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TABLE 1 Body Weight Changes of Dams Exposed to TBDD on Day 8 of Gestation

	Dose ($\mu\text{g}/\text{kg}$ b.w.)			
	0 (Control)	1	10	100
<Gestation Period>				
No. of dams examined	23	25	23	24
Day of gestation				
8	323 \pm 18	318 \pm 22	324 \pm 22	323 \pm 20
10	331 \pm 19	326 \pm 21	323 \pm 22	311 \pm 22 **
15	362 \pm 21	357 \pm 22	352 \pm 26	310 \pm 32 **
20	447 \pm 28	441 \pm 28	437 \pm 34	371 \pm 30 ** a)
<Lactation Period>				
No. of dams examined	8	8	8	8
Day of lactation				
0	352 \pm 12	346 \pm 17	348 \pm 24	320 \pm 9 **
4	356 \pm 14	361 \pm 10	354 \pm 22	291 \pm 20 **
7	364 \pm 13	367 \pm 6	365 \pm 21	289 \pm 19 **
14	380 \pm 15	389 \pm 14	383 \pm 26	308 \pm 15 **
21	365 \pm 10	371 \pm 23	369 \pm 21	314 \pm 15 **

Data represent mean \pm S.D.

Unit : g

** Significantly different from control, $p \leq 0.01$.

a) n = 22.

TABLE 2 Hematological Examination of Dams Exposed to TBDD on Day 8 of Gestation

	Dose ($\mu\text{g}/\text{kg}$ b.w.)			
	0 (Control)	1	10	100
<Day 20 of Gestation>				
No. of dams examined	10	10	10	10
RBC ($10^6/\mu\text{l}$)	5.91 \pm 0.48	5.95 \pm 0.40	6.02 \pm 0.44	6.74 \pm 0.41 **
Reticulocyte (%)	3.4 \pm 0.5	3.5 \pm 0.5	3.4 \pm 0.4	3.0 \pm 0.8
Hemoglobin (g/dl)	11.0 \pm 0.7	10.9 \pm 0.7	11.0 \pm 0.6	12.0 \pm 0.7 *
Hematocrit (%)	30.9 \pm 2.3	30.4 \pm 1.5	30.6 \pm 1.8	33.0 \pm 2.1 *
MCV (fl)	52.2 \pm 1.3	51.1 \pm 2.0	50.9 \pm 2.2	49.0 \pm 0.6 **
MCH (pg)	18.7 \pm 0.5	18.4 \pm 0.9	18.3 \pm 0.9	17.8 \pm 0.4
MCHC (g/dl)	35.8 \pm 0.6	36.0 \pm 0.7	36.0 \pm 0.6	36.3 \pm 0.5
Platelet ($10^3/\mu\text{l}$)	1228 \pm 110	1265 \pm 179	1374 \pm 171	987 \pm 127 **
WBC ($10^3/\mu\text{l}$)	5.52 \pm 1.13	6.20 \pm 1.20	5.48 \pm 1.46	7.81 \pm 2.72
Neutrophil (%)	40.4 \pm 4.9	40.1 \pm 5.9	38.6 \pm 6.1	40.2 \pm 6.8
Lymphocyte (%)	52.1 \pm 4.7	53.3 \pm 6.5	55.1 \pm 6.2	54.2 \pm 7.0
Monocyte (%)	4.7 \pm 1.1	4.1 \pm 0.8	4.1 \pm 0.5	4.1 \pm 1.3
Eosinophil (%)	2.2 \pm 0.8	2.1 \pm 0.5	1.6 \pm 0.4	1.0 \pm 0.5 **
Basophil (%)	0.1 \pm 0.1	0.0 \pm 0.1	0.0 \pm 0.1	0.1 \pm 0.1
PT (sec)	11.9 \pm 0.4	11.8 \pm 0.3	11.3 \pm 0.2 **	11.3 \pm 0.7 **
APTT (sec)	27.4 \pm 5.7 ^{a)}	23.9 \pm 3.8	23.1 \pm 2.4	21.4 \pm 1.9 ^{***b)}
Fibrinogen (mg/dl)	255.9 \pm 25.6	269.5 \pm 29.6	268.7 \pm 40.7	198.0 \pm 46.0 **
<Day 21 of Lactation>				
No. of dams examined	8	8	8	8
RBC ($10^6/\mu\text{l}$)	7.45 \pm 0.33	7.52 \pm 0.42	7.88 \pm 0.60	7.55 \pm 0.49
Reticulocyte (%)	2.1 \pm 0.7	2.1 \pm 0.2	1.9 \pm 0.6	2.3 \pm 0.7
Hemoglobin (g/dl)	14.3 \pm 0.5	14.5 \pm 0.6	14.8 \pm 0.9	13.5 \pm 0.8
Hematocrit (%)	41.1 \pm 1.5	41.0 \pm 2.0	42.3 \pm 2.7	38.7 \pm 1.9
MCV (fl)	55.2 \pm 1.2	54.6 \pm 3.1	53.7 \pm 2.1	51.3 \pm 1.6 **
MCH (pg)	19.2 \pm 0.4	19.3 \pm 1.1	18.8 \pm 0.9	17.8 \pm 0.4 **
MCHC (g/dl)	34.8 \pm 0.4	35.3 \pm 0.5	34.9 \pm 0.5	34.8 \pm 0.6
Platelet ($10^3/\mu\text{l}$)	1057 \pm 104	1285 \pm 145 *	1108 \pm 187	743 \pm 194 **
WBC ($10^3/\mu\text{l}$)	5.37 \pm 1.93	5.48 \pm 1.55	4.49 \pm 1.23	4.89 \pm 2.32
Neutrophil (%)	36.8 \pm 9.6	37.9 \pm 5.3	30.6 \pm 7.9	13.7 \pm 3.5 **
Lymphocyte (%)	58.0 \pm 10.1	56.7 \pm 5.4	64.2 \pm 7.7	82.6 \pm 4.2 **
Monocyte (%)	2.3 \pm 0.7	2.9 \pm 0.8	2.8 \pm 0.6	2.3 \pm 0.8
Eosinophil (%)	2.7 \pm 1.0	2.1 \pm 0.4	2.0 \pm 0.5	1.0 \pm 0.4 **
Basophil (%)	0.1 \pm 0.1	0.1 \pm 0.1	0.1 \pm 0.1	0.1 \pm 0.0
PT (sec)	12.8 \pm 0.6	12.7 \pm 0.4	12.6 \pm 0.5	12.3 \pm 0.7
APTT (sec)	23.2 \pm 5.7	22.2 \pm 4.7	23.2 \pm 6.9	27.0 \pm 12.9 ^{d)}
Fibrinogen (mg/dl)	177.5 \pm 24.1	201.5 \pm 21.4 *	176.7 \pm 6.8	173.0 \pm 16.3

