

## 最終報告書

6-PTU のラットを用いた母動物、胚・胎児発生への影響  
及び甲状腺ホルモン濃度測定試験

(試験番号：P240540)

メディフォード株式会社

試験責任者：

2025年3月21日

大田 泰史

大田 泰史

メディフォード株式会社 熊本研究所

## 1. 目次

1. 目次 .....	2
2. 試験実施概要 .....	3

### Tables

Table 1	Test Article Intake - Summary .....	4
Table 2	Clinical Sign - Summary .....	5
Table 3	Body Weight - Summary .....	6
Table 4	Food Consumption - Summary .....	7
Table 5	Observation on Cesarean Section - Summary .....	8
Table 6	External Examinations - Summary .....	9
Table 7	Thyroid Weight (Absolute and Relative Weights) .....	10
Table 8	Concentrations of TSH, T3, and T4 in the Thyroid and Brain .....	12

### Appendices

Appendix 1	Test Article Intake .....	15
Appendix 2	Clinical Sign .....	16
Appendix 3	Body Weight .....	17
Appendix 4	Food Consumption .....	18
Appendix 5	Observation on Cesarean Section .....	19
Appendix 6	External Examinations .....	21
Appendix 7	Measurement of Test Article Concentrations in Mixed Diet .....	22

## 2. 試験実施概要

表題	6-PTUのラットを用いた母動物，胚・胎児発生への影響及び甲状腺ホルモン濃度測定試験												
試験番号	P240540												
試験の実施基準	適用ガイドラインなし，適用GLPなし												
試験委託者	国立医薬品食品衛生研究所 〒210-9501 神奈川県川崎市川崎区殿町3-25-26 委託責任者：栗形 麻樹子												
試験施設	メディフォード株式会社 熊本研究所 〒869-0425 熊本県宇土市栗崎町1285 番地 試験責任者：大田 泰史												
試験日程	<table border="0"> <tr> <td>試験開始</td> <td>2025年1月8日</td> </tr> <tr> <td>動物入荷</td> <td>2025年1月9日</td> </tr> <tr> <td>交配開始</td> <td>2025年1月14日</td> </tr> <tr> <td>投与開始</td> <td>2025年1月21日</td> </tr> <tr> <td>試料採取</td> <td>2025年2月4日～2025年2月6日</td> </tr> <tr> <td>試験終了</td> <td>本試験報告書への試験責任者署名日とする</td> </tr> </table>	試験開始	2025年1月8日	動物入荷	2025年1月9日	交配開始	2025年1月14日	投与開始	2025年1月21日	試料採取	2025年2月4日～2025年2月6日	試験終了	本試験報告書への試験責任者署名日とする
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試験終了	本試験報告書への試験責任者署名日とする												
試験資料の保存	試験施設の資料保存施設に試験終了後3年間保存する。												
試験場所	<table border="0"> <tr> <td>・名称</td> <td>メディフォード株式会社 鹿島研究所</td> </tr> <tr> <td>・場所番号：実施項目（作業番号，試験主任者）</td> <td>           1：被験物質混合飼料の調製（B240730，佐々木 淳）            2：血漿中及び脳中TSH濃度測定（B240731，野口 彰彦）            3：血漿及び脳中total T3及びT4濃度測定（B240732 原田 智隆）         </td> </tr> </table>	・名称	メディフォード株式会社 鹿島研究所	・場所番号：実施項目（作業番号，試験主任者）	1：被験物質混合飼料の調製（B240730，佐々木 淳） 2：血漿中及び脳中TSH濃度測定（B240731，野口 彰彦） 3：血漿及び脳中total T3及びT4濃度測定（B240732 原田 智隆）								
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**Table 1 Test Article Intake - Summary**  
Unit: mg/kg/day (mean  $\pm$  S.D.)

