Table WEB 1: DBP General Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Animal Number /Sex	Dose*	Body Weight	Organ/Body Weight Ratio	Histopathology	Hematology	Chemistry	Other
Wistar Rats BASF 1992 (*1*)	3-month sub-chronic study. Forty-two day-old rats of both sexes were exposed to DBP in the diet at concentrations of 0, 400, 2,000, or 10,000 ppm and then killed and necropsied. 26 tissues collected, histopathology of control and high dose liver, kidney, and testes examined at all doses. Hematology, clinical chemistry, urinalysis at mid- and end of study. Neurobehavior assessed 3x during study.	10 10 10 10	0 27(M)/ 33(F) 141(M)/ 162(F) 688(M)/ 816(F)	NE NE NE	NE NE ↑Li, Ki(F)	NE NE ↓Lipid in hepatocytes. No testicular effects.	NE NE Transient ↓RBC, Hb, Hct (M).	NE NE ↑Glu, Alb (M). ↓Trigl, T3.	NOAEL ↑ PCoA No neurological effects.

*Dose in mg/kg bw/day.

NA=Not Analyzed
NE=No Effect
↑= Statistically Significant Increase
↓=Statistically Significant Decrease
PCoA=Palmitoyl-CoA Oxidase
M = Male
F = Female
Li = Liver
Ki = Kidney
T3 = Triiodothyronine
Trigl = Triglycerides
Alb = Albumin
RBC = Red Blood Cell
Hb = Hemoglobin
Hct = Hematocrit
Glu = Glucose

Table WEB 2 : DBP General Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Animal Number /Sex	Dose*	Body Weight Gain	Organ/Body Weight Ratio	Histopathology	Hematology	Chemistry	Other
F344/N Rats Marsman 1995 (*2*)	Sub-chronic study (13 weeks), 5–6-week-old rats were fed DBP and then killed and necropsied. Lowest dose was 2,500 ppm, doses then doubled until highest dose of 40,000 ppm achieved. Extensive tissue exam, hematology, clinical chemistry, semen, peroxisome proliferation enzyme evaluation at term.	10	0						
		10	176(M)/ 177(F)	NE	NE	NE	NE	↑Alb (M)	NOAEL
		10	359(M)/ 356(F)	↓(M)	↑Li and Ki (M)	NE	↓Hb (M) ↓RBC (M) ↑Pl (M)	↑Alb (M) ↓Trigl (M) ↑Bile Ac (F)	↑PCoA
		10	720(M)/ 712(F)	↓(M)	↑Li and Ki	Hepatic lesions. Testicular lesions.	↓Hb, Hct (M) ↓RBC (M) ↑MCV ↑Pl (M)	↑Alb (M) ↓Trigl (M) ↑Bile Ac (F) ↑AP (F)	↑PCoA
		10	1,540(M)/ 1,413(F)	↓	↑Li and Ki ↓Te	Hepatic lesions. Testicular lesions, marked hypospermia. ↓ Sperm motility and concentration.	↓Hb, Hct (M) ↓RBC (M) ↑MCV ↑Pl (M)	↑Alb (M) ↓Chol, Trigl ↑Bile Ac ↑AP ↓TP (F)	↑PCoA ↓Testic. Zn ↓Testost.
		10	2,964(M)/ 2,943(F)	↓[a]	↑Li and Ki ↓Te	Hepatic lesions and peroxisomal proliferation. Testicular lesions and hypospermia.	↓Hb, Hct (M) ↓ RBC (M) ↑ MCV (M) ↑Pl (M)	↑Alb(M) ↓TP ↓Chol, Trigl ↑Bile Ac ↑AP	↑PCoA ↓Testic. Zn & serum Zn ↓Testost.

*Dose in mg/kg bw/day.

[a]Food consumption only 58% (M) and 83% (F) of control.