Data represent mean \pm S.D.

* Significantly different from control, $p \leq 0.05$

** Significantly different from control, $p \leq 0.01$

^{a)} n = 8

^{b)} n = 9

^{c)} n = 7

TABLE 3 Biochemical Examination of Dams Exposed to TBDD on Day 8 of Gestation

	Dose ($\mu\text{g}/\text{kg}$ b.w.)			
	0 (Control)	1	10	100
<Day 20 of Gestation>				
No. of dams examined	10	10	10	10
Total protein (g/dl)	5.4 \pm 0.6	5.3 \pm 0.40	5.6 \pm 0.3	4.7 \pm 0.7 *
Albumin (g/dl)	2.9 \pm 0.4	2.9 \pm 0.3	3.0 \pm 0.3	2.6 \pm 0.5
A/G ratio	1.2 \pm 0.1	1.2 \pm 0.1	1.1 \pm 0.2	1.2 \pm 0.2
T-bilirubin (mg/dl)	0.20 \pm 0.05	0.17 \pm 0.01	0.16 \pm 0.03 *	0.12 \pm 0.01 **
Glucose (mg/dl)	130 \pm 9	133 \pm 7	135 \pm 14	123.0 \pm 10
T-cholesterol (mg/dl)	87 \pm 7	85 \pm 12	107 \pm 11 **	104 \pm 15 **
Phospholipid (mg/dl)	202 \pm 20	186 \pm 29	229 \pm 21 *	186 \pm 25
GOT (IU/l)	42 \pm 5	45 \pm 6	49 \pm 6 **	73 \pm 12 **
GPT (IU/l)	28 \pm 4	26 \pm 4	31 \pm 4	37 \pm 7 **
LDH (IU/l)	268 \pm 66	346 \pm 133	258 \pm 48	394 \pm 91 **
γ -GTP (IU/l)	1 \pm 1	1 \pm 1	1 \pm 1	1 \pm 1
CPK (IU/l)	135 \pm 33	153 \pm 40	133 \pm 15	160 \pm 24
BUN (mg/dl)	18.6 \pm 2.9	16.8 \pm 2.8	16.6 \pm 2.3	17.1 \pm 4.5
Creatinine (mg/l)	0.5 \pm 0.0	0.5 \pm 0.0	0.5 \pm 0.0	0.5 \pm 0.0
Sodium (mEq/l)	138.0 \pm 1.2	138.1 \pm 1.0	137.3 \pm 0.9	138.2 \pm 1.2
Potassium (mEq/l)	3.7 \pm 0.4	3.6 \pm 0.3	3.9 \pm 0.4	4.0 \pm 0.5
Chloride (mEq/l)	100.8 \pm 1.7	101.1 \pm 2.1	100.4 \pm 1.2	101.3 \pm 1.6
Calcium (mEq/l)	9.9 \pm 0.5	9.9 \pm 0.4	10.0 \pm 0.5	9.7 \pm 0.8
Inorganic phosphorus (mg/dl)	4.9 \pm 0.8	4.5 \pm 1.1	5.5 \pm 0.7	7.3 \pm 1.2 **
<Lactation Day 21>				
No. of dams examined	8	8	8	8
Total protein (g/dl)	5.6 \pm 0.2	5.8 \pm 0.2	5.9 \pm 0.5	6.7 \pm 0.4 **
Albumin (g/dl)	3.5 \pm 0.1	3.4 \pm 0.1	3.7 \pm 0.3	4.2 \pm 0.4 **
A/G ratio	1.7 \pm 0.2	1.5 \pm 0.1	1.7 \pm 0.2	1.6 \pm 0.2
T-bilirubin (mg/dl)	0.12 \pm 0.01	0.12 \pm 0.02	0.15 \pm 0.03	0.16 \pm 0.04 *
Glucose (mg/dl)	163 \pm 23	171 \pm 17	163 \pm 15	168 \pm 14
T-cholesterol (mg/dl)	86 \pm 8	92.0 \pm 11	100 \pm 19	120 \pm 18 **
Phospholipid (mg/dl)	174 \pm 15	180 \pm 15	198 \pm 27	209 \pm 31 *
GOT (IU/l)	72 \pm 19	65 \pm 12	70 \pm 12	79 \pm 24
GPT (IU/l)	62 \pm 10	60 \pm 17	55 \pm 17	31 \pm 5 **
LDH (IU/l)	182 \pm 130	128 \pm 84	216 \pm 151	166 \pm 66
γ -GTP (IU/l)	1 \pm 1	1 \pm 1	1 \pm 1	1 \pm 1
CPK (IU/l)	116 \pm 42	106 \pm 39	115 \pm 61	65 \pm 20
BUN (mg/dl)	30.4 \pm 2.7	31.7 \pm 4.5	27.2 \pm 3.5	19.0 \pm 1.8 **
Creatinine (mg/l)	0.5 \pm 2.7	0.6 \pm 0.0	0.5 \pm 0.0	0.6 \pm 0.1
Sodium (mEq/l)	139.8 \pm 0.1	138.9 \pm 1.4	138.5 \pm 1.4	139.9 \pm 0.8
Potassium (mEq/l)	3.6 \pm 1.8	3.6 \pm 0.4	3.8 \pm 0.4	4.1 \pm 0.5
Chloride (mEq/l)	103.1 \pm 0.2	100.5 \pm 1.5 *	101.6 \pm 2.3	103.8 \pm 1.3
Calcium (mEq/l)	9.8 \pm 1.4	10.1 \pm 0.5	10.0 \pm 0.6	10.9 \pm 0.3 **
Inorganic phosphorus (mg/dl)	1.9 \pm 0.363	2.9 \pm 1.3	2.7 \pm 1.5	5.4 \pm 0.8 **