<b>Test article</b>	<b>6-PTU</b>	
<b>Dose (ppm)</b>	<b>5</b>	
<b>No. of animals</b>	<b>10</b>	
<b>Treatment</b>		
<b>Gestation period</b>	<b>6</b>	<b>0.344 <math>\pm</math> 0.035</b>
	<b>7</b>	<b>0.346 <math>\pm</math> 0.031</b>
	<b>9</b>	<b>0.317 <math>\pm</math> 0.052</b>
	<b>11</b>	<b>0.342 <math>\pm</math> 0.024</b>
	<b>13</b>	<b>0.316 <math>\pm</math> 0.039</b>
	<b>15</b>	<b>0.305 <math>\pm</math> 0.038</b>
	<b>17</b>	<b>0.319 <math>\pm</math> 0.039</b>
	<b>19</b>	<b>0.296 <math>\pm</math> 0.037</b>
	<b>Mean</b>	<b>0.324 <math>\pm</math> 0.026</b>

Table 2 Clinical Sign - Summary

Test article	Control	6-PTU
Dose (ppm)	0	5
No. of animals	10	10
Pre-treatment		
Gestation period		
No. of animals	10	10
Normal	10	10
Treatment		
Gestation period		
No. of animals	10	10
Normal	10	10

**Table 3 Body Weight - Summary**  
Unit: g (mean  $\pm$  S.D.)

Test article		Control	6-PTU
Dose (ppm)		0	5
No. of animals		10	10
<b>Pre-treatment</b>			
Gestation period	0	258.71 $\pm$ 14.81	255.42 $\pm$ 12.85
<b>Treatment</b>			
Gestation period	6	291.95 $\pm$ 19.49	290.11 $\pm$ 12.32
	7	297.71 $\pm$ 20.22	293.84 $\pm$ 13.70
	8	300.00 $\pm$ 19.74	299.88 $\pm$ 13.24
	10	308.39 $\pm$ 21.76	310.61 $\pm$ 12.67
	12	323.08 $\pm$ 24.06	320.50 $\pm$ 12.26
	14	337.97 $\pm$ 24.37	333.53 $\pm$ 14.33
	16	354.94 $\pm$ 25.71	350.56 $\pm$ 17.26
	18	383.66 $\pm$ 29.49	378.11 $\pm$ 18.82
	20	419.58 $\pm$ 30.34	408.92 $\pm$ 22.87

Not significantly different from the control group

Table 4 Food Consumption - Summary  
Unit: g (mean  $\pm$  S.D.)

Test article		Control	6-PTU
Dose (ppm)		0	5
No. of animals		10	10
<b>Pre-treatment</b>			
Gestation period	0	18.08 $\pm$ 2.11	17.01 $\pm$ 3.08
	5	22.90 $\pm$ 4.35	23.57 $\pm$ 3.75
<b>Treatment</b>			
Gestation period	6	20.93 $\pm$ 2.59	20.15 $\pm$ 2.37
	7	20.34 $\pm$ 3.62	20.77 $\pm$ 2.07
	9	21.53 $\pm$ 2.77	19.58 $\pm$ 3.04
	11	24.04 $\pm$ 4.67	21.88 $\pm$ 1.38
	13	22.66 $\pm$ 1.98	21.11 $\pm$ 2.76
	15	22.82 $\pm$ 2.43	21.44 $\pm$ 3.17
	17	25.32 $\pm$ 3.70	24.01 $\pm$ 3.35
	19	27.30 $\pm$ 3.30	24.22 $\pm$ 3.81

Not significantly different from the control group

Table 5 Observation on Cesarean Section - Summary  
(mean  $\pm$  S.D.)

Test article		Control		6-PTU	
Dose (ppm)		0		5	
No. of animals		10		10	
No. of corpora lutea (A)	Total	155		159	
		15.5 $\pm$ 1.4		15.9 $\pm$ 1.6	
No. of implants (B)	Total	150		158	
		15.0 $\pm$ 2.5		15.8 $\pm$ 1.8	
Pre-implantation loss (A-B)/(A)	Total	5		1	
	(%)	3.8 $\pm$ 9.7		0.7 $\pm$ 2.3	
No. of dead implants					
Early resorptions	Total	9		18	
	(%)	6.1 $\pm$ 3.7		10.3 $\pm$ 22.1	
Late resorptions	Total	0		0	
	(%)	0.0 $\pm$ 0.0		0.0 $\pm$ 0.0	
Dead fetuses	Total	0		0	
	(%)	0.0 $\pm$ 0.0		0.0 $\pm$ 0.0	
Post-implantation loss (C)/(B)	Total	9		18	
	(%)	6.1 $\pm$ 3.7		10.3 $\pm$ 22.1	
No. of live fetuses		14.1 $\pm$ 2.4		14.0 $\pm$ 3.5	
Male		70		60	
Female		71		80	
Total		141		140	
Sex ratio M/(M+F) (%)		50.1 $\pm$ 8.5		45.2 $\pm$ 17.1	
Weight of fetuses (g)					
Male		3.94 $\pm$ 0.17		3.81 $\pm$ 0.17	
Female		3.75 $\pm$ 0.17		3.60 $\pm$ 0.20	

