Appendices

Appendix Table 1: Summary of the Atrazine Two Year and One Year Bioassays Using the SD Strain of Rat

Study	Duration	Doses Tested	Female Mammary Fibroadenoma Incidence (doses are in ppm)	Fibroadenoma P Values Adjusted for Survival (Trend is indicated at control)	Female Mammary Carcinoma Incidence (doses are in ppm)	Carcinoma P Values Adjusted for Survival (Trend is indicated at control)
Mayhew, *et al.*, 1986	2 year	0, 10, 70 , 500 or 1000 ppm (0, 0.5, 3.5, 25 or 50 mg/kg/day)	0= 23%; 10= 37%; 70= 30%; 500= 31%; 1000=22 %	0= 0.446; 10=0.110; 70= 0.373 ; 500= 0.373; 1000= 0.468	0= 17%; 10=24 %; 70=39 %; 500= 40%; 1000=51 %	0=0.00 ; 10=0.39; 70= 0.024 ; 500= 0.019; 1000= 0.000
Thakur, 1991a	2- year with serial sacrifices	0, 70 and 400 ppm (0, 4.23 and 26.23 mg/kg/day)	0= 11.6%; 70= 17.9%; 400= 18.8%	0=0.484 ; 70=0.213; 400=0.084[2]	0=13% ; 70=6%; 400=15.9%	0=0.092 ; 70=0.254; 400=0.619[2]
Thakur, 1992a	2- year	0, 70 and 400 ppm (0, 3.79 and 23.01 mg/kg/day)	0= 65%; 70=51 %; 400= 68.3%	0=not meaningful ; 70= 0.914; 400=0.107[2]	0=28% ; 70=22%; 400=33.6%	0= not meaningful; 70=0.832; 400=0.159[2]
Morseth, 1998[1]	2 year	0, 25, 50, 70 and 400 ppm (0, 1.5, 3.1, 4.2, 24.4 mg/kg/day)	0= 21%; 25= 32%; 50=44 % 70=37 %; 400=32%	0=0.23; 25=0.03; 50=0.00; 70=0.014;400=0.014	0= 15% ; 25=22% 50=25% ; 70=18% ; 400= 34%	0=0.002; 25=0.112; 50=0.067; 70=0.395; 400=0.007

Study	Duration	Doses Tested	Female Mammary Fibroadenoma Incidence (doses are in ppm)	Fibroadenoma P Values Adjusted for Survival (Trend is indicated at control)	Female Mammary Carcinoma Incidence (doses are in ppm)	Carcinoma P Values Adjusted for Survival (Trend is indicated at control)
Pettersen, and Turnier, 1995[3]	1 year	0, 15, 30, 50, 70, or 400 ppm (0, 0.8, 1.7, 2.8, 4.1, or 23.9 mg/kg/day)	0= 5.9%; 15= 5.9% 30= 5.9%; 50=0 %; 70= 11.3%; 400= 11.9%	Survival was similar between groups. Thus, a survival adjusted analysis is not meaingful.	0= 2.9%; 15=2.9 % 30=2.9%; 50= 5.9%; 70=2.9%; 400= 17.1%	Survival was similar between groups. Thus, a survival adjusted analysis is not meaingful.

[1]This study employed both ovarectomized and intact animals. However, no ovarectomized animal was found to have a mammary tumor. Thus, results shown are for intact animals only.
[2] Based on Cox-Tarone .
[3] Incidence rates are based on 9 and 12 month timepoints only

Appendix Table 2: The Thakur Study Design

Type of study	Sacrifice	Strain	Sex	Doses	MRID
Serial Sacrifice	at 1, 3, 9, 12, 15, 18 and 24 months	one study with SD one study with F-344	Females only in both strains	0, 10, 70, 200 and 400 ppm for F-344 0, 70 and 400 ppm for SD	42085001 -SD 42146101 - F-344
Terminal Sacrifice	after 24 months	one study with SD one study with F-344	Females only for SD both sexes for F-344	0, 10, 70, 200 and 400 ppm for F-344 0, 70 and 400 ppm for SD	42204401 - SD 42227001 - F-344
Estrous cycle and hormone evaluations	serial sacrifices	one study with SD one study with F-344	Females only	all doses	42743903 - F-344 42743902 - SD

Appendix Table 3: Tumor Incidence by timepoints in Thakur, 1991a. Values shown are the number of rats with that type of mammary tumor. Mammary tumors found in animals which died an unscheduled death are included in the data for the timepoint which immediately followed the animals death.

	Control	4.23 mg/kg/day	26.63 mg/kg/day
1 month	no mammary tumors of any type	no mammary tumors of any type	no mammary tumors of any type
3 month	no mammary tumors of any type	no mammary tumors of any type	no mammary tumors of any type
9 month	no mammary tumors of any type	no mammary tumors of any type	Fibroadenomas= 2 Carcinomas=4
12 month	Fibroadenomas= 1 Carcinomas=0	Fibroadenomas=0 Carcinomas=1	Fibroadenomas= 2 Carcinomas=2
15 month	Fibroadenomas= 2 Carcinomas= 2	Fibroadenomas=5 Carcinomas=0	Fibroadenomas=1 Carcinomas=1
18 month	Fibroadenomas=2 Carcinomas=5	Fibroadenomas=4 Carcinomas=2	Fibroadenomas=4 Carcinomas=4
24 month	Fibroadenomas=3 Carcinomas=2	Fibroadenomas=3 Carcinomas=1	Fibroadenomas=4 Carcinomas=0
0-12 month total	Fibroadenomas= 1 Carcinomas= 0	Fibroadenomas= 0 Carcinomas= 1	Fibroadenomas= 4 Carcinomas= 6
0-24 month total	Fibroadenomas= 8 Carcinomas= 9	Fibroadenomas= 12 Carcinomas= 4	Fibroadenomas= 13 Carcinomas= 11

Appendix Table 4: All 20 Guideline studies with Atrazine, Propazine, Simazine or Atrazine mammalian metabolites that have been submitted and found acceptable by HED

