finding test

Conc. in diet	Cage number	(g/day/rat)			
		week 1	2	3	4
0% ^{a)}	16	13	13	15	15
	17	13	14	16	16
	18	14	16	14	13
	Mean	13	14	15	15
5%	19	12	10	16	14
	20	12	15	15	16
	21	16	14	16	14
	Mean	13	13	15	15
10%	22	13	12	11	14
	23	14	15	14	12
	24	14	14	17	14
	Mean	14	14	14	13
0% ^{b)}	25	14	14	15	16
	26	14	14	15	13
	27	13	15	15	16
	Mean	14	14	15	15
20%	28	14	15	14	15
	29	12	14	13	13
	30	13	13	12	13
	Mean	13	14	13	14

a):Control I b):Control II

Appendix 3 Individual food consumption of male rats fed the dry beef-contained diet in a 28day dose range-finding test

Conc. in diet	Cage number	(g/day/rat)			
		week 1	2	3	4
0% ^{a)}	1	17	20	21	21
	2	18	21	22	22
	3	18	22	24	22
	Mean	18	21	22	22
5%	4	16	17	18	18
	5	19	20	24	23
	6	18	21	21	22
	Mean	18	19	21	21
10%	7	17	18	18	17
	8	17	19	20	19
	9	18	20	22	19
	Mean	17	19	20	18
0% ^{b)}	10	16	18	21	17
	11	18	21	20	17
	12	17	17	18	17
	Mean	17	19	20	17
20%	13	17	18	15	9
	14	17	21	21	17
	15	15	15	16	18
	Mean	16	18	17	15

a):Control I b):Control II

Appendix 5 - 1

Individual urinary findings of male rats fed the dry beef-contained diet in a 28day dose range-finding test

Conc. in diet	Animal number	Color	Cloudy	pH	Protein	Glucose	Ketone body	Occult blood	Urobilinogen	Bilirubin
0% ^{a)}	001	PY	-	6.5	●	-	●	-	0.1	-
	002	PY	-	6.0	±	-	-	-	0.1	-
	003	PY	-	6.0	-	-	-	-	0.1	-
	004	PY	-	6.0	-	-	-	-	0.1	-
	005	PY	-	6.0	±	-	±	-	0.1	-
	006	PY	-	6.0	±	-	-	-	0.1	-
5%	007	PY	-	6.0	±	-	-	-	0.1	-
	008	PY	-	6.0	±	-	-	-	0.1	-
	009	PY	-	6.0	±	-	-	-	0.1	-
	010	PY	-	6.0	-	-	-	-	0.1	-
	011	PY	-	6.0	-	-	±	-	0.1	-
	012	PY	-	6.0	-	-	-	-	0.1	-
10%	013	PY	-	6.5	±	-	-	-	0.1	-
	014	PY	-	6.0	±	-	±	-	0.1	-
	015	PY	-	6.0	±	-	-	-	0.1	-
	016	PY	-	6.0	±	-	-	-	0.1	-
	017	PY	-	7.0	+	-	-	+	0.1	-
	018	PY	-	6.0	-	-	-	+	0.1	-

Color : PY (pale yellow)
 Cloudy : - (negligible)
 Protein : - (negligible), ± (15~30mg/dL), + (30mg/dL)
 Glucose : - (negligible)
 Ketone body : - (negligible), ± (5mg/dL)
 Occult blood : - (negligible), ± (trace), + (slight)
 Urobilinogen : Ehrlich unit/dL
 Bilirubin : - (negligible)
 a) : Control I

Appendix

Conc. in diet
0%^{a)}

5%

10%

Color : PY
 Cloudy : -
 Protein : -
 Glucose : -
 Ketone body : -
 Occult blood : -
 Urobilinogen : -
 Bilirubin : -
 a) : Control I

Appendix 5 - 2

Individual urinary findings of male rats fed the dry beef-contained diet in a 28day dose range-finding test

Conc. in diet	Animal number	Color	Cloudy	pH	Protein	Glucose	Ketone body	Occult blood	Urobilinogen	Bilirubin
0% ^{b)}	019	PY	-	6.0	●	-	-	-	0.1	-
	020	PY	-	6.0	±	-	-	-	0.1	-
	021	PY	-	6.0	+	-	-	-	0.1	-
	022	PY	-	6.0	●	-	-	-	0.1	-
	023	PY	-	6.0	-	-	-	-	0.1	-
	024	PY	-	6.0	±	-	-	-	0.1	-
20%	025	PY	-	6.5	-	-	-	±	0.1	-
	026	PY	-	6.0	±	-	-	-	0.1	-
	027	PY	-	6.0	●	-	-	-	0.1	-
	028	PY	-	6.0	-	-	-	-	0.1	-
	029	PY	-	6.0	-	-	-	-	0.1	-
	030	PY	-	6.0	+	-	-	-	0.1	-

b) : Control II

Appendix

Conc. in diet
0%^{b)}

20%

b) : Control II

Appendix 6 - 1

Individual urinary findings of female rats fed the dry beef-contained diet
in a 28day dose range-finding test