NE= No Effect
↑= Statistically Significant Increase
↓=Statistically Significant Decrease
Hb = Hemoglobin
M= Male
F= Female
Li = Liver
Ki = Kidney
RBC= Red Blood Cell Count
Te =Testes
Tp = Total Protein
Alb = Albumin
Chol = Cholesterol
Trigl = Triglycerides
AP = Alkaline Phosphatase
Bile Ac = Bile Acids
PCoA = Palmitoyl-CoA Oxidase
MCV= Mixed Cell Volume
Zn = Zinc
Pl = Platelets
Testost = Testosterone
HCT= Hematocrit

Table WEB 3: DBP General Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Animal Number /Sex	Dose*	Body Weight Gain	Organ/Body Weight Ratio	Histopathology	Hematology	Chemistry	Other
F344/N Rats Marsman 1995 (2)	Rats were exposed to 0 or 10,000 ppm DBP during prenatal development until 8 weeks of age. At 8 weeks of age, the rats were then fed DBP in the diet for 13 weeks, killed and necropsied.	10 10 10 10 10 10	0** 0 138(M)/ 147(F) 279(M)/ 294(F) 571(M)/ 593(F) 1,262(M)/ 1,182(F) 2,495(M)/ 2,445 (F)	↑[a] ↓F[b], M[ab] ↓[ab] ↓[a,b,c]	↑Te[a] ↑Ki(F)[b], Li(F)[a] ↑Te[a] ↑Ki(F)[b](M)[a] ↑Li (F)[a](M)[a,b] ↑Te[a] ↑Ki(F)[b](M)[a,b] ↑Li [a,b] ↑Te[a] ↑Ki[a,b] ↑Li[a,b] ↓Te[a,b] ↑Ki[a,b] ↑Li[a,b] Te[a,b]	NE NE NE Hepatic and testicular lesions. Hepatic and testicular lesions. ↓Sperm counts and hypospermia of epididymis. Hepatic lesions, peroxisomal proliferation, and testicular lesions. ↓Sperm counts and hypospermia of epididymis.	NE NE NE ↓ Hct ↓Hb ↓RBC(M)[b] ↑Pl(M)[b] NE ↓Hct ↓Hb ↓RBC [a,b] ↑Pl(M)[a,b]	↓Test [a] ↑Alb(F)[a] ↑Alb[a,b] ↓Trigl(M)[a,b] ↑Alb[a,b] ↓ Chol[a,b] ↓Trigl [a,b] ↑ AP [a,b] ↓Tot Prot[a,b] ↑Alb(M)[a,b] ↓ Chol[a,b] ↓Trigl[a,b] ↑ AP[a,b] ↑Bile Ac (F)[b], (M)[a,b] ↓Test [a]	↑PCoA at weaning. ↑PCoA(M) [a,b] No-effect level for liver and testes. ↑PCoA [a,b] ↑Zn in serum(M)[a,b] ↑PCoA [a,b] ↑Zn in serum(M)[b] ↓Testicular Zn[a,b] ↑PCoA [a,b]

*Dose in mg/kg bw/day. ** No prenatal exposure [a]Significant compared to control with no perinatal DBP exposure
[b]Significant compared to control with 10,000 ppm DBP perinatal exposure [c] Significant reduction in food consumption, rats emaciated

NA=Not Analyzed
NE=No Effect
↑= Statistically Significant Increase
↓=Statistically Significant Decrease
M = Male
F = Female
Li= Liver
Ki = Kidney
Te = Testes
Tot Prot = Total Protein
Alb = Albumin
Chol = Cholesterol
Trigl = Triglycerides
AP = Alkaline Phosphatase
Bile Ac = Bile Acids
PCoA = Palmitoyl-CoA Oxidase
Zn = Zinc
Pl = Platelets
Test = Testosterone
Hct = Hematocrit
Hb = Hemoglobin
RBC = Red Blood cells