Data represent mean \pm S.D.

* Significantly different from control, $p \leq 0.05$

** Significantly different from control, $p \leq 0.01$

TABLE 4 Thyroid Hormones of Dams Exposed to TBDD on Day 8 of Gestation

	Dose ($\mu\text{g}/\text{kg}$ b.w.)			
	0 (Control)	1	10	100
<Day 20 of Gestation>				
No. of dams examined	15	17	15	14
TSH (ng/ml)	9.9 \pm 1.4	10.1 \pm 1.5	10.8 \pm 2.3	9.2 \pm 1.9
T3 (ng/ml)	2.1 \pm 0.3	2.1 \pm 0.3	2.0 \pm 0.2	1.9 \pm 0.5
T4 (ng/ml)	66.3 \pm 13.0	70.2 \pm 12.1	62.4 \pm 11.5	64.5 \pm 23.6
<Day 21 of Lactation >				
No. of dams examined	8	8	8	8
TSH (ng/ml)	13.8 \pm 1.7	14.7 \pm 1.5	14.4 \pm 3.0	9.3 \pm 1.0 **
T3 (ng/ml)	1.7 \pm 0.2	1.8 \pm 0.2	2.0 \pm 0.3	3.0 \pm 0.4 **
T4 (ng/ml)	89.4 \pm 14.4	86.0 \pm 10.3	96.5 \pm 16.6	92.5 \pm 10.8

Data represent mean \pm S.D.

** Significantly different from control, $p \leq 0.01$

TABLE 5 Organ Weights of Dams Exposed to TBDD on Day 8 of Gestation

		Dose ($\mu\text{g}/\text{kg}$ b.w.)			
		0 (Control)	1	10	100
<Day 20 of Gestation>					
No. of dams examined		11	10	11	10
Body weight	(g)	446 \pm 35	434 \pm 34	432 \pm 32	367 \pm 27 **
Liver	(g)	16.377 \pm 2.089	15.356 \pm 1.554	17.024 \pm 1.104	17.187 \pm 2.590
	(%)	3.663 \pm 0.228	3.538 \pm 0.162	3.944 \pm 0.153	4.711 \pm 0.857
Kidneys	(g)	2.117 \pm 0.192	2.022 \pm 0.172	2.116 \pm 0.156	2.035 \pm 0.110
	(%)	0.475 \pm 0.018	0.467 \pm 0.032	0.491 \pm 0.035	0.558 \pm 0.059
Thymus	(g)	0.423 \pm 0.072	0.399 \pm 0.056	0.336 \pm 0.042 **	0.186 \pm 0.046 **
	(%)	0.095 \pm 0.014	0.092 \pm 0.011	0.078 \pm 0.010 **	0.051 \pm 0.012 **
Spleen	(g)	0.993 \pm 0.124	1.012 \pm 0.158	0.917 \pm 0.082	0.833 \pm 0.105 *
	(%)	0.223 \pm 0.022	0.233 \pm 0.030	0.213 \pm 0.018	0.228 \pm 0.033
Brain	(g)	1.942 \pm 0.130	1.923 \pm 0.089	1.936 \pm 0.059	1.941 \pm 0.067
	(%)	0.438 \pm 0.042	0.445 \pm 0.026	0.450 \pm 0.037	0.532 \pm 0.038 **
Thyroid	(g)	0.034 \pm 0.006	0.035 \pm 0.008	0.030 \pm 0.004	0.032 \pm 0.004
	(%)	0.008 \pm 0.002	0.008 \pm 0.002	0.007 \pm 0.001	0.009 \pm 0.001
Pituitary	(g)	0.019 \pm 0.003	0.017 \pm 0.001	0.017 \pm 0.002	0.018 \pm 0.002
	(%)	0.004 \pm 0.001	0.004 \pm 0.000	0.004 \pm 0.001	0.005 \pm 0.001 **
<Day 21 of Lactation>					
No. of dams examined		8	8	8	8
Body weight	(g)	365 \pm 10	371 \pm 23	369 \pm 21	314 \pm 15 **
Liver	(g)	16.542 \pm 1.220	17.250 \pm 1.261	16.612 \pm 1.706	14.256 \pm 1.238 **
	(%)	4.533 \pm 0.347	4.652 \pm 0.273	4.518 \pm 0.573	4.539 \pm 0.374
Kidneys	(g)	2.537 \pm 0.140	2.515 \pm 0.177	2.504 \pm 0.303	2.110 \pm 0.084 **
	(%)	0.695 \pm 0.028	0.678 \pm 0.036	0.678 \pm 0.063	0.683 \pm 0.043
Thymus	(g)	0.295 \pm 0.057	0.326 \pm 0.050	0.304 \pm 0.064	0.168 \pm 0.043 **
	(%)	0.081 \pm 0.017	0.088 \pm 0.015	0.083 \pm 0.019	0.054 \pm 0.014 **
Spleen	(g)	0.817 \pm 0.095	0.842 \pm 0.108	0.789 \pm 0.109	0.734 \pm 0.066
	(%)	0.224 \pm 0.028	0.228 \pm 0.032	0.214 \pm 0.028	0.234 \pm 0.024
Brain	(g)	1.915 \pm 0.129	1.955 \pm 0.083	1.912 \pm 0.070	1.865 \pm 0.088
	(%)	0.525 \pm 0.042	0.528 \pm 0.040	0.521 \pm 0.048	0.594 \pm 0.028 **
Thyroid	(g)	0.030 \pm 0.004	0.029 \pm 0.007	0.028 \pm 0.004	0.028 \pm 0.007
	(%)	0.008 \pm 0.001	0.008 \pm 0.002	0.008 \pm 0.001	0.009 \pm 0.002
Pituitary	(g)	0.019 \pm 0.003	0.019 \pm 0.003	0.017 \pm 0.002	0.016 \pm 0.002
	(%)	0.005 \pm 0.001	0.005 \pm 0.001	0.005 \pm 0.001	0.005 \pm 0.001