Not significantly different from the control group

**Table 6 External Examinations - Summary**  
(mean  $\pm$  S.D.)

Test article	Control	6-PTU
Dose (ppm)	0	5
No. of animals (F0)	10	10
No. of fetuses examined	141	140
<b>Anomalies</b>		
Frequencies	0	0
(%)	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0
<b>Not significantly different from the control group</b>		

Table 7 Thyroid Weight (Absolute and Relative Weights)

Dose (ppm)	Animal number	Body weight (g)		Thyroid (mg)								
		Male	Female	Male				Female				
				1st	2nd	3rd	Mean	1st	2nd	3rd	Mean	
0	184	3.31	3.30	0.96	0.96	0.92	0.95	1.56	1.61	1.08	1.42	
	185	3.42	3.62	1.25	1.20	1.21	1.22	0.71	0.67	0.67	0.68	
	186	4.00	3.78	1.21	1.13	1.21	1.18	1.09	1.11	1.11	1.10	
	187	4.23	3.81	1.13	1.06	1.12	1.10	0.97	0.90	0.92	0.93	
	188	4.23	3.58	1.06	0.99	1.07	1.04	0.79	0.75	0.76	0.77	
	Mean	3.76	3.61				1.10					0.98
	S.D.	0.15	0.54				0.11					0.29
5	193	3.80	3.46	1.47	1.45	1.51	1.48	0.83	0.67	0.72	0.74	
	194	3.67	3.41	1.21	1.17	1.15	1.18	1.37	1.36	1.34	1.36	
	195	3.87	3.46	1.63	1.61	1.59	1.61	1.65	1.62	1.62	1.63	
	196	3.98	3.87	1.12	1.12	1.14	1.13	1.81	1.84	2.02	1.89	
	197	4.00	3.55	1.30	1.28	1.28	1.29	1.28	1.26	1.20	1.25	
	Mean	4.14	3.51				1.34					1.37
	S.D.	0.38	0.41				0.20					0.43

Table 7 Thyroid Weight (Absolute and Relative Weights) (Continued)

Dose (ppm)	Animal number	Body weight (g)		Thyroid ( $\times 10^{-3}\%$ )								
		Male	Female	Male				Female				
				1st	2nd	3rd	Mean	1st	2nd	3rd	Mean	
0	184	3.31	3.30	29.00	29.00	27.79	28.60	47.27	48.79	32.73	42.93	
	185	3.42	3.62	36.55	35.09	35.38	35.67	19.61	18.51	18.51	18.88	
	186	4.00	3.78	30.25	28.25	30.25	29.58	28.84	29.37	29.37	29.19	
	187	4.23	3.81	26.71	25.06	26.48	26.08	25.46	23.62	24.15	24.41	
	188	4.23	3.58	25.06	23.40	25.30	24.59	22.07	20.95	21.23	21.42	
	Mean	3.76	3.61				28.91					27.36
	S.D.	0.15	0.54				4.27					9.51
5	193	3.80	3.46	38.68	38.16	39.74	38.86	23.99	19.36	20.81	21.39	
	194	3.67	3.41	32.97	31.88	31.34	32.06	40.18	39.88	39.30	39.78	
	195	3.87	3.46	42.12	41.60	41.09	41.60	47.69	46.82	46.82	47.11	
	196	3.98	3.87	28.14	28.14	28.64	28.31	46.77	47.55	52.20	48.84	
	197	4.00	3.55	32.50	32.00	32.00	32.17	36.06	35.49	33.80	35.12	
	Mean	4.14	3.51				34.60					38.45
	S.D.	0.38	0.41				5.46					11.03