Table WEB 4: DBP General Toxicity, Mice

Species, Strain, and Source	Experimental Regimen	Animal Number/ Sex	Dose*	Body Weight	Organ/Body Weight Ratio	Histopathology	Hematology	Chemistry
$B6C3F_1$ Mice Marsman 1995 (*2*)	13 week sub-chronic study. 6 week-old mice were exposed to DBP in the diet at levels of 0,1,250, 2,500, 5,000, 10,000, or 20,000 ppm for 13 weeks and then killed and necropsied. Organ weights, histological exam of tissues. Hematology, sperm morphology and vaginal cytology.	10 10	0 163(M)/ 238(F)	NE	↑Ki(F)	NE	NE	NA
		10	353(M)/ 486(F)	NE	↑Ki(F)	NE	NE	NA
		10	812(M)/ 971(F)	↓	↑Li ↑Ki(F)	NE	NE	NA
		10	1,601(M)/ 2,137(F)	↓	↑Li ↑Ki(F)	Liver lesions (M).	NE	NA
		10	3,689(M)/ 4,278(F)	↓	↑Li ↑Ki(F)	Liver lesions. No testicular lesions or other adverse reproductive effects	↓ Hct (F)	NA

*Dose in mg/kg bw/day.

NA=Not Analyzed
NE=No Effect
↑= Statistically Significant Increase
↓=Statistically Significant Decrease
M=Male
F=Female
Li=Liver
Ki=Kidney
Zn=Zinc
Hct=Hematocrit

Table WEB 5: DBP Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Number[a]	Dose*	Maternal Effects	Fetal Effects
ICR-JCL Mice Shiota et al. 1980; Shiota and Mishimura 1982 (*3, 4*)	Prenatal developmental toxicity study. Mice were fed diets with 0, 0.05, 0.1, 0.2, 0.4, or 1% DBP from gd 0–18. Body weights were measured on gd 0–18. Dams were sacrificed on gd 18. Corpora lutea were counted and pups were examined for skeletal and soft tissue malformations.	8	0		
		7	80	NE	LOAEL[b] Delayed ossification.
		8	180	NE	Delayed ossification.
		6	350	NE	Delayed ossification.
		9	660	NOAEL	↓ Fetal weight. Delayed ossification.
		15	2,100	↓ Bodyweight gain.	↑ Resorptions (98.4 vs 5%). ↓ Fetal weight. Delayed ossification. ↑ Neural tube defects (2/3 fetuses).[c]

*Dose in mg/kg bw/day.

[a]Number of pregnant females at sacrifice. [b]Differs from author's selection of effect level. [c]Effect not statistically significant.

↑=Statistically Significant Increase
↓=Statistically Significant Decrease
NE=No effects

Table WEB 6: DBP Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Number[a]	Dose*	Maternal Effects	Fetal Effects
Wistar Rats Ema et al. 1993 (*5*)	Prenatal developmental toxicity study. Rats were gavaged with DBP from gd 7–15. Body weights and food intake were measured daily. Dams were sacrificed on gd 20. Implantation sites were examined. Pups were sexed, weighed, and evaluated for external malformations. Two-thirds of fetuses were examined for skeletal malformations and 1/3 for visceral malformations.	11(11) 11(11) 12(12) 12(12) 11(9)	0 500 630 750 1,000	 NOAEL ↓Weight gain. ↓Adjusted weight gain (38%). ↓Adjusted weight gain (71%).	 NOAEL Complete resorption in 2/12 litters. ↓Live fetuses/litter (43%). ↓ Fetal weight (9–10%). Complete resorption in 10/12 litters. ↓ Live fetuses/litter (93%). ↓ Fetal weight (14–18%). ↑ External malformations (cleft palate) in 6/10 fetuses (2 litters) vs 0/118 fetuses in control. Complete resorption in 9/9 litters.