Data represent mean \pm S.D.* Significantly different from control, $p \leq 0.05$ ** Significantly different from control, $p \leq 0.01$

TABLE 6 Histopathological Examination of Liver in Dams Exposed to TBDD on Day 8 of Gestation

	Dose ($\mu\text{g}/\text{kg b w}$)			
	0 (Control)	1	10	100
<Day 20 of Gestation>				
No of dams examined	5	5	5	5
cytoplasmic basophilia tigroid <slight>	0	0	5	0
hepatocellular hypertrophy <slight>	0	0	0	5
vacuolic change liver cell <slight>	0	0	0	5
<Day 21 of Lactation>				
No of dams examined	5	5	5	5
cytoplasmic basophilia tigroid <moderate>	0	0	0	5
hepatocellular hypertrophy <slight>	0	0	0	5
vacuolic change liver cell <slight>	0	0	0	5
multinuclear liver cell <slight>	0	0	0	4
inflammatory cell nest <slight>	0	0	0	3
fibrosis central <slight>	0	0	0	2

TABLE 7 Reproductive Performance and Summary of Development Obtained by Cesarean on Day 20 of Gestation

	Dose ($\mu\text{g}/\text{kg b w}$)			
	0 (Control)	1	10	100
No of dams examined	15	14	12	13
No of corpora lutea	17.6 \pm 1.5	16.4 \pm 1.8	17.7 \pm 1.8	17.8 \pm 1.5
No of implantations	16.3 \pm 2.0	15.7 \pm 2.0	17.1 \pm 2.3	16.6 \pm 1.8
Implantation rate (%)	92.6 \pm 10.2	96.1 \pm 6.4	96.5 \pm 6.0	93.3 \pm 8.4
No of intrauterine death	1.0 \pm 0.7	1.1 \pm 0.9	1.9 \pm 1.2*	10.0 \pm 6.3**
Placental remnants	1.0 \pm 0.7	1.1 \pm 0.9	1.9 \pm 1.2	8.8 \pm 6.5**
Macerated fetuses	0.0 \pm 0.0	0.0 \pm 0.0	0.0 \pm 0.0	1.2 \pm 1.1**
Implantation loss (%)	6.5 \pm 4.9	7.1 \pm 5.0	11.5 \pm 7.4	59.4 \pm 35.9**
No of live fetuses	15.3 \pm 2.3	14.6 \pm 1.7	15.2 \pm 2.7	6.6 \pm 5.9**
Males	7.8 \pm 2.5	6.7 \pm 2.6	7.4 \pm 2.1	2.6 \pm 3.2**
Females	7.5 \pm 2.2	7.9 \pm 1.7	7.8 \pm 2.9	4.0 \pm 3.8*
Sex ratio	0.51 \pm 0.14	0.45 \pm 0.15	0.50 \pm 0.14	0.33 \pm 0.26
Fetal body weights (g)				
Males	4.16 \pm 0.27	4.17 \pm 0.29	4.18 \pm 0.25	3.42 \pm 0.32**
Females	3.96 \pm 0.21	3.95 \pm 0.26	3.99 \pm 0.30	2.90 \pm 0.51**
Placental weights (g)				
Males	0.52 \pm 0.07	0.53 \pm 0.06	0.47 \pm 0.04	0.43 \pm 0.07**
Females	0.50 \pm 0.05	0.50 \pm 0.07	0.45 \pm 0.05	0.41 \pm 0.04**

Data represent mean \pm S D

Implantation rate (%) = (No of implantations / No of corpora lutea) \times 100

Implantation loss (%) = (No of intrauterine death / No of implantations) \times 100

Sex ratio = No of males / No of live fetuses

* Significantly different from control, $p \leq 0.05$

** Significantly different from control, $p \leq 0.01$

TABLE 8 Morphological Observations of Fetuses in Dams Exposed to TBDD on Day 8 of Gestation