Chemical	Study Type	Endpoint	Cell type/Species	Results	MRID
Atrazine	Ames Test	Gene Mutation	TA 98, 100, 1535, 1537 and 1538	Negative when tested with and w/o activation up to the limit dose of 5000 µg/plate	0060642
Atrazine	Ames Test	Gene Mutation	TA 98, 100, 1535 and 1537	Negative when tested with and w/o activation up to the limit dose of 5000 µg/plate	40246601
Atrazine	Unscheduled DNA Synthesis	DNA Damage	Isolated rat hepatocytes strain- Tif:RAIf	Negative when tested up to the solubilty limit	00161790/ 40246602
Atrazine	Unscheduled DNA Synthesis	DNA Damage	Isolated rat hepatocytes strain- Tif:RAIf	Negative when tested up to the solubilty limit	42547105
Atrazine	Micronucleus Assay	Clastogenicity (Chromosomal aberrations)	Mouse Strain-Tif:MAGf	Negative up to a dose causing death in the mouse	40722301
Atrazine	Dominant Lethal Assay	Genotoxicity to germinal tissue (effects which cause embry. or fetal death)	Mouse Strain-Tif:MAGf	Negative when tested in doses which induced toxicity	42637003

Appendix Table 4 cont.

Chemical	Study Type	Endpoint	Cell type/Species	Results	MRID
Simazine	Ames Test	Gene Mutation	TA 98, 100, 1535, 1537, and 1538	Negative both with and w/o activation when tested up to the solubility limit	40614406
Simazine	Unscheduled DNA Synthesis	DNA Damage	Isolated rat hepatocytes strain- Tif:RAIf	Negative when tested up to the solubilty limit	4144902
Simazine	Micronucleus Assay	Clastogenicity (Chromosomal aberrations)	Mouse strain-Tif:MAGf	Negative up to the limit dose of 5000 mg/kg	41442901
Propazine	In vitro mammalian cell gene mutation assay	Gene Mutation	V79 cell line - Chinese Hamster, fibroblast - like	Positive dose-related response (5-23x background) w/o activation at 800 and 1000 µg/ml Weak (5x background and non-dose related) mutagenic response with activation at 2000 µg/ml	0016322
Propazine	Unscheduled DNA Synthesis	DNA Damage	Isolated rat hepatocytes strain- Tif:RAIf	Negative when tested up to the solubilty limit	00150623
Propazine	Micronucleus Assay	Clastogenicity (Chromosomal aberrations)	Female Chinese Hamsters	Negative up to the limit dose of 5000 mg/kg	00150622
DACT	Ames Test	Gene Mutation	TA 98, 100, 1535, and 1537	Negative with and w/o activation up to the limit dose of 5000 µg/plate	40722302
DACT	Unscheduled DNA Synthesis	DNA Damage	CRL 1521 cell line - human fibroblast - like	Negative without activation only when tested up to solubilty limits	40722303
G-28279	Ames Test	Gene Mutation	TA 98, 100, 1535, and 1537	Negative when tested with and w/o activation up to the limit dose of 5000 µg/plate	43049101
G-28279	Unscheduled DNA Synthesis	DNA Damage	Isolated rat hepatocytes strain- Tif:RAIf	Negative up the cytotoxic dose of 800 µg/ml	43049105

Appendix Table 4 cont.

Chemical	Study Type	Endpoint	Cell type/Species	Results	MRID
G-28279	Micronucleus Assay	Clastogenicity (Chromosomal aberrations)	Mouse strain-Tif:MAGf	Negative up to the maximum tolerated dose of 480 mg/kg	43093103
G-30033	Ames Test	Gene Mutation	TA 98, 100, 1535, and 1537	Negative when tested with and w/o activation up to the limit dose of 5000 µg/plate	43093102
G-30033	Unscheduled DNA Synthesis	DNA Damage	Isolated rat hepatocytes strain- Tif:RAIf	Negative in doses up to the cytotoxic dose of 1000 µg/ml	43093106
G-30033	Micronucleus Assay	Clastogenicity (Chromosomal aberrations)	Mouse strain-Tif:MAGf	Negative up to the maximum tolerated dose of 480 mg/kg	43903104