*Dose in mg/kg bw/day.
[a]Number of pregnant rats (Number of litters evaluated)

↑=Statistically Significant Increase
↓=Statistically Significant Decrease

Table WEB 7: DBP Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Number[a]	Dose*	Maternal Effect	Fetal Effects
Wistar Rats Ema et al. 1998 (*6*)	Prenatal developmental toxicity study. Rats were fed diets with 0, 0.5, 1.0, or 2.0% DBP on gd 11–21. Body weights and food intake were measured. Dams were sacrificed on gd 21. Implantation sites were examined. Pups were sexed, weighed, and evaluated for external malformations. Two-thirds of fetuses were examined for skeletal malformations and 1/3 for visceral malformations.	11 11 11 11	0 331 555 661	NOAEL ↓Corrected weight gain.[b] ↓Food intake. ↓Corrected weight gain.[b] ↓Food intake.	NOAEL. ↓Anogenital distance in males. ↑Undescended testes (15% vs 0 in 7/11 litters). ↓Fetal weight (22%). ↓Anogenital distance in males. ↑Undescended testes (53% vs 0 in 11/11 litters). ↑External (cleft palate; 4% vs 0 in 4/11 litters) and skeletal (fused sternebrae; 55% vs 0 in 11/11 litters) malformations

*Dose in mg/kg bw/day.
[a]Number of pregnant rats and litters evaluated [b]Body weight excluding gravid uterus

↑=Statistically Significant Increase
↓=Statistically Significant Decrease

Table WEB 8: DBP Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Animal Number	Dose*	Maternal Effects	F_1 Offspring Effects
F344/N Rat Marsman et al. 1995 (*2*)	Pre- and post-natal exposure study. DBP administered in feed to dams throughout gestation and lactation. Dams were weighed on gd 0 and 18, and weekly during lactation. Uteri of nulliparous rats in high-dose group were stained with ammonium sulfide. Gestation index[a], litter size, and pup survival were examined. Pups were weighed at birth and pnd 0, 4, and weekly thereafter.	28[b]	0		
		15	92 (1,250 ppm)[d]	NE	NE
		15	184 (2,500 ppm)	NOAEL	↓ Weight days 21–28.
		13	368 (5,000 ppm)	↓ Gestation index(68 vs. 93%).[a] ↓ Gestation length.	↓ Weight days 1–28.
		14	551 (7,500 ppm)	NE	↓ Weight days 0-28.
		16	736 (10,000 ppm)	↓ Weight gain during lactation.	↓ Weight days 0-28. ↓ Percent live pups/litter (89 vs. 96%).
		14	1,472 (20,000 ppm)	↓ Gestation index (21 vs. 93%).[a] ↓ Gestational weight gain.	↓ Pup weight day 0. ↓ Litter size (72%) and % live pups/litter (29 vs 99) Complete pup mortality by pnd 1.
	After weaning on day 28, pups were administered DBP in feed for 4 weeks at the same levels administered to their mothers (1,250, 2,500, 5,000, 7,500, 10,000 ppm). Body weights were measured weekly. Necropsies were conducted and organ weights determined for all groups. Histopathology was evaluated in control and high dose rats. Testis evaluated in dose groups receiving 2,500 ppm and higher.	10[c]	0		
		10	133(F)/143(M)[e]		↑ Kidney (M) & liver to body weight ratio (M). ↑ Weight gain in females.
		10	275(F)/284(M)		↑ Kidney (M) to body weight ratio (M). ↑ Liver to body weight ratio.
		10	500(F)/579(M)		Hypospermia in 4/10 males. ↑ Kidney & liver to body weight ratio .
		10	836(F)/879(M)		Hypospermia in 10/10 males. ↓ Weight gain in males. ↑ Kidney & liver to body weight ratios.
		10	1,104(F)-1165(M)		Hypospermia in 10/10 males. ↓Testis to body weight ratio (11%). ↓ Weight gain in males. ↑ Kidney & liver to body weight ratios .

*Dose in mg/kg bw/day.

[a]Delivery of ≥ 1 live pup per sperm positive female

[b]Number of rats delivering litters

[c]Number of pups/sex

[d]Doses estimated by CERHR, see Section 3 for explanation.