Conc. in diet	Animal number	Color	Cloudy	pH	Protein	Glucose	Ketone body	Occult blood	Urobilinogen	Bilirubin
0% ^{a)}	501	PY	-	6.0	±	-	-	-	0.1	-
	502	PY	-	6.0	±	-	-	-	0.1	-
	503	PY	-	6.0	-	-	-	-	0.1	-
	504	PY	-	6.5	±	-	-	-	0.1	-
	505	PY	-	6.0	-	-	-	-	0.1	-
	506	PY	-	6.0	±	-	-	-	0.1	-
5%	507	PY	-	7.0	-	-	-	-	0.1	-
	508	PY	-	6.0	-	-	-	-	0.1	-
	509	PY	-	6.5	-	-	-	-	0.1	-
	510	PY	-	6.5	-	-	-	+	0.1	-
	511	PY	-	6.0	±	-	-	±	0.1	-
	512	PY	-	6.0	-	-	-	±	0.1	-
10%	513	PY	-	7.5	+	-	-	-	0.1	-
	514	PY	-	6.0	-	-	-	-	0.1	-
	515	PY	-	6.0	±	-	-	-	0.1	-
	516	PY	-	7.0	-	-	-	-	0.1	-
	517	PY	-	6.0	±	-	-	-	0.1	-
	518	PY	-	7.0	-	-	-	-	0.1	-

Color : PY(pale yellow)

Cloudy : - (negligible)

Protein : - (negligible), ±(15~30mg/dL), + (30mg/dL)

Glucose : - (negligible)

Ketone body : - (negligible)

Occult blood : - (negligible), ±(trace), + (slight)

Urobilinogen : Ehrlich unit/dL

Bilirubin : - (negligible)

a) : Control I

Appendix 6 - 2

Individual urinary findings of female rats fed the dry beef-contained diet
in a 28day dose range-finding test

Conc. in diet	Animal number	Color	Cloudy	pH	Protein	Glucose	Ketone body	Occult blood	Urobilinogen	Bilirubin
0% ^{b)}	519	PY	-	7.5	±	-	-	-	0.1	-
	520	PY	-	6.0	-	-	-	-	0.1	-
	521	PY	-	6.0	±	-	-	-	0.1	-
	522	PY	-	6.0	-	-	-	-	0.1	-
	523	PY	-	6.5	±	-	-	±	0.1	-
	524	PY	-	6.0	±	-	-	-	0.1	-
20%	525	PY	-	6.5	-	-	-	-	0.1	-
	526	PY	-	6.0	-	-	-	-	0.1	-
	527	PY	-	6.0	-	-	-	-	0.1	-
	528	PY	-	7.5	±	-	-	-	0.1	-
	529	PY	-	6.0	-	-	-	-	0.1	-
	530	PY	-	6.0	±	-	-	-	0.1	-

b) : Control II

Appendix 7-1

Individual hematological findings of male rats fed the dry beef-contained diet in a 28-day dose range-finding test