Appendix Table 5: Database for the Genotoxicity of Atrazine*

Test system	Results[a] Without Exogenous Metabolic Activation	With Exogenous Metabolic Activation	Dose[b] (LED or HID)	Reference**
MUTATION				
Bacteriophage T4, forward mutation	-	NT	20 ug/plate	Andersen *et al.* (1972)
Bacteriophage, reverse mutation	-	NT	1000 ug/plate	Andersen *et al. (1972)*
Salmonella typhimurium, forward mutation, $8AG^R$	-	-	250 ug/ml	Adler (1980)
Salmonella typhimurium TA100, TA98, TA1535, TA1537, TA1538 reverse mutation	-	-	5000 ug/plate	Poole & Simmon (1977; DER)
Salmonella typhimurium TA100, TA98, TA1535 reverse mutation	-	-	100 ug/plate	Lusby *et al.* (1979)
Salmonella typhimurium TA100, TA98 reverse mutation	NT	-	1100 ug/plate	Bartsch *et al. (1980)*
Salmonella typhimurium TA100, TM677 reverse mutation	NT	-[c]	30000 ug/plate	Sumner *et al.* (1984)
Salmonella typhimurium TA100, TA98, TA97, TA1535, TA1537, TA1539 reverse mutation	-	-	1000 ug/plate	Kappas(1988)
Salmonella typhimurium TA100, reverse mutation	NT	+[c]	NG	Means *et al.* (1988)
Salmonella typhimurium TA100, TA98, TA97, TA102 reverse mutation	-	-	1000 ug/plate	Mersch-Sundermann *et. al.* (1988)
Salmonella typhimurium TA100, TA98, TA97, TA1535, TA1537, TA1538 reverse mutation	-	-	1000 ug/plate	Zeiger *et al*, (1988)
Salmonella typhimurium TA100, TA98, TA97 reverse mutation	-	NT	2000 ug/plate	Butler & Hoagland (1989)
Salmonella typhimurium TA100, TA98, TA102, TA1535, TA1537 reverse mutation	-	-	1000 ug/plate	Ruiz & Marzin (1997)
Salmonella typhimurium TA100, TA98, TA1535, TA1537 reverse mutation	-	-	5000 ug/plate	Deparde (1986; DER)
Salmonella typhimurium TA100, TA98 reverse mutation	-	-	1000 ug/plate	Morichetti *et al.* (1992)
Salmonella typhimurium TA1530, TA1531, TA1532, TA1534, *his* G45 reverse mutation (spot test)	-	NT	NG	Seiler (1973)
Salmonella typhimurium, (eight unidentified strains) reverse mutation	-	NT	NG	Andersen *et al. (972*)
Salmonella typhimurium, (strains not identified) reverse mutation	-	-	NG	Adler (1980)
Escherichia coli, forward mutation, AMP^R	-	-	430 ug/plate	Adler, (1980)
Saccharomyces cerevisiae, reverse mutation (stationary phase cells)	-	NT	75600 ug/ml	Morichetti *et al.* (1992)
Saccharomyces cerevisiae, reverse mutation (logarithmic phase cells)	(+)	NT	2160 ug/ml	Morichetti *et. al.* (1992)
Saccharomyces cerevisiae, forward mutation	-	NT	50 ug/ml	Emnova *et al.* (1987)
Schizosaccharomyces pombe, reverse mutation	+	NT	17.5 ug/ml	Mathias (1987)
Schizosaccharomyces pombe, reverse mutation	+	+[c]	70 ug/ml	Mathias (1987)
Aspergillus nidulans, forward mutation	-	+	2500 ug/ml	Benigni *et al.* (1979)
Gene mutation, Chinese hamster lung V79 cells, *hprt* locus	-	-[e]	2000 ug/ml	Adler (1980)
Host-mediated assay, *Escherichia* coli Amp^R in mouse		+	100 po x 1	Adler (1980)
Drosophila melanogaster, somatic mutation	+		1000 ug/g feed	Torres *et al.* (1992)
Drosophila melanogaster, somatic mutation	+		200 ug/g feed	Tripathy *et al.* (1993)
Drosophila melanogaster, sex-linked recessive lethal mutation	(+), I^G		100 ug/g feed	Murnik & Nash (1977)
Drosophila melanogaster, sex-linked recessive lethal mutation	-		2000 ug/g feed	Adler (1980)
Drosophila melanogaster, sex-linked recessive lethal mutation	(+), I^E		200 ug/g feed	Tripathy *et al.* (1993)
Drosophila melanogaster, dominant lethal mutation	(+) I^G,		100 ug/g feed	Murnik & Nash (1977)
Drosophila melanogaster, sex-linked recessive lethal mutation			10,000 ug/g feed	Njagi *et al.* (1980)

Table 5 (cont)

Test system	Results[a] Without Exogenous Metabolic Activation	With Exogenous Metabolic Activation	Dose[b] (LED or HID)	Reference
CHROMOSOME ABERRATIONS--IN VITRO				
Chromosomal aberrations, Chinese hamster CHO cells *in vitro*	-	-	2000 ug/ml	Adler (1980)
Chromosomal aberrations, human lymphocytes *in vitro*	+	NT	0.15 ug/ml	Lioi *et. al*. (1998)
Chromosomal aberrations, Chinese hamster CHO cells *in vitro*	-	NT	250 ug/ml	Ishidate (1988)
Chromosomal aberrations, human lymphocytes *in vitro*	-	NT	50 ug/ml	Kligerman *et al*. (1999)
Chromosomal aberrations, human lymphocytes *in vitro*	(+)	NT	0.1 ug/ml	Meisner *et al*. (1992)
Chromosomal aberrations, human lymphocytes *in vitro*	(+)	NT	1.0 ug/ml	Meisner *et al*. (1993)
CHROMOSOME ABERRATIONS-IN VIVO				
Micronucleus formation, Tif.MAGf female mouse bone-marrow cells *in vivo*	-		2250mg/kg po x 1	Ceresa (1988a; DER)
Micronucleus formation, Tif.-MAGf male mouse bone-marrow cells *in vivo*	-		2250mg/kg po x 1	Ceresa (1988a; DER)
Micronucleus formation, NMRI female mouse bone-marrow cells *in vivo*	(+)		1400mg/kg: po x 1	Gebel *et al.* (1997)
Micronucleus formation, NMRI male mouse bone-marrow cells *in vivo*			1750mg/kg po x 1	Gebel *et al*. (1997)
Micronucleus formation, female mouse bone-marrow cells *in vivo*	-		500mg/kg ip x 2	Kligerman *et al*. (1999)
Chromosome aberrations, mouse bone-marrow cells *in vivo*			20 ppm dw	Meisner *et al*. (1992)
OTHER INDICATORS OF DNA DAMAGE				
Escherichia coli PQ37	-	-	1000 *ug/ml*	Ruiz & Marzin *(1997)*
Saccharomyes cerevisiae, gene conversion	-	+C	10 *ug/ml*	Plewa and Gentile *(1976)*
Saccharomyes cerevisiae, gene conversion	-	-	2000 *ug/ml*	Adler (1980)
Saccharomyes cerevisiae, gene conversion			4000 *ug/ml*	de Bertoldi *et al. (1980)*
Saccharomyes cerevisiae, gene conversion (stationary phase cells)	+	NT	64800 *ug/ml*	Morichetti *et al. (1992)*
Saccharomyes cerevisiae, gene conversion (logarithmic phase cells)	-	NT	540 *ug/ml*	Morichetti *et al.* (1992)
Saccharomyes cerevisiae, mitotic recombination	-	NT	50 *ug/ml*	Emnova *et al.* (1987)
Aspergillus nidulans, gene conversion	-	NT	8000 ug/ml	de Bertoldi *et al*. (1980)
Aspergillus nidulans, mitotic recombination	-	+	NG	Adler (1980)
Aspergillus nidulans, mitotic recombination	-	-	1000 ug/ml	Kappas(1988)
DNA damage, human lymphocytes in vitro	(+)	-	100 ug/ml	Ribas *et al*, (1995)
Unscheduled DNA synthesis, human EUE cells *in vitro*	-	-[e]	650 ug/ml	Adler (1980)
Unscheduled DNA synthesis, rat primary hepatocytes *in vitro*	-	NT	139 ug/ml	Hertner (1992; DER)
Unscheduled DNA synthesis, rat primary hepatocytes *in vitro*	-	NT	150 ug/ml	Puri & Muller (1984; DER)
DNA strand breaks, rat stomach, liver and kidney *in vivo*	(+)		875mg/kg po x 1	Pino *et al.* (1988)
DNA strand breaks, rat stomach, liver and kidney *in vivo*	(+)		350mg/kg po x 15	Pino, *et al.* (1988)
DNA strand breaks, rat lung *in vivo*	(+)		875mg/kg po x 1	Pino *et al.* (1988)
DNA strand breaks, rat lung *in vivo*	(+)		350mg/kg po x 15	Pino *et al.* (1988)
Rana catesbeiana tadpoles, DNA damage	+[d], I[E]		4.8 mg/kg	Clements *et al.* (1997)
Sister chromatid exchanges, human lymphocytes *in vitro*	-,I[G]	NT	NG	Ghiazza *et al.* (1984)
Sister chromatid exchanges, human lymphocytes *in vitro*	-	-	10 ug/ml	Dunkelberg *et al.* (1994)
Sister chromatid exchanges, human lymphocytes *in vitro*	-	NT	50 ug/ml	Kligerman *et al*. (19 99)
Sister chromatid exchanges, human lymphocytes *in vitro*	(+)	NT	0.1 ug/ml	Lioi *et. al*. (1998)
Sister chromatid exchange, Chinese hamster CHO cells *in vitro*	-	-	2000 ug/ml	Adler (1980)
DNA repair exclusive of unscheduled DNA synthesis, human lymphocytes in vitro	-	NT	25 ug/ml	Surralles *et al.* (1995)