[e]Author calculated doses for females and males, respectively

NE=No effect

↑=Statistically Significant Increase

↓=Statistically Significant Decrease

Table WEB 9: DBP Developmental Toxicity, Mice

Species, Strain, and Source	Experimental Regimen	Animal Number	Dose*	Maternal effects	Offspring effects
$B6C3F_1$ Mouse Marsman et al. 1995 (*2*)	Pre- and post-natal exposure study. DBP administered in feed to dams throughout gestation and lactation. Dams were weighed on gd 0 and 17, and weekly during lactation. Uteri of nulliparous mice in high-dose group were stained with ammonium sulfide. Litter size, and pup survival were examined. Pups were weighed at birth and pd 0, 4, and weekly thereafter.	11[a]	0		
		10	227 (1,250 ppm)[c]	NE	NE
		12	454 (2,500 ppm)	↑ Gestation length (2%).	↓ Litter size.
		9	908 (5,000 ppm)	↑ Gestation length (3%).	NE
		11	1,359 (7,500 ppm)	↓ Gestational weight gain (18%). ↑ Gestation length (5%).	↓ Litter size (28%). ↓ Live pups/litter (48%).
		5	1,816 (10,000 ppm)	↓ Gestational weight gain (34%). ↑ Gestation length (6%).	↓ Litter size (48%). ↓ Live pups/litter (89%). ↓ Pup birth weight (14%).
		0	3,632 (20,000 ppm)	No live deliveries.	
	After weaning, pups were administered DBP in feed for 4 weeks at the same levels administered to their mothers (0, 1,250, 2,500, 5,000, 7,500, 10,000 ppm). Body weights were measured weekly. Necropsies were conducted and organ weights determined for all groups. Histopathology was evaluated in controls and the 1,060–1,286 mg/kg bw/day group.	10[b]	0		
		10	170(F)/199(M)[d]		↑ Liver to body weight ratio (M). ↑ Kidney to body weight ratio (F).
		10	399(F)/437(M)		↓Male body weights (7%). ↑ Liver to body weight ratio in males. ↑ Kidney to body weight ratio in females.
		10	714(F)/750(M)		↓Male body weights (11%). ↑ Liver to body weight ratio in males. ↑ Kidney to body weight ratio in females.
		10	1,060(F) /1,286(M)		↓Male body weights (12%). ↓ Female body weight (11%). ↑ Liver to body weight ratio in males. ↑ Kidney to body weight ratio in females.
		1	3,804(M)		

*Dose in mg/kg bw/day.
[a]Number of mice delivering litters [b]Number of pups/sex [c]Doses estimated by CERHR, see section 3 for explanation.
[d]Author calculated doses for females and males respectively ↑=Statistically Significant Increase
NE=No Effect (M)=Male (F)=Female

Table WEB 10: DBP Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Number[a]	Dose*	Maternal effects	Offspring effects
CD Rat Mylchreest et al. 1998 (*7*)	Pre- and post-natal developmental toxicity study. Rats were gavaged with DBP from gd 3 until the end of lactation. Body weights were measured daily and food intake was measured weekly. Dams were killed and necropsied following weaning of pups. Implantation sites were examined. Pups were sexed, weighed, and evaluated for sexual maturation. Pups were sacrificed on pnd 100–105. All males and up to 3 females/litter were necropsied. Histological exams were conducted on malformed rats and ≤ 2 normal rats/litter. Sperm analysis was conducted at necropsy.	9 8 7 4	0 250 500 750	NE ↓Uterine weight. ↓Uterine weight (non-significant).	↑Hypospadia (1/32 pups), underdeveloped or absent epididymis (3/32 pups; 2 litters) and seminal vesicles (0 pups), and undescended testes (1/32 pups). ↓Anogenital distance in males (pnd 1). ↑Hypospadia (7/34 pups; 4 litters), underdeveloped or absent epididymis (17/34 pups; 6 litters) and seminal vesicles (2/34 pups; 2 litters), and undescended testes (2/34 pups; 2 litters). ↓Testis (24%) and seminal vesicle weight (16%). ↓Live pups/litter (27%). ↓Pup survival during lactation (85 vs 96%). ↓Anogenital distance in males (pnd 1). ↑Hypospadia (6/14 pups; 2 litters), underdeveloped or absent epididymis (10/14 pups; 3 litters) and seminal vesicles (7/14 pups; 3 litters), and undescended testes (4/14 pups; 2 litters). ↓Testis (33%), seminal vesicle (32%), epididymis (34%), and prostate weight (27%) . ↓Kidney weight. No effects on female sexual development or estrous cycles.