Table 8 Concentrations of TSH, T3, and T4 in the Thyroid and Brain

Dose (ppm)	Animal number	Plasma								
		Dams			Male fetuses			Female fetuses		
		TSH (ng/mL)	T3 (pg/mL)	T4 (pg/mL)	TSH (ng/mL)	T3 (pg/mL)	T4 (pg/mL)	TSH (ng/mL)	T3 (pg/mL)	T4 (pg/mL)
0	181	6.49	241.9	7896	6.38	16.69	2866	7.71	15.28	2441
	182	6.80	514.0	16960	5.20	23.75	3028	5.94	21.34	3399
	183	7.53	530.2	16640	5.77	17.26	2721	8.16	15.12	2366
	184	6.06	298.3	9322	7.47	13.83	2594	6.95	11.81	1995
	185	7.58	323.7	10120	6.48	12.67	1871	6.99 a	12.11	1433
	186	7.95	424.3	12720	8.37	19.40	1734	9.85	19.89	2005
	187	5.13	374.5	7995	7.65	18.49	2125	6.17	16.12	1831
	188	6.02	357.5	11270	6.82	16.02	2100	7.03	15.06	1847
	189	6.51	352.5	11120	8.83	12.11	2089	7.89 a	11.75	1731
	190	7.16	373.2	11220	7.31	15.75	2612	7.70	13.35	2184
	Mean	6.72	379.0	11530	7.03	16.60	2374	7.44	15.18	2123
	S.D.	0.86	89.9	3160	1.13	3.45	444	1.11	3.28	539
5	191	8.43	200.5	2269	15.34	6.161	282.2	17.98	7.059	247.3
	192	18.57	436.7	3235	14.73	12.36	464.8	13.83	10.98	418.1
	193	17.70	372.6	2577	16.66	8.850	350.0	18.97	9.302	266.1
	194	15.36	262.8	2757	13.42	9.055	279.7	14.86	8.713	186.1
	195	10.55	336.9	2982	12.37	12.27	367.7	15.04	11.22	364.8
	196	8.09	524.9	5483	13.92	7.419	201.3	<1.00 b	11.50 c	197.1 c
	197	13.24	419.4	3520	12.70 a	13.63	420.1	16.24	15.20	451.1
	198	28.13	237.1	1810	14.95 a	5.818	193.3	12.43	5.802	132.3
	199	14.64	215.0	1679	15.29	6.733	335.8	14.01	6.665	270.7
	200	12.26	496.5	3032	13.31	8.698	435.7	13.55	5.896	305.2
	Mean	14.70	350.2	2934	14.27	9.099	333.1	13.69	9.233	283.9
	S.D.	5.90	118.3	1074	1.35	2.774	93.9	5.22	3.023	102.7

a: Due to insufficient sample volume, the sample was diluted 2-fold and measured.

b: Due to insufficient sample volume, the sample was diluted 10-fold and measured.

c: Although 50 µL of plasma was required, only 20 µL of plasma was collected. As the value calculated from the measured value was shown.

Calculated value (pg/mL) = measured value/20×50

Table 8 Concentrations of TSH, T3, and T4 in the Thyroid and Brain (Continued)

Dose (ppm)	Animal number	Brain					
		Male fetuses			Female fetuses		
		TSH (ng/mL)	T3 (pg/mL)	T4 (pg/mL)	TSH (ng/mL)	T3 (pg/g)	T4 (pg/g)
0	181	11.08	803.1	657.7	9.32	800.5	749.0
	182	6.06	954.5	861.7	7.44	784.4	853.5
	183	8.22	684.9	831.9	6.32	730.3	784.8
	184	5.85	610.3	686.2	6.70	694.0	873.6
	185	6.53	625.6	617.0	6.17	553.5	614.3
	186	8.19	992.9	1132	9.00	601.6	641.4
	187	5.97	541.9	595.2	6.06	624.3	559.5
	188	6.40	675.9	671.1	6.60	835.6	773.5
	189	7.78	625.0	798.5	6.66	658.7	631.7
	190	5.91	599.0	668.0	6.70	781.8	865.8
		Mean	7.20	711.3	751.9	7.10	706.5
	S.D.	1.66	154.6	161.5	1.15	95.1	115.1
5	191	6.91	203.5	85.29	6.28	192.3	72.33
	192	5.93	232.2	86.29	6.12	291.2	92.34
	193	6.33	268.8	62.84	7.35	186.2	62.08
	194	6.07	339.4	112.4	5.41	244.5	111.5
	195	6.31	245.5	63.52	6.22	343.7	155.7
	196	6.63	279.0	77.87	7.35	282.4	102.5
	197	7.07	354.1	105.1	5.91	226.6	66.29
	198	6.44	219.6	<50	6.29	89.09	<50
	199	5.69	142.8	<50	8.29	192.5	72.53
	200	6.73	238.2	99.94	8.08	166.5	57.85
		Mean	6.41	252.3	69.33	6.73	221.5
	S.D.	0.44	62.4	39.97	0.97	72.7	40.68