Table 5. cont.

Test system	Results[a] Without Exogenous Metabolic Activation	With Exogenous Metabolic Activation	Dose[b] (LED or HID)	Reference
PLANT TESTS				
Hordeum vulgare, mutation	+	NT	1000 mg/kg	Wuu & Grant (1966)
Hordeum vulgare, mutation	-	NT	200 mg/kg	Stroev (1968)
Zea mays, mutation	+	NT	200 mg/kg	Morgun *et al.* (1982)
Zea mays, mutation	+	NT	NG	Plewa *et al.* (1984)
Nicotiana tabacum, mutation		-	NT	NG Briza (1999)
Tradescantia pa*ludosa,* micronucleus formation	-	NT	200 mg/kg	Ma et al, (1984)
Hordeum vulgare, chromosomal aberrations	+	NT	500 mg/ kg spray	Wuu & Grant (1967 a)
Hordeum Vulgare, chromosomal aberrations	-	NT	2000 mg/kg	Muller *et* 471. (1972)
Vicia faba, chromosomal aberrations	+	NT	400 mg/kg	Wu & Grant (1967b)
Vicia faba, chromosomal aberrations	-	NT	200 mg/kg	Khudoley *et* al, (1997)
Sorghum sp., chromosomal aberrations	+	NT	NG[d]	Liang & Liang. (1972)
Sorghum sp., chromosomal aberrations	-	NT	NG	Muller *et* al. (1972)
Sorghum sp., chromosomal aberrations	+	NT	NG	Lee *et al.* (1974)
Nigella damascena, chromosomal aberrations	-	NT	320 mg/kg	Mathias (1987)
Nigella damascena, chromosomal aberrations	+	NT	40[d] mg/kg	Mathias (1987)
Zea mays, chromosomal aberrations	-	NT	200 mg/kg	Morgun *et al.* (1992)
ANEUPLOIDY[f]				
Aspergillus nidulans	-	+	2000 ug/ml	Benigni *et al.* (1979)
Neurospora crassa,	+	NT	NG	Griffiths (1979)
Drosophila melanogaster	+		100 ug/g feed	Murnik & Nash (1977)
GERM CELL EFFECTS				
Dominant lethal effects mouse (all germ cell stages)	-		2400mg/kg PO x 1	Hertner (1993; DER)
Dominant lethal effects mouse spermatids	+		1500mg/kg po x 1	Adler (1980)
Sperm morphology, mouse	-		600mg/kg ip x 4	0sterloh

* This Table was adopted and updated from Dearfield et al., 1993

** DER, data entry record-study was submitted by registrant and considered acceptable guideline study after review by EPA's Office of Pesticide Program.

[a] +, positive; (+) weakly positive; -, negative; IG, determined to be inconclusive finding by the GeneTox Panel; IE, determine to be an inconclusive finding by EPA review; NT, not tested

[b] LED, lowest effective dose; HID, highest ineffective does; in vitro test, mg/kg bw/day; NG, not given; po, oral (gavage or gastric intubation); dw, drinking water; d , days; ip, intraperitoneal

[c] Tested extracts of atrazine-treated Zea *mays*

[d] Commercial pesticide

[e]Positive with potato microsomes at doses up to 3 mM

[f] Aneuploidy, chromosome loss or gain is not typically associated with a DNA reactive mutagenic mechanism but usually involves disruption of spindle formation or chromosomal segreagation