*Dose in mg/kg bw/day.

[a]The number of litters evaluated. ↑ Statistically Significant Increase ↓ Statistically Significant Decrease

Table WEB 11: DBP Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Number*	Dose*	Maternal effects	Offspring effects
CD Rat Mylchreest et al. 1999 (*8*)	Pre- and post-natal developmental toxicity study. Rats were gavaged with DBP from gd 12–21. Body weights were measured daily during dosing and weekly at other times. Food intake was measured weekly. Dams were killed and necropsied following weaning of pups. Implantation sites were examined. Pups were sexed, weighed, and evaluated for sexual maturation. Male pups were sacrificed on pnd 100–105 and a histological examination of sex organs was conducted. Females were sacrificed on pnd 25–30 and their reproductive tracts were evaluated for gross abnormalities.	10	0		
		9	100	NE	↑Age of preputial separation (5%).
		10	250	NE	↓Anogenital distance in males (9%). ↑Retained thoracic nipples (35/62 pups; 5 litters). ↑Absent or underdeveloped epididymis (6/62 pups; 4 litters).
		9	500	Large weight loss (16%) and complete litter death in one dam.	↓Anogenital distance in males (24%). ↑ Retained thoracic nipples (47/54 pups; 8 litters). ↑Age of preputial separation (9%). ↑Hypospadias (21/52 pups; 4 litters), absent prostate (3/52 pups; 1 litter), absent or underdeveloped epididymis (26/52 pups; 8 litters) and vas deferens (14/52 pups; 4 litters). ↑Testicular and epididymal lesions. ↑Interstitial adenoma (2/45 in 1 litter versus 0/51 pups in control). ↑Intra-abdominal testes (5/52 pups; 3 litters). ↓Absolute testes (16%), epididymis (26%), and seminal vesical (21%) weight. ↓Absolute kidney weight.
	Results were compared to those induced by the antiandrogenic drug, flutamide.	*5*	*100 flutamide*	*¯Body weight gain.*	*¯Anogenital distance in males.* *- Retained thoracic nipples.* *-Hypospadias, underdeveloped or absent seminal vesicles,* *complete lack of prostate and epididymis, and vas deferens development.* *-Testicular lesions.* *-Suprainguinal testes.* *¯Absolute testes, epididymis, and seminal vesical weight.*

*Dose in mg/kg bw/day.
*Numbers of litters evaluated NE=No Effect ↑=Statistically Significant Increase ↓=Statistically Significant Decrease

Table WEB 12: DBP Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Number[a]	Dose*	Maternal effects	Offspring effects
Sprague-Dawley Rat Mylchreest et al. 2000 (*9*)	Pre- and post-natal developmental toxicity study. Rats were gavaged with DBP in corn oil from gd 12–21. Dams delivered litters and pups were examined and weighed at birth. After the pups were weaned, dams were killed and organ weights and implantation sites were evaluated. Pups were weighed weekly and evaluated for sexual maturation until killed at puberty. Male and female pup organs were weighed and testes and epididymides were examined histologically.	19 20 19 20 20 11	0 0.5 5 50 100 500	No effects observed at any dose level.	NE NE NOAEL ↑Seminiferous tubule degeneration (3% of rats in 2/10 litters). ↑Retained areolas or nipples in males (31% of rats in 16/20 litters). ↑Seminiferous tubule degeneration (56% of rats in 3/5 litters). ↑Retained areolas or nipples in males (90% of rats in 11/11 litters). ↓Anogenital distance in males. ↑Hypospadias (9% of rats in 4/11 litters). ↑Agenesis of epididymis (36% of rats in 9/11 litters), vas deferens (28% of rats in 9/11 litters), and prostate (1/58 rats). ↓Testis, epididymis, prostate, and levator ani muscle weight. ↑Interstitial cell hyperplasia (35% of rats in 3/5 litters) and adenoma (1/23 rats). ↑Intra-abdominal testes (4 rats/3 litters). No effect on vaginal opening or on female reproductive organ weight or histology.