	Dose ($\mu\text{g}/\text{kg b w}$)							
	0 (Control)		1		10		100	
<External observation>								
No of fetuses (litters) examined	229	(15)	204	(14)	182	(12)	83	(9)
No of fetuses (litters) with external malformations	0	(0)	0	(0)	1	(1)	23	** (4) **
Anasarca	0	(0)	0	(0)	0	(0)	19	** (2)
Cleft palate	0	(0)	0	(0)	0	(0)	11	** (4) **
Thread like tail	0	(0)	0	(0)	1	(1)	0	(0)
<Visceral observation>								
No of fetuses (litters) examined	112	(15)	98	(14)	88	(12)	43	(9)
No of fetuses (litters) with visceral malformations	0	(0)	0	(0)	0	(0)	11	** (6) **
Hydronephrosis	0	(0)	0	(0)	0	(0)	5	** (3) *
Diaphragmatic hernia	0	(0)	0	(0)	0	(0)	1	(1)
Ventricular septum defect	0	(0)	0	(0)	0	(0)	6	** (4) **
No of fetuses (litters) with visceral variations	13	(6)	16	(9)	34	** (11) **	42	** (9) **
Small spleen	0	(0)	0	(0)	0	(0)	38	** (9) **
Malpositioned thymus	12	(5)	12	(8)	28	** (10) **	22	** (7) *
Dilated renal pelvis	0	(0)	1	(1)	1	(1)	3	** (2)
Left umbilical artery	0	(0)	2	(2)	7	** (4) *	18	** (6) **
Supernumerary right coronary orifice	1	(1)	2	(2)	2	(2)	2	(2)
<Skeletal observation>								
No of fetuses (litters) examined	117	(15)	106	(14)	94	(12)	40	(8)
No of fetuses (litters) with skeletal variations	16	(9)	26	* (12)	14	(7)	17	** (7)
Short supernumerary rib	10	(5)	16	(9)	7	(6)	6	(3)
Cervical rib	4	(3)	3	(2)	5	(2)	2	(1)
Wavy rib	1	(1)	2	(2)	0	(0)	0	(0)
Short rib	0	(0)	1	(1)	0	(0)	0	(0)
Dumbbell thoracic centrum	1	(1)	5	(4)	2	(2)	6	** (6) **
Bipartite thoracic centrum	1	(1)	0	(0)	0	(0)	7	** (4) *
No of fetuses (litters) with delayed ossification	0	(0)	0	(0)	1	(1)	15	** (5) **
Supraoccipital	0	(0)	0	(0)	0	(0)	8	** (4) **
Cervical arch	0	(0)	0	(0)	1	(1)	13	** (4) **
No of ossified sacral caudal vertebrae	8.4 \pm 0.6 ^{a)}		8.3 \pm 0.4		8.2 \pm 0.5		6.5 \pm 1.3 **	

^{a)} Mean \pm S D

* Significantly different from control, $p \leq 0.05$

** Significantly different from control, $p \leq 0.01$

TABLE 9 Summary of Development of Pups from Dams Exposed to TBDD on Day 8 of Gestation

	Dose ($\mu\text{g}/\text{kg b w}$)			
	0 (Control)	1	10	100
No of dams	8	8	8	8
No of dams with live pups	8	8	8	0
Gestation rate (%) ¹⁾	100	100	100	0 **
Gestation length (days)	22.1 \pm 0.4	22.3 \pm 0.5	22.5 \pm 0.5	23.6 \pm 0.5 **
No of implantations	15.8 \pm 1.4	16.9 \pm 1.6	16.5 \pm 5.4	16.4 \pm 2.4
No of pups born	14.1 \pm 2.3	15.5 \pm 1.9	14.6 \pm 4.5	0 **
Delivery index (%) ²⁾	89.6 \pm 11.4	91.9 \pm 6.7	90.2 \pm 8.2	0 **
Birth index (%) ³⁾	85.7 \pm 19.5	91.2 \pm 6.0	77.7 \pm 27.0	0 **
PND 0 No of live pups	13.5 \pm 3.4	15.4 \pm 1.6	12.4 \pm 5.7	
Males	6.5 \pm 2.7	7.5 \pm 1.2	4.4 \pm 2.3	
Females	7.0 \pm 2.8	7.9 \pm 1.5	8.0 \pm 4.4	
Sex ratio ⁴⁾	0.5 \pm 0.2	0.5 \pm 0.1	0.4 \pm 0.2	
Live birth index (%) ⁵⁾	94.8 \pm 14.7	99.3 \pm 1.9	85.8 \pm 27.5	
PND 4 No of live pups	13.0 \pm 4.1	15.3 \pm 1.5	11.6 \pm 5.7	
Males	6.3 \pm 2.9	7.5 \pm 1.2	4.3 \pm 2.3	
Females	6.8 \pm 2.9	7.8 \pm 1.3	7.4 \pm 4.2	
Viability index (%) ⁶⁾	93.9 \pm 15.0	99.3 \pm 2.1	92.0 \pm 4.0	
PND 4 No of pups after culling	7.5 \pm 1.4	8.0 \pm 0.0	6.8 \pm 2.4	
Males	3.6 \pm 0.7	4.0 \pm 0.0	3.3 \pm 0.9	
Females	3.9 \pm 1.4	4.0 \pm 0.0	3.5 \pm 1.7	
PND 21 No of live pups	7.4 \pm 1.4	8.0 \pm 0.0	6.0 \pm 2.8	
Males	3.6 \pm 0.7	4.0 \pm 0.0	2.6 \pm 1.2	
Females	3.8 \pm 1.4	4.0 \pm 0.0	3.4 \pm 1.7	
Viability index (%) ⁶⁾	98.4 \pm 4.4	100.0 \pm 0.0	81.3 \pm 34.1	

Data represent mean \pm S D

* Significantly different from control, $p \leq 0.05$

** Significantly different from control, $p \leq 0.01$

¹⁾ Gestation rate = (No of dams with live pups / No of dams) \times 100

²⁾ Delivery index = (No of pups born / No of implantations) \times 100

³⁾ Birth index = (No of live pups on PND 0 / No of implantations) \times 100

⁴⁾ Sex ratio = No of male live pups on PND 0 / No of live pups on PND 0

⁵⁾ Live birth index = (No of live pups on PND 0 / No of pups born) \times 100

⁶⁾ Viability index = (No of live pups on PND 4 or 21 / No of live pups on PND 0 or PND 4 after culling) \times 100

TABLE 10 Body Weight Changes of Pups from Dams Exposed to TBDD on Day 8 of Gestation