Conc. in diet	Animal number	RBC (10 ⁶ /μL)	Hb (g/dL)	Ht (%)	MCV (fL)	MCH (pg)	MCHC (%)	PT (sec)	APTT (sec)	WBC (10 ⁶ /μL)
0% ^{a)}	001	711	13.7	39.3	55	19.3	34.9	13.2	21.7	69
	002	777	13.2	38.6	50	17.0	34.2	12.9	17.9	55
	003	749	15.0	42.3	56	20.0	35.5	12.9	20.2	58
	004	739	13.3	39.2	53	18.0	33.9	12.3	18.6	67
	005	721	14.3	42.4	59	19.8	33.7	13.0	17.4	55
	006	722	14.4	42.5	59	19.9	33.9	12.6	20.7	53
	Mean		737	14.0	40.7	55	19.0	34.4	12.8	19.4
5%	007	794	14.8	42.2	53	18.8	35.1	12.9	18.5	85
	008	784	14.3	42.0	54	18.2	34.0	13.6	19.0	32
	009	739	13.8	40.8	55	18.7	33.8	13.8	18.7	57
	010	780	14.5	43.1	55	18.6	33.6	13.5	17.5	46
	011	761	15.4	44.0	58	20.2	35.0	13.2	20.8	88
	012	780	14.5	42.8	55	18.6	33.9	13.0	18.4	64
	Mean		773	14.6	42.5	55	18.8	34.2	13.3	18.8
10%	013	792	15.1	42.3	53	19.1	35.7	13.0	20.8	45
	014	699	14.6	40.1	57	20.9	36.4	14.4	20.2	46
	015	727	14.4	42.1	58	19.8	34.2	13.3	19.9	54
	016	776	14.7	42.8	55	18.9	34.3	12.8	18.3	39
	017	618	11.5	34.3	56	18.6	33.5	14.7	18.4	46
	018	771	14.7	43.6	57	19.1	33.7	13.2	17.1	42
	Mean		731	14.2	40.9	56	19.4	34.6	13.6	19.1
0% ^{b)}	019	794	13.1	39.1	49	18.5	33.5	12.8	16.8	49
	020	758	14.3	41.4	55	18.9	34.5	12.4	16.7	69
	021	696	14.6	42.5	61	21.0	34.4	13.5	18.6	67
	022	820	15.8	46.5	57	19.3	34.0	15.2	23.4	32
	023	707	14.7	43.2	61	20.8	34.0	13.3	22.7	31
	024	762	14.8	44.2	58	19.4	33.5	13.4	20.1	57
	Mean		756	14.6	42.8	57	19.3	34.0	13.4	19.7
20%	025	718	10.0	32.2	46	13.9	31.1	13.9	18.7	32
	026	820	15.4	44.1	54	18.8	34.9	14.1	16.3	25
	027	822	15.5	43.2	53	18.9	35.9	13.4	19.3	47
	028	916	14.6	42.4	46	15.9	34.4	13.4	18.1	51
	029	807	14.7	42.5	53	18.2	34.6	13.6	18.8	31
	030	847	15.4	43.8	52	18.2	35.2	13.4	17.8	43
	Mean		822	14.3	41.4	51	17.3	34.4	13.6	18.2

a): Control I, b): Control II

Appendix 7-2

Individual hematological findings of male rats fed the dry beef-contained diet in the 28-day repeat dose toxicity test

Conc. in diet	Animal number	Differential leukocyte counts (%)							Plat. (10 ⁶ /μL)
		Baso.	Eosin.	Neutro.		Lymph.	Mono.	Other	
				Stab.	Seg.				
0% ^{a)}	001	0	1	0	14	83	2	0	130
	002	1	0	0	10	87	2	0	138
	003	0	0	0	16	83	1	0	128
	004	0	2	0	22	74	2	0	146
	005	0	1	0	16	80	3	0	119
	006	0	0	0	8	92	0	0	130
	Mean		0	1	0	14	83	2	0
5%	007	0	0	0	20	78	2	0	137
	008	0	0	0	10	87	3	0	126
	009	0	1	0	10	88	1	0	96
	010	0	0	0	12	87	1	0	131
	011	0	1	0	19	80	0	0	105
	012	0	1	0	13	86	0	0	116
	Mean		0	1	0	14	84	1	0
10%	013	0	1	0	12	85	1	0	125
	014	0	0	0	8	92	0	0	122
	015	0	1	0	7	90	2	0	127
	016	0	0	0	12	87	1	0	131
	017	0	0	0	19	77	4	0	239
	018	0	4	0	12	83	1	0	113
	Mean		0	1	0	12	86	2	0
0% ^{b)}	019	0	0	0	12	88	0	0	128
	020	0	0	0	11	87	2	0	110
	021	0	1	0	22	76	1	0	97
	022	0	1	0	17	80	2	0	142
	023	0	0	1	18	81	0	0	142
	024	0	0	0	12	87	1	0	124
	Mean		0	0	0	15	83	1	0
20%	025	0	0	0	7	92	1	0	234
	026	0	0	0	11	89	0	0	126
	027	0	2	0	13	84	1	0	104
	028	0	1	0	15	83	1	0	102
	029	0	0	0	15	83	2	0	123
	030	0	1	0	12	87	0	0	114
	Mean		0	1	0	12	86	1	0