*Dose in mg/kg bw/day.

[a]Number of litters evaluated. ↑=Statistically Significant Increase ↓=Statistically Significant Decrease NE=No Effect

Table WEB 13: DBP Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Number[a]	Dose*	Maternal effects	Offspring effects
Sprague Dawley Rat	Pre- and post-natal developmental toxicity study.	9	0		
	DBP administered in oil by gavage from gd 14 to lactation day 3. Male pups were examined for sexual maturation. At 5 months of age, male offspring were killed and necropsied. Organ weights were measured and a histological examination was conducted on reproductive organs.	8	500	Not reported	↓Anogenital distance (2.79 vs 3.70mm). ↑Percentage of areolas (55 vs 0%) and numbers of areolas/nipples at birth (n=2.7 vs 0) and adulthood (2.2 vs 0). ↑% Hypospadias (6.2 vs 0%) and testicular and epididymal atrophy or agenesis (46 vs 0%). ↓Seminal vesicle, prostate, epididymis, testes, levator ani, and penis weight.
LE Hooded Rats	LE Hooded Rats were gavaged with DBP from gd 16–19.	6	0		
Gray et al. 1999 (*10*)	All other details are as described above for longer exposure in Sprague-Dawley rats.	4	500	Not reported	↓Anogenital distance (2.83 vs 3.21 mm). ↑Percentage of areolas (87 vs 0%) and numbers of areolas/nipples at birth and adulthood (1.9 vs 0). ↓Seminal vesicle, prostate, and levator ani muscle weight.

*Dose in mg/kg bw/day.

[a]Number of pregnant rats. ↑ Statistically Significant Increase ↓ Statistically Significant Decrease

Table WEB 14: DBP Reproductive Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Number[b]	Dose[c] (mg/kg bw/day)	Effects
CD Rats	Fertility assessment through a continuous breeding study.	40	0	
Wine et al. 1997 (*11*)[a]	DBP administered in feed at 1,000, 5,000 or 10,000 ppm. Breeding pairs housed together for 112 days; female body weight was measured on days of littering and both sexes at necropsy; clinical signs, and food intake were recorded; litters were counted, sexed, weighed, and removed following birth. In a crossover breeding study, high-dose F_0 males and females were mated with control animals for 1 week. At the end of the study Necropsy and a histopathological examination were conducted.	20	52(M)/80(F)	↓ Live pups/litter.
		19	256(M)/385(F)	↓ Live pups/litter. ↓ Pup weight.
		20	509(M)/794(F)	↓ Live pups/litter. ↓ Pup weight. ↑ Liver and kidney to body weight ratio. ↓ Pup weight from treated females in crossover.
	Final F_1 litters from continuous breeding study were weaned and mated within dose groups for 1 week. Rats continued to receive the same DBP concentrations as their parents.	20	0	
		20	52(M)/80(F)	↓ F_2 Pup weight.
		20	256(M)/385(F)	↑ Kidney to body weight ratio (M). ↓ F_2 Pup weight. ↑ Degeneration of seminiferous tubules.
		20	509(M)/794(F)	30% mating, 5% pregnancy, 17% fertility indices ↓ Sperm count (49%). ↑ Degeneration of seminiferous tubules, interstitial cell hyperplasia, underdeveloped epididymis, and malformed penises and prepuces. ↓ Prostate and seminal vesicle to body weight ratio. ↓ Testis weight. ↓ Body weight in males and females. ↑ Liver and kidney to body weight ratio in males. ↓ F_2 Pup weight

[a]This study is also addressed in Marsman et al. 1995

[b]Number of male and female pairs

[c]Author-calculated male and female doses, respectively.