Table 6. Database for the Genotoxicity of Simazine

Test system	ResuIts[a]	Dose b (LED or HID)	Reference

	With Exogenous Metabolic Activation		Without Exogenous Metabolic Activation		
MUTATION					
Escherichia coli PQ37, SOS chromotest	NT		-	NG	Mersch-Sundermann *et al.* (1988)
Salmonella typhimurium TA1978/TA1538 and SL525/SL4700 differential toxicity	-		NT	2000 ug/disc	USEPA (1984)
Bacillus subtilis rec strains, differential toxicity	-		NT	1000 ug/disc	Kuroda *et al.* (1992)
Salmonella typhimurium TA100, TA98, TA1535, TA1537, TA1538, reverse mutation	NT		-	NG	Simmon *et al.* (1977)
Salmonella typhimurium TA100, TA98, reverse mutation	-		-	5000 ug/plate	USEPA (1984)
Salmonella typhimurium TA100, TA1535, TA1537, TA1538, reverse mutation	-		-	1000 ug/plate	USEPA(1977)
Salmonella typhimurium TA100, reverse mutation	NT		+[C]	NG	Means *et al.* (1988)
Salmonella typhimurium TA100, TA102, TA97, reverse mutation	-		-	1000 ug/plate	Mersch-Sundermann *et al.* (1988)
Salmonella typhimurium TA1530, TA1531, TA1532, TA1534, G46, reverse mutation (spot test)	-		NT	NG	Sieler (1973)
Salmonella typhimurium, (eight unidentified strains) reverse mutation	-		NT	NG	Andersen *et al.* (1972)
Escherichia coli, forward mutation	-		NT	NG	Fahrig (1974)
Escherichia coli WP2 uvr, reverse mutation	-		-	1000 ug/plate	USEPA (1984)
Serratia marcescens, reverse mutation	-		NT	NG	Fahrig (1974)
OTHER INDICATIONS OF DNA DAMAGE					
Saccharomyces cerevisiae, gene conversion	-		NT	NG	Fahrig (1974)
Saccharomyces cerevisiae, gene conversion	-		NT	1000[d]	Siebert & Lemperle (1974)
Saccharomyces cerevisiae D3, homozygosis by recombination	-		-	50000	USEPA (1977)
Saccharomyces cerevisiae D7, mitotic recombination	-		-	25000	USEPA (1984)
Saccharomyces cerevisiae D7, reverse mutation	-		-	25000	USEPA (1984)
Saccharomyces cerevisiae D7, gene conversion	-		-	25000	USEPA (1984)
Saccharomyces cerevisiae, reverse mutation	-		NT	5	Emnova et al. (1987)
Drosophila melanogaster, somatic mutation	+			2000 ug/g feed	Tripathy *et al.* (1995)
Drosophila melanogaster, sex-linked recessive lethal mutation				10 ng/fly inj	Benes & Sram (1969)
Drosophila melanogaster, sex-linked recessive lethal mutation	+			6 ng/fly inj	Murnik & Nash (1977)
Drosophila melanogaster, sex-linked recessive lethal mutation				6000 ug/g feed	Murnik & Nash (1977)
Drosophila melanogaster, sex-linked recessive lethal mutation	+			2000 ug/g feed	Tripathy *et al.* (1995)
Drosophila melanogaster, dominant lethal test	+			6000 ug/g feed	Murnik & Nash (1977)
Drosophila melanogaster, aneuploidy	-			6000 ug/g feed	Murnik & Nash (1977)
Gene mutation, mouse lymphoma L5178Y cells *in vitro, tk locus in vitro*	-		*(+)I*	*300*	Jones et al. (1984)
CHROMOSOME ABERRATION					
Chromosomal aberrations, Chinese hamster ovary CHO cells *in vitro*	-	NT	0.01	Biradar & Rayburn (1995)	
Chromosomal aberrations, human lymphocytes *in vitro*	-	NT	37.5	Kligerman et al. (1999)	
Micronucleus formation, mouse bone-marrow and peripheral blood cells *in vivo*		NT	500 po x 2	USEPA (1984)	
Micronucleus formation, both sexes,mouse bone-marrow *in vivo*	-	NT	5000 po x 1	Ceresa (1988a)	

Table 6 (cont)

Test system	Results[a]		Doseb (LED or HID)	Reference
	Without Exogenous Metabolic Activation	With Exogenous Metabolic Activation		
OTHER INDICATORS OF DNA DAMAGE				
Sister chromatid exchange, Chinese hamster ovary CHO cells *in vitro*	-	NT	1700	USEPA (1984)
Sister chromatid exchange, Chinese hamster lung V79 cells *in vitro*	-	NT	2	Kuroda *et al.* (1992)
Sister chromatid exchange, human lymphocytes *in vitro*	-	NT	37.5	Kligerman et al. (1999)
Sister chromatid exchange, human lymphocytes *in vitro*	(+), I	NT	NG	Ghiazza *et al.* (1984)
Sister chromatid exchange, human lymphocytes *in vitro*			*10*	Dunkelberg *et al.* (1994)
Unscheduled DNA synthesis, human lung WI 38 fibroblasts *in vitro*	-		*200*	USEPA (1984)
Unscheduled DNA synthesis, rat primary heptocytes	-	NT		Hertner (1992)
PLANT ASSAYS				
Hordeum vulgare, mutation	+	NT	1000	Wuu & Grant (1966)
Hordeum vulgare, mutation		NT	200	Stroev (1968a)
Rizobium meliloti, mutation		NT	5000	Kaszubiak (1968)
Zea mays, chlorophyll mutation	+	NT	200	Morgun et al. (1982)
Zea mays, mutation	+	NT	NG	Plewa et al. (19 84)
Fragaria ananassa, mutation	+	NT	2	Malone & Dix (1990)
Tradescantia paludosa, micronuclei		NT	200	Ma et al. (1984)
Hordeum vulgare, chromosomal aberrations	+	NT	500	Wuu & Grant (1966)
Hordeum vulgare, chromosomal aberrations	+	NT	500 spray	Wuu & Grant (1967a)
Hordeum vulgare, chromosomal aberrations	(+)	NT	500	Stroev (1968b)
Hordeum vulgare, chromosomal aberrations	(+)	NT	500'	Kahlon (1980)
Vicia faba, chromosomal aberrations	+	NT	200'	Wuu & Grant (I 967b)
Vicia faba, chromosomal aberrations	+	NT	5	Hakeem & Shehab (1974)
Vicia faba, chromosomal aberrations	(+)	NT	1000	de Kergommeaux *et al.* (1983)
Allium cepa, chromosomal aberrations	+	NT	20	Chubutia & Ugulava (1973)
Crepis capillaris, chromosomal aberrations	+	NT	1000	Voskanyan & Avakyan (1984)
ANEUPLOIDY TESTS				
Neurospara crassa, aneuploidy	-	NT	NG	Griffiths (1979)

a +, positive; (+), weakly positive; -, negative; NT, not tested

b LED, lowest effective dose; HID, highest ineffective dose; unless **otherwise stated, in-vitro** test, ug/mL; in-vivo test, mg/kg bw/day; NG, not given; inj, injection; po, oral