		Dose ($\mu\text{g}/\text{kg b w}$)		
		0 (Control)	1	10
No of litters with pups		8	8	8
Male Pups				
PND	0	6.4 \pm 0.4 (52)	6.5 \pm 0.3 (60)	6.0 \pm 0.3 (35)
	4	10.5 \pm 1.0 (50)	10.6 \pm 1.2 (60)	9.1 \pm 1.4 (34)
	7	16.1 \pm 2.4 (29)	16.3 \pm 2.2 (32)	13.3 \pm 2.4 (26)
	14	33.5 \pm 3.4 (29)	34.5 \pm 4.2 (32)	28.2 \pm 8.2 (23)
	21	57.7 \pm 5.5 (29)	59.1 \pm 5.3 (32)	53.5 \pm 4.8 (21) ^{a)}
Female Pups				
PND	0	6.0 \pm 0.4 (56)	6.3 \pm 0.3 (63)	5.7 \pm 0.5 (64)
	4	9.7 \pm 1.1 (54)	10.2 \pm 1.2 (62)	9.4 \pm 1.3 (59) ^{a)}
	7	14.8 \pm 2.3 (31)	15.7 \pm 2.2 (32)	13.9 \pm 1.4 (28) ^{a)}
	14	30.7 \pm 4.6 (31)	33.8 \pm 3.3 (32)	29.7 \pm 4.2 (28) ^{a)}
	21	51.9 \pm 7.1 (30)	57.4 \pm 4.5 (32)	50.0 \pm 5.1 (27) ^{a)}

Data represent mean \pm S D

Unit g

() No of pups examined

^{a)} The number of litters with pups is 7

TABLE 11 Anogenital Distance (AGD) of PND 4 Pups from Dams Exposed to TBDD on Day 8 of Gestation

	Dose ($\mu\text{g}/\text{kg b w}$)		
	0 (Control)	1	10
Male Pups			
No of dams	8	8	8
No of male pups examined / litter	3 6 \pm 0 7	4 0 \pm 0 0	3 3 \pm 0 9
Body weight of pups / litter	10 8 \pm 1 3	10 8 \pm 1 3	9 2 \pm 1 5
AGD (mm) / litter	4 6 4 \pm 0 4 1	4 9 1 \pm 0 3 4	4 4 1 \pm 0 5 1
Relative AGD / litter	2 1 0 \pm 1 1 4	2 2 3 \pm 0 1 6	2 1 1 \pm 0 1 5
Female Pups			
No of dams	8	8	7
No of female pups examined / litter	3 9 \pm 1 4	4 0 \pm 0 0	3 5 \pm 1 7
Body weight of pups / litter	9 9 \pm 1 2	10 3 \pm 1 2	9 6 \pm 1 2
AGD (mm) / litter	2 5 1 \pm 0 1 8	2 6 9 \pm 0 2 1	2 6 9 \pm 0 1 8
Relative AGD / litter	1 1 7 \pm 0 1 0	1 2 4 \pm 0 0 9	1 2 6 \pm 0 0 6

Data represent mean \pm S D

TABLE 12 Physical Development of Pups from Dams Exposed to TBDD on Day 8 of Gestation

	Dose ($\mu\text{g}/\text{kg b w}$)		
	0 (Control)	1	10
Male Pups			
No of dams	8	8	8
No of male pups examined	29	32	26
Incisor eruption (day)	96 \pm 0.9	94 \pm 0.8	86 \pm 0.3 *
Eye opening (day)	150 \pm 1.0	141 \pm 0.4	137 \pm 1.1 *
Female Pups			
No of dams	8	8	7
No of female pups examined	31	32	28
Incisor eruption (day)	95 \pm 0.9	97 \pm 1.0	88 \pm 0.4
Eye opening (day)	149 \pm 0.9	140 \pm 0.5	137 \pm 0.9 *

Data represent mean \pm S D

* Significantly different from control, $p \leq 0.05$

TABLE 13 Hematological Examination of PND 21 Pups from Dams Exposed to TBDD on Day 8 of Gestation

	Dose ($\mu\text{g}/\text{kg b w}$)		
	0 (Control)	1	10
Male Pups			
No of pups examined	7	8	7
RBC ($10^6/\mu\text{l}$)	4 95 \pm 0 20	4 81 \pm 0 17	4 38 \pm 0 56 *
Reticulocyte (%)	20 1 \pm 1 8	21 2 \pm 2 7	22 2 \pm 2 3
Hemoglobin (g/dl)	9 3 \pm 0 8	9 0 \pm 0 5	8 3 \pm 1 0
Hematocrit (%)	30 5 \pm 2 3	29 5 \pm 1 2	28 3 \pm 3 4
MCV (fl)	61 4 \pm 2 7	61 4 \pm 2 4	64 8 \pm 4 7
MCH (pg)	18 8 \pm 1 2	18 7 \pm 0 8	19 1 \pm 1 9
MCHC (g/dl)	30 5 \pm 0 8	30 4 \pm 0 8	29 4 \pm 0 9
Platelet ($10^3/\mu\text{l}$)	1024 \pm 137	1111 \pm 151	816 \pm 179 *
WBC ($10^3/\mu\text{l}$)	4 01 \pm 0 45	3 36 \pm 1 18	2 43 \pm 1 28 *
Neutrophil (%)	16 3 \pm 2 2	16 0 \pm 2 0	14 1 \pm 1 6
Lymphocyte (%)	79 2 \pm 2 4	79 2 \pm 1 5	81 9 \pm 1 8 *
Monocyte (%)	3 0 \pm 0 8	3 3 \pm 1 4	2 9 \pm 0 6
Eosinophil (%)	1 1 \pm 0 2	1 0 \pm 0 3	0 7 \pm 0 2 *
Basophil (%)	0 1 \pm 0 1	0 1 \pm 0 1	0 1 \pm 0 1
Female Pups			
No of pups examined	6	8	7
RBC ($10^6/\mu\text{l}$)	4 94 \pm 0 21	5 07 \pm 0 31	4 49 \pm 0 50
Reticulocyte (%)	20 6 \pm 2 9	21 7 \pm 2 2	21 4 \pm 3 2
Hemoglobin (g/dl)	9 5 \pm 1 0	9 8 \pm 0 5	8 7 \pm 0 6
Hematocrit (%)	31 0 \pm 2 5	31 7 \pm 1 8	29 3 \pm 1 5
MCV (fl)	62 8 \pm 3 5	62 5 \pm 1 1	65 7 \pm 5 6
MCH (pg)	19 2 \pm 1 5	19 3 \pm 0 3	19 4 \pm 1 7
MCHC (g/dl)	30 5 \pm 0 9	30 9 \pm 0 2	29 6 \pm 0 6 *
Platelet ($10^3/\mu\text{l}$)	1014 \pm 81	1077 \pm 138	906 \pm 266
WBC ($10^3/\mu\text{l}$)	3 93 \pm 0 82	3 65 \pm 0 72	2 67 \pm 0 53 **
Neutrophil (%)	17 0 \pm 3 1	16 2 \pm 1 9	15 4 \pm 3 8
Lymphocyte (%)	78 8 \pm 3 3	79 5 \pm 2 0	80 1 \pm 4 5
Monocyte (%)	2 6 \pm 0 3	2 9 \pm 0 5	3 0 \pm 0 7
Eosinophil (%)	1 2 \pm 0 3	1 0 \pm 0 2	1 0 \pm 0 5
Basophil (%)	0 1 \pm 0 1	0 1 \pm 0 0	0 1 \pm 0 1