↑=Statistically Significant Increase
↓=Statistically Significant Decrease

(F)=Female
(M)=Male

Table WEB 15: DBP Reproductive Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Animal Number	Dose*	Effects
LE Hooded Rats Gray et al. 1999 (*10*)	Multigeneration reproductive study. Male and female rats (F_0) were gavaged with DBP from puberty through adulthood, mating, and lactation. Sexual maturation and estrous cycles were evaluated. Treated rats were mated with untreated controls. Following weaning of F_1 pups, F_0 rats were killed. At necropsy, serum hormone levels, organ weights, testicular histology, and implantation sites were examined.	24[a]	0	
		10	250	↑Age of F_0 preputial separation (42.6 vs 39.5 days). ↑Malformed F_1 pups (14.5 vs 0.7%) and litters with malformed pups (50 vs 5.5%).
		4	500	↑Age of F_0 preputial separation (43.4 vs 39.5 days). ↑Malformed F_1 pups (33 vs 0.7%) and litters with malformed pups (100 vs 5.5%). ↓Fertility in F_0 males and females. ↑Testicular atrophy in F_0 males. ↓Sperm production in F_0 males. ↑Midterm abortions in F_0 females.
		8–12[b] (males only)	1,000	↑Age of F_0 preputial separation (44.4 vs 39.5 days). ↑Testicular atrophy in F_0 males. ↓Sperm production in F_0 males.
	The F_1 rats were not exposed to DBP following weaning. Some F_1 pups from treated dams were mated within dose groups for 11 cycles, and the remainder were necropsied. F_2 pups were counted and discarded.	18[c]	0[d]	
		18	250	↓Fecundity in F_1. ↓Number of F_2 pups born. ↓Caudal sperm levels in F_1 (non-significant; 19%).
		4	500	↓Fecundity in F_1. ↓Number of F_2 pups born. ↓Caudal sperm levels in F_1 (34%).

*Dose in mg/kg bw/day.
[a]Number of litters evaluated [b]Number of males, only males treated with highest dose [c]Number of breeding pairs
[d]Maternal (F_0) exposure levels ↑=Statistically Significant Increase ↓=Statistically Significant Decrease

Table WEB 16: DBP Reproductive Toxicity, Mice

Species, Strain, and Source	Experimental Regimen	Number[b]	Dose[c] (mg/kg bw/day)	Effects
CD-1 Mice Reel et al. 1984; Lamb 1987 (*12, 13*)[a]	Fertility assessment through a continuous breeding study. DBP administered in feed. Breeding pairs housed together for 98 days; body weight was measured on 7 days, clinical signs, and food intake were recorded; litters were counted, sexed, weighed, and removed following birth. In a crossover breeding study, high dose males and females were mated with control mice. Breeding pairs were housed together for 7 days or until a copulatory plug was observed. Necropsy and a histopathological examination were conducted.	39 20 18 20	0 52.5 525 1,750	 NE NOAEL ↓ Number of fertile pairs. ↓ Number of litters delivered/pair. ↓ Litter size. ↓ Live pups. ↑ Percentage of male pups. ↓ Pup weight. ↓ Uterus to body weight ratio in F_0 females. ↓ Body weight in F_0 males. ↑ Liver to body weight ratio in F_0 males and females. No effects on estrous cycles, sperm morphology, or sex organs in F_0 mice.

[a]This study is also addressed in Marsman et al. 1995 [b]Number of male and female pairs [c]Author-calculated doses

NE=No Effect
↑=Statistically Significant Increase
↓=Statistically Significant Decrease

WEB Table 17: MBuP Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Number[a]	Dose*	Maternal effects	Offspring effects
Wistar-King A rats. Imajima et al. 1997 (*14*)	Pre and postnatal developmental toxicity study with prenatal exposure. Rats were gavage dosed with 0 or 300 mg/day MBuP in sesame oil from gd 15-18. Testicular descent was evaluated in male offspring on gd 20 or pnd 30-40.	19 / 15 15 / 26	0 1,000	Not reported.	↑ Testicular ascent on gd 20. ↑ Chryptorchidism in 22/26 male pups on pnd 30–40 with 87% of the undescended testes in abdominal cavity and 13% in the inguinal ring.

*Dose in mg/kg bw/day.
[a]Number of male fetuses evaluated on gd 20 / pnd 30-40.
↑ Statistically significant increase

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