'Tested with extracts of simazine-treated *Zea mays*

d Commercial pesticide tested

Table 7. Database for the Genotoxicity of Propazine

Test system	Results[a]		Dose[b]	Reference**
Without Exogenous Metabolic Activation	With Exogenous Metabolic Activation	(LED or HID)		
MUTATION				
Bacteriophage, forward mutation	-	NT	100 ug/plate	Andersen *et al.* (1972)
Bacteriophage, reverse mutation	-	NT	2000 ug/plate	Andersen *et al.* (1972)
Salmonella typhimurium TA100,TA98,TA1535,TA1537,TA1538 reverse mutation	-	-	5000 ug/plate	Kappas(1988)
Gene mutation, Chinese hamster lung V79 cells, *hprt* locus	(+)	-	400	Ciba-Geigy (1986; DER)
CHROMOSOME ABERRATIONS--IN VITRO				
Chromosomal aberrations, Chinese hamster CHO cells *in vitro*	-	-	3000 ug/ml	Ishidate (1983)
CHROMOSOME ABERRATIONS--IN VIVO				
Micronucleus formation, Hamsters *in vivo*	-		50000 po x 1	Ciba-Geigy (1984; DER)
OTHER INDICATORS OF DNA DAMAGE				
Unscheduled DNA synthesis, rat primary hepatocytes-	NT	62.5	Puri (1984)	
Aspergillus nidulans, crossing over	-	-	800	Kappas (1988)

**DER, data entry record-study was submitted by registrant and considered acceptable guideline study after review by EPA's Office of Pesticide Program.

[a] +, positive; (+), weakly positive; -, negative; I^G, determined to be an inconclusive finding by the GeneTox Panel; I^E, determined to be an inconclusive finding by EPA review; NT, not tested

[b] LED, lowest effective dose; HID, highest ineffective dose; in-vivo test, mg/kg bw/day; NG, not given; po, oral (gavage or gastric intubation); dw, drinking water; d, days; ip, intraperitoneal

Appendix Table 8: Data from Eldridge, 1993a. DI=Diestrus; PR=Proestrus; ES=Estrus

% days in stages of estrous cycle in SD rats						
mg/kg/day▾	3 months	9 months	12 months	15 months	18 months	24 months
0	DI= 46.1±7.1 PR= 29.5 ±4.6 ES= 24.8±7.7	DI= 44.8@-- ±7.6 PR= 30.9 ±5.7 ES= 24.2@++ ±7.6	DI= 31.1@-- ±5.3 PR= 26.0±7.9 ES= 42.6@+ ±10.1	DI= 36.7±15.1 PR= 19.2±8.2 ES= 44.4±12.2	DI= 31.0 @--±5.5 PR= 24.4@-±4.1 ES= 44.9@++ ±5.7	DI= 31.6 ±22.2 PR= 21.0±5.7 ES= 47.8±18.9
4.23	DI= 42.6±7.4 PR=32.5 ±7.6 ES= 25.2±4.9	DI= 36.2*±7.9 PR= 29.4±6.5 ES= 34.4*±9.0	DI= 26.9±8.5 PR= 26.1±8.4 ES= 47.2±13.7	DI= 32.8±14.0 PR= 24.6±8.7 ES= 42.7±12.6	DI= 23.0*±9.0 PR= 20.1±6.4 ES= 57.2*±12.5	DI= 37.0±32.8 PR= 13.3±8.1 ES= 50.0±27.3
26.23	DI= 42.0±6.7 PR= 30.2±6.3 ES= 27.8±7.6	DI= 25.9**±9.1 PR= 29.4±6.2 ES= 44.8**±11.6	DI= 22.4*±7.5 PR= 24.6±7.3 ES= 53.3±11.2	DI= 28.0±11.3 PR= 22.4±5.1 ES= 49.6±12.2	DI= 25.5*±17.3 PR= 18.7±7.9 ES= 55.9*±20.7	DI= 55.0±9.9 PR= 21.5±10.6 ES= 24.0±0.0

@+ Dose-related trend is statistically significant, in positive direction, at $p \leq 0.05$
@++ Dose-related trend is statistically significant, in positive direction, at $p \leq 0.01$
@- Dose-related trend is statistically significant, in negative direction, at $p \leq 0.05$
@-- Dose-related trend is statistically significant, in negative direction, at $p \leq 0.01$
* Statistically Significant at $p < 0.05$
** Statistically signficant at $p<0.01$

Appendix Table 9. Data from Morseth, 1996a. Data from One Month study exposing SD females through the diet

Days in Estrus vs. Time					
Dose ▸	0 mg/kg/day	2.5 mg/kg/day	5 mg/kg/day	40 mg/kg/day	200 mg/kg/day
# normally cycling animals	67 (74.4%)	66 (73.3%)	65 (72.2%)	50 (55.6%)	33 (36.7%)
# animals with diestrus blocks	21 (23.3%)	20 (22.2%)	21 (23.3%)	36 (40%)	51 (56.7%)
# animals with estrus blocks	3 (3.3%)	3 (3.3%)	4 (4.4%)	6 (6.6%)	11 (12.2%)

Appendix Table 10 : Data from Morseth, S., 1996b. Six month study exposing SD females through the diet