a): Control I, b): Control II

Appendix

Conc. in diet
0%^{a)}5%

10%

0%^{b)}

20%

a): Control

Animal Cloning: A Risk Assessment

DRAFT

Conc. in diet(%)	Animal numbers	B.W. (g)	Brain (%)	Liver (%)	Kidney (%)	Spleen (%)	Heart (%)	Lung (%)	Thymus (%)	Thyr. (mg%)	Pitui. (mg%)	Adrenal (mg%)	Ovary (mg%)	Uterus (%)
0 ^a	501	191	0.95	3.02	0.88	0.21	0.35	0.50	0.21	9.2	7.6	25.2	31.6	0.23
	502	205	0.81	3.00	0.88	0.19	0.36	0.49	0.19	10.5	6.8	30.9	37.6	0.21
	503	201	0.90	3.00	0.96	0.23	0.37	0.52	0.32	11.0	6.1	26.0	31.9	0.18
	504	224	0.78	3.29	0.76	0.25	0.32	0.42	0.25	8.1	6.9	25.8	30.2	0.20
	505	215	0.88	2.85	0.85	0.18	0.40	0.42	0.26	9.6	6.2	29.0	32.5	0.21
	506	187	0.94	2.71	0.82	0.19	0.36	0.50	0.21	12.2	4.9	27.4	34.7	0.36
	Mean	204	0.88	2.98	0.86	0.21	0.36	0.48	0.24	10.1	6.4	27.4	33.1	0.23
5	507	186	0.91	2.72	0.75	0.21	0.34	0.53	0.24	9.9	5.8	21.6	41.0	0.19
	508	221	0.82	2.83	0.86	0.21	0.40	0.48	0.16	7.9	6.6	27.9	43.6	0.22
	509	201	0.88	3.27	0.79	0.26	0.39	0.56	0.23	12.1	6.4	28.6	36.5	0.32
	510	197	0.90	2.71	0.84	0.21	0.36	0.48	0.27	10.5	5.7	24.0	28.2	0.14
	511	228	0.82	3.29	0.80	0.24	0.38	0.46	0.21	7.5	6.4	27.6	36.0	0.22
	512	213	0.88	2.93	0.77	0.17	0.35	0.46	0.20	11.8	7.3	21.4	27.9	0.29
	Mean	208	0.87	2.96	0.80	0.22	0.37	0.50	0.22	10.0	6.4	25.2	35.5	0.23
10	513	181	0.98	2.55	0.81	0.25	0.38	0.51	0.22	10.8	6.5	27.7	33.8	0.19
	514	179	1.07	2.80	0.85	0.18	0.38	0.51	0.23	12.0	6.8	30.2	43.4	0.25
	515	201	0.94	2.80	0.82	0.24	0.37	0.51	0.23	10.8	7.4	28.8	50.0	0.28
	516	204	0.86	2.56	0.79	0.21	0.35	0.48	0.24	10.3	6.6	23.6	34.5	0.16
	517	204	0.87	2.81	0.80	0.21	0.33	0.50	0.20	8.8	6.0	32.2	37.9	0.25
	518	219	0.84	2.82	0.92	0.22	0.33	0.47	0.25	10.0	6.6	30.0	33.2	0.26
	Mean	198	0.93	2.72	0.83	0.22	0.36	0.50	0.23	10.5	6.7	28.8	38.8	0.23
0 ^b	519	198	0.89	2.78	0.81	0.21	0.37	0.48	0.29	10.7	5.4	26.5	35.2	0.20
	520	234	0.81	3.09	0.90	0.20	0.32	0.44	0.26	8.8	7.6	28.9	37.1	0.20
	521	190	0.93	2.72	0.80	0.22	0.35	0.45	0.25	13.4	5.7	31.3	34.7	0.19
	522	223	0.83	2.90	0.80	0.22	0.36	0.46	0.26	9.9	5.7	33.9	32.2	0.36
	523	221	0.84	3.14	0.80	0.16	0.40	0.52	0.23	8.9	6.9	28.7	32.2	0.21
	524	224	0.84	2.92	0.75	0.17	0.33	0.44	0.18	8.8	6.3	25.1	34.9	0.33
	Mean	215	0.86	2.93	0.81	0.20	0.36	0.47	0.25	10.1	6.3	29.1	34.4	0.25
20	525	218	0.83	2.87	0.78	0.17	0.41	0.44	0.21	10.4	7.1	25.5	37.8	0.16
	526	209	0.89	2.43	0.72	0.17	0.35	0.47	0.28	10.7	5.6	21.3	29.3	0.18
	527	191	0.93	2.52	0.87	0.18	0.35	0.48	0.23	10.4	6.1	26.0	36.0	0.19
	528	201	0.91	2.83	0.85	0.20	0.36	0.53	0.31	9.1	6.5	33.7	34.9	0.21
	529	172	1.03	2.56	0.85	0.20	0.38	0.51	0.22	10.3	6.5	27.3	31.5	0.31
	530	226	0.79	2.70	0.76	0.32	0.36	0.51	0.19	8.8	6.5	25.8	34.3	0.29
	Mean	203	0.90	2.65	0.81	0.21	0.37	0.49	0.24	10.0	6.4	26.6	34.0	0.22

a): Control I ; b): Control II