Table 8 Concentrations of TSH, T3, and T4 in the Thyroid and Brain (Continued)

	Results of significance test (p-value)					
	Plasma TSH	Plasma T3	Plasma T4	Brain TSH	Brain T3	Brain T4
Factor: Dose	0.0000 **	0.0000 **	0.0000 **	0.1186	0.0000 **	0.0000 **
Factor: Sex	0.9256	0.5238	0.1912	0.7656	0.5862	0.9124
Interaction (Dose × Sex)	0.5815	0.4413	0.3766	0.5636	0.6914	0.6792

Significantly different from the control group ; \*\*:p<0.01 (Two-Way ANOVA)

There were no significant differences from the control group in terms of the factor sex and the interaction between dose and sex.

Appendix 1 Test Article Intake  
Unit: mg/kg/day

Test article	Dose (ppm)	Animal number	Animal status (day)	Treatment								
				Gestation period								
				6	7	9	11	13	15	17	19	Mean
6-PTU	5	191		0.35	0.35	0.34	0.35	0.36	0.30	0.30	0.28	0.33
		192		0.33	0.34	0.30	0.35	0.30	0.29	0.29	0.30	0.31
		193		0.42	0.38	0.28	0.32	0.37	0.38	0.38	0.38	0.36
		194		0.33	0.35	0.31	0.34	0.28	0.26	0.29	0.30	0.31
		195		0.32	0.37	0.28	0.33	0.26	0.29	0.29	0.30	0.31
		196		0.33	0.34	0.29	0.34	0.31	0.31	0.34	0.32	0.32
		197		0.38	0.36	0.29	0.32	0.33	0.34	0.34	0.29	0.33
		198		0.35	0.31	0.34	0.37	0.32	0.28	0.31	0.27	0.32
		199		0.29	0.28	0.29	0.31	0.27	0.26	0.27	0.24	0.28
		200		0.34	0.38	0.45	0.39	0.36	0.34	0.38	0.28	0.37

## Appendix 2 Clinical Sign

Test article	Dose (ppm)	Animal number	Animal status(day)	Observations	Severity	Pre-treatment	Treatment
						Gestation	Gestation
Control	0	181	PG	Normal			
		182	PG	Normal			
		183	PG	Normal			
		184	PG	Normal			
		185	PG	Normal			
		186	PG	Normal			
		187	PG	Normal			
		188	PG	Normal			
		189	PG	Normal			
		190	PG	Normal			
6-PTU	5	191	PG	Normal			
		192	PG	Normal			
		193	PG	Normal			
		194	PG	Normal			
		195	PG	Normal			
		196	PG	Normal			
		197	PG	Normal			
		198	PG	Normal			
		199	PG	Normal			
		200	PG	Normal			

PG : Pregnancy

Appendix 3 Body Weight  
Unit: g

Test article	Dose (ppm)	Animal number	Animal status (day)	Gestation period									
				Pre-treatment	Treatment								
				0	6	7	8	10	12	14	16	18	20
Control	0	181		245.6	282.0	289.1	295.1	300.6	315.4	326.1	344.8	371.9	408.7
		182		256.2	282.7	289.0	293.4	294.8	309.4	320.0	327.4	350.9	372.2
		183		279.8	327.7	334.5	341.8	348.5	365.0	378.9	394.6	422.2	455.7
		184		257.9	299.3	298.0	308.0	317.7	327.8	346.8	365.9	397.6	433.7
		185		274.1	312.3	319.1	309.6	330.5	351.5	372.6	392.4	429.8	467.8
		186		257.3	279.6	284.5	288.2	295.6	305.8	320.0	342.2	370.8	402.0
		187		233.3	261.3	264.9	268.0	274.1	283.8	301.0	315.8	341.8	383.2
		188		249.3	279.5	287.3	287.7	298.3	310.6	330.6	346.4	381.8	413.9
		189		277.9	307.0	316.4	313.8	325.4	342.2	350.7	369.3	405.9	440.2
		190		255.7	288.1	294.3	294.4	298.4	319.3	333.0	350.6	363.9	418.4
6-PTU	5	191		242.9	271.0	275.8	279.1	297.0	307.0	321.8	335.7	365.2	383.9
		192		247.9	282.8	287.1	290.8	297.8	319.9	320.1	337.8	364.7	395.7
		193		257.7	302.2	313.4	314.1	327.6	341.3	360.7	384.1	411.5	444.4
		194		261.7	296.7	301.3	307.8	319.5	324.2	343.7	369.8	398.7	427.7
		195		257.1	299.1	302.1	310.2	320.3	329.1	336.5	358.0	381.7	416.1
		196		262.9	297.1	300.6	308.2	316.4	325.7	339.3	346.8	353.0	377.2
		197		231.2	270.6	278.8	286.5	293.8	304.3	322.4	341.8	370.1	404.4
		198		256.1	282.6	275.9	285.9	299.0	304.3	313.6	327.2	362.5	391.9
		199		279.5	302.2	308.6	315.6	324.1	330.3	344.7	359.4	396.8	439.4
		200		257.2	296.8	294.8	300.6	310.6	318.9	332.5	345.0	376.9	408.5