% Days in Estrus or Diestrus							
Dose (mg/ kg/day)▾	1-2 weeks	5-6 weeks	9-10 weeks	13-14 weeks	17-18 weeks	21-22 weeks	25-26 weeks
0	DI= 58 ± 9.2 ES=22 ± 5.2	DI= 55 ± 8.7 ES= 23 ± 5.1	DI= 54 ± 7.5 ES= 25 ± 9.4	DI= 49 ± 17.2 ES= 31 ± 22.4	DI= 47 ± 18.1 ES= 34 ± 24.2	DI= 51 ± 22.3 ES= 32 ± 25.4	DI= 40 ± 25.7 ES= 47 ± 32.2
1.8	DI= 57 ± 10.2 ES= 22 ± 5.6	DI= 55 ± 7.6 ES= 23 ± 4.5	DI= 54 ± 7.5 ES= 25 ± 4.8	DI= 53 ± 15.1 ES= 28 ± 18	DI= 49 ± 19.4 ES= 33 ± 24.7	DI= 43 ± 24.6 ES= 41 ± 31.9	DI= 42 ± 29.6 ES= 48 ± 35.5
3.65	DI= 56 ± 10.2 ES= 22 ± 5.4	DI= 53 ± 10.9 ES= 25 ± 10	DI= 51 ± 8.7 ES= 26 ± 10.2	DI= 49 ± 16 ES= 31 ± 21.1	DI= 47 ± 18.8 ES= 36 ± 25.1	**DI= 39 ± 23.9**** **ES= 45 ± 32.2***	DI= 34 ± 27.3 ES= 54 ± 35.1
29.4	DI= 61 ± 11.5 ES= 21 ± 7	DI= 55 ± 10 ES= 24 ± 7.4	DI= 52 ± 10 ES= 26 ± 9.3	DI= 44 ± 21.6 **ES= 40 ± 27.6***	DI= 41 ± 25.2 **ES= 45 ± 32.1***	**DI= 37 ± 27.7**** **ES= 51 ± 34.8****	**DI= 29 ± 30.2*** **ES= 63 ± 37.0***

* p≤ 0.05; ** p≤ 0.01

Appendix Table 11: Data from Thakur, 1999

Days in Estrus vs. Time					
Dose▸ Study Weeks	Control	1.5 mg/kg/day	3.1 mg/kg/day	4.2 mg/kg/day	24.4 mg/kg/day
1-14	26.12 ± 0.71	28.57 ± 0.86	26.38±0.87	26.45±0.72	28.91± 0.97
17-26	45.79 ± 2.05	50.28 ± 2.05	48.67 ± 2.25	48.34 ± 2.1	61.3 ± 2.3
29-38	77.22 ± 2.13	74.63 ± 2.2	71.4 ± 2.29	67.4 ± 2.36	80.75 ± 2.02
41-46	81.51 ± 2.44	75.77 ± 2.73	70.8 ± 2.81	73.41 ± 2.84	83.74 ± 2.24

Appendix Table 12: Data from Thakur, 1999

Percent of Animals with Estrus Blocks of at least 7 days					
Dose ▸ Study Weeks ▾	Control	1.5 mg/kg/day	3.1 mg/kg/day	4.2 mg/kg/day	24.4 mg/kg/day
17-18	17.5	15	21.52	17.5	26.35
21-22	22.78	28.75	31.65	33.74	50.63
25-26	30.38	36.25	36.71	33.75	50.63

Appendix Table 13: Data from Thakur, 1999

Percent Days in Estrus During Weeks 1-46 and Tumor Response for all Dose Groups Combined			
	No Tumor	Fibroadenoma	Carcinoma
Mean percent days in estrus	50.869	55.275#	60.346*
Standard Error	1.27	1.074	1.596
N	217	128	91

p=0.0341 compared to animals with no tumor
*p=0.0000 compared to animals with no tumor

Appendix Table 14: Data from Thakur, 1999

Percent Days in Estrus During Weeks 17-26 and Tumor Response for all Dose Groups Combined			
	No Tumor	Fibroadenoma	Carcinoma
Mean percent days in estrus	48.077	52.223	60.803*
Standard Error	1.864	2.489	2.995
N	216	128	91

*p=0.0003 compared to animals with no tumor

Appendix Table 15: Data from Eldridge, 1993a. E=Estradiol; PROG=Progesterone; PRL= Prolactin

Serum hormone levels in SD rats (E in pg/ml; PROG and PRL in ng/ml)						
mg/kg/day▾	3 months	9 months	12 months	15 months	18 months	24 months
0	E= 3.5±6.4 PROG= 15.6 ±7.9 PRL= N/A	E= 22.6±20.6 PROG= 11.6±11.9 PRL= 17.8 ±12.4 &	E= 13.1±10.6 PROG= 4.0±1.5 PRL= 13.2±2.9	E= 17.3±12.8 PROG= 14.2 ±19 PRL= 16.1±15.2	E= 3.7 ±3.6 PROG= 19.6 ±29.3 PRL= 20.8 ±8.8	E= 2.1±3.3 PROG= 2.8±1.2 PRL=20.3 ±4.9
4.23	E= 11.2±12.6* PROG= 16.5±10.7 PRL= N/A	E= 20.7±26.1 PROG= 8.2±6.6 PRL= 24.3±10.4	E= 12.5±21.6 PROG= 6.9±11.4 PRL= 11.9±6.8	E= 18.8±18 PROG= 4.1±3 PRL= 11.2±7.6	E= 16.1±21.6 PROG= 11.7*±28.7 PRL= 17±6.3	E= 3.4±5.3 PROG= 13.3±22.1 PRL= 14.2± 6.4
26.23	E= 16.2±13* PROG= 14.3±7.3 PRL= N/A	E= 31.2±28.1 PROG= 7.4±4.1 PRL= 45.8±20**	E= 11.7±7.5 PROG= 3.2±1.4 PRL= 15±3.6	E= 18.4±7.6 PROG= 20±24.5 PRL= 15±11	E= 5.6±7.1 PROG= 4.4±4.9 PRL= 17.5±8.7	E= 0.9± 0.9 PROG= 3.9±0.6 PRL= 13.5±1.1

& Dose-related trend is statistically significant, in positive direction, at $p \leq 0.05$
@ Dose-related trend is statistically significant, in negative direction, at $p \leq 0.05$
* Statistically Significant at $p < 0.05$
** Statistically Significant at $p < 0.01$
N/A - samples from the 1 and 3 month timepoints were not available for analysis because these samples were inavertatly hydrolyzed.