Data represent mean \pm S D

* Significantly different from control, $p \leq 0.05$

** Significantly different from control, $p \leq 0.01$

TABLE 14 Biochemical Examination of PND 21 Pups from Dams Exposed to TBDD on Day 8 of Gestation

	Dose ($\mu\text{g}/\text{kg b w}$)		
	0 (Control)	1	10
Male Pups			
No of pups examined	8	8	7
Total protein (g/dl)	46 \pm 0.2	47 \pm 0.1	48 \pm 0.3
Albumin (g/dl)	31 \pm 0.2	32 \pm 0.1	32 \pm 0.2
A/G ratio	2.2 \pm 0.2	2.1 \pm 0.3	2.1 \pm 0.2
T bilirubin (mg/dl)	0.17 \pm 0.02	0.18 \pm 0.02	0.18 \pm 0.03
Glucose (mg/dl)	170 \pm 8	177 \pm 8	166 \pm 7
T cholesterol (mg/dl)	124 \pm 13	111 \pm 15	131 \pm 32
Phospholipid (mg/dl)	225 \pm 21	211 \pm 23	225 \pm 42
GOT (IU/l)	84 \pm 4	88 \pm 7	91 \pm 10
GPT (IU/l)	29 \pm 4	25 \pm 2*	22 \pm 4**
LDH (IU/l)	266 \pm 99	317 \pm 150	425 \pm 124
γ GTP (IU/l)	1 \pm 1	1 \pm 1	1 \pm 0
CPK (IU/l)	278 \pm 52	295 \pm 54	224 \pm 38
BUN (mg/dl)	20.7 \pm 2.3	18.4 \pm 2.4	20.2 \pm 2.9
Creatinine (mg/l)	0.3 \pm 0.1	0.4 \pm 0.1	0.4 \pm 0.0
Sodium (mEq/l)	137.1 \pm 0.8	137.0 \pm 0.9	136.6 \pm 1.3
Potassium (mEq/l)	5.6 \pm 0.4	5.6 \pm 0.3	5.7 \pm 0.3
Chloride (mEq/l)	102.6 \pm 1.1	102.6 \pm 1.3	102.3 \pm 0.8
Calcium (mEq/l)	11.7 \pm 0.2	11.6 \pm 0.2	11.4 \pm 0.4
Inorganic phosphorus (mg/dl)	8.9 \pm 0.4	9.0 \pm 0.5	9.3 \pm 0.5
Female Pups			
No of pups examined	7	8	7
Total protein (g/dl)	46 \pm 0.1	47 \pm 0.2	47 \pm 0.3
Albumin (g/dl)	31 \pm 0.1	32 \pm 0.1	32 \pm 0.2
A/G ratio	2.1 \pm 0.3	2.1 \pm 0.2	2.1 \pm 0.1
T bilirubin (mg/dl)	0.17 \pm 0.01	0.18 \pm 0.03	0.21 \pm 0.10
Glucose (mg/dl)	167 \pm 6	176 \pm 8	166 \pm 8
T cholesterol (mg/dl)	124 \pm 14	117 \pm 12	148 \pm 35
Phospholipid (mg/dl)	224 \pm 22	215 \pm 20	259 \pm 50
GOT (IU/l)	91 \pm 10	86 \pm 9	97 \pm 19
GPT (IU/l)	30 \pm 4	23 \pm 2**	22 \pm 5**
LDH (IU/l)	305 \pm 104	338 \pm 152	470 \pm 248
γ GTP (IU/l)	1 \pm 1	1 \pm 0	1 \pm 0
CPK (IU/l)	280 \pm 40	287 \pm 42	208 \pm 27**
BUN (mg/dl)	22.2 \pm 3.6	18.5 \pm 1.8*	21.5 \pm 2.5
Creatinine (mg/l)	0.3 \pm 0.1	0.3 \pm 0.1	0.3 \pm 0.0
Sodium (mEq/l)	137.3 \pm 0.8	137.1 \pm 0.8	136.7 \pm 1.1
Potassium (mEq/l)	5.5 \pm 0.4	5.5 \pm 0.3	5.5 \pm 0.3
Chloride (mEq/l)	103.1 \pm 1.1	102.5 \pm 1.8	101.9 \pm 1.1
Calcium (mEq/l)	11.4 \pm 0.2	11.5 \pm 0.2	11.8 \pm 0.3
Inorganic phosphorus (mg/dl)	8.8 \pm 0.2	9.0 \pm 0.6	9.4 \pm 0.5