Appendix 4 Food Consumption  
Unit: g

Test article	Dose (ppm)	Animal number	Animal status (day)	Pre-treatment		Treatment							
				Gestation period									
				0	5	6	7	9	11	13	15	17	19
Control	0	181		19.0	20.8	20.6	21.3	21.7	24.9	23.4	21.7	21.2	22.3
		182		18.3	23.2	19.9	21.0	21.3	24.5	21.7	20.7	24.7	28.3
		183		22.6	28.7	25.2	28.8	27.1	33.2	24.5	26.0	25.8	29.9
		184		17.8	21.8	17.3	20.3	19.6	22.2	22.1	21.9	24.4	26.0
		185		19.7	30.1	21.7	18.4	23.1	29.2	24.4	26.5	30.9	34.4
		186		16.0	21.8	21.2	19.7	19.0	20.3	17.7	21.3	28.7	24.7
		187		15.8	14.8	16.8	15.7	17.8	17.3	23.9	21.8	19.5	25.5
		188		15.6	23.2	24.0	16.9	22.3	23.4	22.6	25.7	29.2	27.1
		189		18.5	19.9	21.6	18.7	19.4	19.7	22.7	19.5	26.8	26.1
		190		17.5	24.7	21.0	22.6	24.0	25.7	23.6	23.1	22.0	28.7
6-PTU	5	191		17.3	23.2	19.5	19.7	20.2	21.6	23.3	20.0	21.6	21.8
		192		16.6	20.1	18.9	19.5	17.6	22.7	19.3	19.4	20.8	23.8
		193		21.6	27.4	26.5	23.8	18.1	22.1	26.6	29.1	31.0	34.1
		194		20.1	22.4	19.8	21.8	19.8	22.3	19.5	19.4	23.5	25.6
		195		18.1	23.2	19.2	22.9	18.0	21.5	17.8	20.9	21.8	25.0
		196		19.6	22.2	19.6	20.8	18.2	21.9	21.2	21.6	24.2	23.8
		197		11.7	21.3	21.0	20.7	17.2	19.3	21.0	23.3	24.9	23.6
		198		13.8	22.0	19.2	17.8	20.1	22.3	20.0	18.5	22.6	21.2
		199		14.2	21.2	17.9	17.9	18.9	20.5	18.4	19.0	21.2	20.7
		200		17.1	32.7	19.9	22.8	27.7	24.6	24.0	23.2	28.5	22.6