Data represent mean \pm S D* Significantly different from control, $p \leq 0.05$ ** Significantly different from control, $p \leq 0.01$

TABLE 15 Thyroid Hormones of PND 21 Pups from Dams Exposed to TBDD
on Day 8 of Gestation

	Dose ($\mu\text{g}/\text{kg b w}$)		
	0 (Control)	1	10
Male Pups			
No of pups examined	14	16	12
TSH (ng/ml)	77 \pm 17	88 \pm 15	96 \pm 17 *
T3 (ng/ml)	31 \pm 04	29 \pm 03	30 \pm 03
T4 (ng/ml)	1100 \pm 116	1134 \pm 135	854 \pm 60 **
Female Pups			
No of pups examined	15	16	13
TSH (ng/ml)	96 \pm 34	95 \pm 23	107 \pm 24
T3 (ng/ml)	30 \pm 02	28 \pm 02 *	30 \pm 03
T4 (ng/ml)	1183 \pm 159	1150 \pm 103	917 \pm 138 **

Data represent mean \pm S D

* Significantly different from control, $p \leq 0.05$

** Significantly different from control, $p \leq 0.01$

TABLE 16 Organ Weights of PND 21 Pups from Dams Exposed to TBDD on Day 8 of Gestation

	Dose ($\mu\text{g}/\text{kg b w}$)		
	0 (Control)	1	10
<Male Pups>			
No of pups examined	15	16	10
Body weight (g)	56.7 \pm 6.7	58.8 \pm 6.1	53.3 \pm 6.0
Liver (g)	2.169 \pm 0.356	2.448 \pm 0.350	2.611 \pm 0.444 *
(%)	3.808 \pm 0.238	4.152 \pm 0.253 **	4.880 \pm 0.386 **
Kidneys (g)	0.633 \pm 0.084	0.665 \pm 0.076	0.657 \pm 0.115
(%)	1.116 \pm 0.055	1.131 \pm 0.059	1.226 \pm 0.102 **
Thymus (g)	0.205 \pm 0.021	0.230 \pm 0.040	0.173 \pm 0.043
(%)	0.365 \pm 0.044	0.392 \pm 0.058	0.321 \pm 0.055
Spleen (g)	0.332 \pm 0.069	0.372 \pm 0.093	0.363 \pm 0.106
(%)	0.583 \pm 0.083	0.631 \pm 0.147	0.672 \pm 0.134
Brain (g)	1.421 \pm 0.069	1.441 \pm 0.041	1.392 \pm 0.072
(%)	2.535 \pm 0.283	2.478 \pm 0.272	2.638 \pm 0.289
Testes (g)	0.034 \pm 0.006	0.035 \pm 0.008	0.030 \pm 0.004
(%)	0.008 \pm 0.002	0.008 \pm 0.002	0.007 \pm 0.001
Epididymides (g)	0.058 \pm 0.008	0.058 \pm 0.005	0.057 \pm 0.010
(%)	0.102 \pm 0.013	0.100 \pm 0.012	0.107 \pm 0.012
Prostate (ventral) (g)	0.030 \pm 0.005	0.036 \pm 0.009	0.021 \pm 0.009 *
(%)	0.054 \pm 0.008	0.061 \pm 0.013	0.039 \pm 0.015 **
Seminal vesicles (g)	0.017 \pm 0.005	0.018 \pm 0.004	0.014 \pm 0.003
(%)	0.030 \pm 0.009	0.031 \pm 0.008	0.027 \pm 0.007
<Female Pups>			
No of dams examined	13	16	14
Body weight (g)	53.7 \pm 5.2	57.5 \pm 5.0	49.2 \pm 3.8 *
Liver (g)	2.027 \pm 0.265	2.332 \pm 0.313 *	2.355 \pm 0.311 *
(%)	3.768 \pm 0.200	4.042 \pm 0.232 *	4.776 \pm 0.327 **
Kidneys (g)	0.619 \pm 0.060	0.667 \pm 0.066	0.613 \pm 0.051
(%)	1.154 \pm 0.054	1.159 \pm 0.053	1.247 \pm 0.066 **
Thymus (g)	0.208 \pm 0.041	0.246 \pm 0.030	0.169 \pm 0.037
(%)	0.391 \pm 0.083	0.430 \pm 0.053	0.342 \pm 0.055
Spleen (g)	0.315 \pm 0.052	0.336 \pm 0.071	0.287 \pm 0.050
(%)	0.586 \pm 0.069	0.579 \pm 0.082	0.583 \pm 0.088
Brain (g)	1.364 \pm 0.060	1.394 \pm 0.041	1.343 \pm 0.052
(%)	2.564 \pm 0.276	2.438 \pm 0.200	2.743 \pm 0.191
Ovaries (g)	0.027 \pm 0.005	0.028 \pm 0.005	0.025 \pm 0.005
(%)	0.051 \pm 0.008	0.050 \pm 0.008	0.051 \pm 0.010
Uterus (g)	0.043 \pm 0.007	0.048 \pm 0.006	0.045 \pm 0.007
(%)	0.080 \pm 0.009	0.084 \pm 0.012	0.092 \pm 0.015 *

Data represent mean \pm S D* Significantly different from control, $p \leq 0.05$ ** Significantly different from control, $p \leq 0.01$

TABLE 17 Histopathological Examination of Liver in PND 21-Pups from Dams Exposed to TBDD on Day 8 of Gestation

	Dose ($\mu\text{g}/\text{kg b w}$)		
	0 (Control)	1	10
Male pups			
No of pups examined	8	8	7
vacuolic change liver cell <slight>	0	0	7
Female pups			
No of pups examined	7	8	7
vacuolic change liver cell <slight>	0	0	7