## Appendix 5 Observation on Cesarean Section

Test article	Dose (ppm)	Animal number	Animal status (day)	No. of corpora lutea (A)	No. of implants (B)	Pre-implantation loss (A-B)/(A)(%)	Post-implantation loss							
							E.R.(C)	(C)/(B)(%)	L.R.(D)	(D)/(B)(%)	D.F.(E)	(E)/(B)(%)	Total(F)	(F)/(B)(%)
Control	0	181		15	15	0.0	1	6.7	0	0.0	0	0.0	1	6.7
		182		13	9	30.8	1	11.1	0	0.0	0	0.0	1	11.1
		183		16	16	0.0	1	6.3	0	0.0	0	0.0	1	6.3
		184		16	16	0.0	0	0.0	0	0.0	0	0.0	0	0.0
		185		17	17	0.0	1	5.9	0	0.0	0	0.0	1	5.9
		186		14	13	7.1	0	0.0	0	0.0	0	0.0	0	0.0
		187		15	15	0.0	1	6.7	0	0.0	0	0.0	1	6.7
		188		16	16	0.0	1	6.3	0	0.0	0	0.0	1	6.3
		189		15	15	0.0	1	6.7	0	0.0	0	0.0	1	6.7
		190		18	18	0.0	2	11.1	0	0.0	0	0.0	2	11.1
6-PTU	5	191		16	16	0.0	1	6.3	0	0.0	0	0.0	1	6.3
		192		14	14	0.0	1	7.1	0	0.0	0	0.0	1	7.1
		193		16	16	0.0	1	6.3	0	0.0	0	0.0	1	6.3
		194		17	17	0.0	0	0.0	0	0.0	0	0.0	0	0.0
		195		14	13	7.1	0	0.0	0	0.0	0	0.0	0	0.0
		196		18	18	0.0	13	72.2	0	0.0	0	0.0	13	72.2
		197		18	18	0.0	2	11.1	0	0.0	0	0.0	2	11.1
		198		15	15	0.0	0	0.0	0	0.0	0	0.0	0	0.0
		199		17	17	0.0	0	0.0	0	0.0	0	0.0	0	0.0
		200		14	14	0.0	0	0.0	0	0.0	0	0.0	0	0.0

E.R.: Early resorbed, L.R.: Late resorbed, D.F.: Dead fetuses, M: Male, F: Female

## Appendix 5 Observation on Cesarean Section (Continued)

Test article	Dose (ppm)	Animal number	Animal status (day)	No. of live fetuses			Sex ratio M/(M+F) (%)	Mean weight of fetuses (g)	
				M	F	M+F		M	F
Control	0	181		6	8	14	42.9	4.16	3.86
		182		5	3	8	62.5	4.19	4.06
		183		7	8	15	46.7	3.73	3.51
		184		8	8	16	50.0	3.76	3.61
		185		9	7	16	56.3	3.91	3.77
		186		5	8	13	38.5	3.90	3.69
		187		7	7	14	50.0	4.15	3.86
		188		7	8	15	46.7	3.96	3.66
		189		9	5	14	64.3	3.79	3.91
		190		7	9	16	43.8	3.87	3.62
6-PTU	5	191		6	9	15	40.0	3.67	3.50
		192		5	8	13	38.5	3.92	3.91
		193		7	8	15	46.7	3.76	3.35
		194		8	9	17	47.1	3.68	3.47
		195		5	8	13	38.5	4.01	3.67
		196		4	1	5	80.0	4.05	3.87
		197		2	14	16	12.5	4.00	3.79
		198		6	9	15	40.0	3.69	3.62
		199		10	7	17	58.8	3.69	3.42
		200		7	7	14	50.0	3.60	3.41

E.R.: Early resorbed, L.R.: Late resorbed, D.F.: Dead fetuses, M: Male, F: Female

## Appendix 6 External Examinations

Test article	Dose (ppm)	Animal number	No. of fetuses examined	External findings		Types	Number	(%)
				No. of fetuses	(%)			
Control	0	181	14	0	0.0			
		182	8	0	0.0			
		183	15	0	0.0			
		184	16	0	0.0			
		185	16	0	0.0			
		186	13	0	0.0			
		187	14	0	0.0			
		188	15	0	0.0			
		189	14	0	0.0			
		190	16	0	0.0			
6-PTU	5	191	15	0	0.0			
		192	13	0	0.0			
		193	15	0	0.0			
		194	17	0	0.0			
		195	13	0	0.0			
		196	5	0	0.0			
		197	16	0	0.0			
		198	15	0	0.0			
		199	17	0	0.0			
		200	14	0	0.0			

## Appendix 7 Measurement of Test Article Concentrations in Mixed Diet

Nominal concentration (ppm)	Measured concentration					
	Layer	1st (ppm)	2nd (ppm)	Mean (ppm)	Overall Mean (ppm)	RSD (%)
500	Upper	472.9	469.5	471.2 [94.2*]	475.8 [95.1*]	0.9
	Middle	480.3	478.1	479.2 [95.8*]		
	Lower	475.6	478.6	477.1 [95.4*]		

\*:Indicates the ratio to nominal concentration (unit:%)