Appendix Table 16: Histomorphology Analysis in the SD, McConnell, 1995

Values shown below are Index Weighted Scores at 1, 3, 9 and 12 months into the study.

Index Weighted Score[1] at 1, 3, 9 and 12 months				
Finding▸ Dose▾	Acinar Development (Estrogen)	Acinar/Lobular Development (Prolactin)	Secretory Activity (Prolactin)	Dilated Ducts with Secretion (Prolactin)
Control	1=15 3= 20 9= 28 12= 31	1= 9 3= 22 9= 23 12= 25	1= 15 3= 17 9= 24 12= 31	1= 9 3= 12 9= 17 12= 23
4.23 mg/kg/day	1= 22 3= 24 9= 33 12= 33	1= 10 3= 17 9= 28 12= 30	1= 14 3= 14 9= 28 12= 36	1= 12 3= 11 9= 24 12= 25
26.23 mg/kg/day	1= 21 3= 27 9= 45 12= 41	1= 12 3= 16 9= 42 12= 36	1= 12 3= 17 9= 46 12= 39	1= 9 3= 15 9= 45 12= 41

1 The index weighted score is calculated as such: the severity of the findings, as determined by the examining pathologist, is converted to a numerical value and the numerical values for each group are summed. The score of absent= 1; minimal =2; mild=3; moderate=4 and marked=5.

Appendix Table 17: Galactocele Incidence and Severity in the SD Female, Thakur, 1991a

Finding▸ Dose▾	One and Three month	Nine Months	12 Months	15 Months
Control	None at either timepoint	1 (slight)[1]	5 (4- minimal; 1 moderate)	7 (2- slight; 1- moderate; 1- moderatly severe; 3- severe
4.23 mg/kg/day	None at either timepoint	4 (2-minimal;1-slight; 1-moderate)	5 (1-minimal; 3-slight; 1- moderately severe)	7 (3 - minimal;4- slight)
26.23 mg/kg/day	None at either timepoint	8 (2-minimal; 1- moderate; 5 moderately severe)	10 (5-slight; 4-moderate; 1- moderately severe)	9 (2- minimal; 3- slight; 2- moderate; 1- moderatly severe; 1- severe)

1 The scores are: minimal; slight; moderate; moderately severe and marked

Appendix Table 18: Data from Morseth, 1996a and 1996b*

Timepoints for measurement of LH surge in both the one and six month studies				
Biologic time	# animals for non-repeat bleed	# animals for repeat bleed	Expected state of serum LH levels	In a normally cycling rat this is equivalent to:
1100	10	10	baseline	proestrus morning
1400	15	10	baseline	early afternoon proestrus
1600	15	10	LH surge	mid- afternoon proestrus
1800	15	10	LH surge	Late afternoon proestrus
2000	15	10	LH surge	Proestrus evening
2300	10	10	baseline	Proestrus evening

* There were 90 females in each group: 10 + 15 + 15 + 15 + 15 + 10 non-repeat bleed animals = 80 animals plus the 10 repeat bleed animals equals 90 animals per group.

Appendix Table 19: Data from Morseth, 1996a . Doses are in mg/kg/day. LH values given are in picograms/ml.

LH data from the one-month study						
Biologic Time▸	1100	1400	1600	1800	2000	2300
mean and SD *nonrepeat bleed*	0= 998 ± 614 2.5= 943 ± 614 5.0= 1140 ±715 40= 1219 ±467 200= 873 ±656	0= 1122 ± 564 2.5= 1171 ±802 5.0= 882 ±926 40= 1125 ±795 200= 1099 ±863	0= 3315 ± 2684 2.5= 20951 ±1315 5.0= 3099 ±2521 40= 3518 ±4514 200= 1685 ±2962	0= 5138 ± 4403 2.5= 4489 ±4345 5.0= 2804 ±13 40= 3246 ±1981 200= 2752 ±3137	0= 2242 ± 1850 2.5= 1118 ±412 5.0= 1554 ±14 40= 1740 ±1157 200= 1853 ±1138	0= 761 ± 288 2.5= 486 ±138 5.0= 508 ±317 40= 689 ±373 200= 1126 ±81645
mean and SD *repeat bleed*	0= 732 ± 461 2.5= 1101 ±652 5.0= 810 ±519 40= 755 ±389 200= 514 ±503	0= 786 ± 557 2.5= 2222 ±1220 5.0= 1678 ±1602 40= 1037 ±829 200= 453 ±313	0= 1301 ± 1031 2.5= 3029 ±2383 5.0= 4971 ±5047 40= 1137 ±629 200= 552 ±311	0= 2650 ± 2389 2.5= 3015 ±3220 5.0= 2717 ±25 40= 1450 ±857 200= 812 ±470	0= 2606 ± 2076 2.5= 1731±1447 5.0= 2954 ±3515 40= 1477 ±1296 200= 1140 ±328	0= 1671 ± 674 2.5= 1475 ± 456 5.0= 1431±345 40= 1362 ±329 200= 1080 ±30142

Appendix Table 20: Data from Morseth, 1996b. Doses are in mg/kg/day. LH values given are in picograms/ml.

LH data from the six-month study						
Biologic Time▸	1100	1400	1600	1800	2000	2300
mean and SD *nonrepeat bleed*	0= 1900 ±775 1.8= 1816 ±543 3.65= 1581 ±791 29.4= 1863 ±788	0= 2326 ±1082 1.8= 1606 ±926 3.65= 1799 ±933 29.4= 1420 ±622	0= 2669 ±1464 1.8= 2507 ±1008 3.65= 2463 ±1201 29.4= 1913 ±799	0= 3458 ±2310 1.8= 3235 ±2751 3.65= 3175 ±1685 29.4= 1356 ±760	0= 2327 ±1668 1.8= 2249 ±1498 3.65= 1899 ±752 29.4= 1308 ±477	0= 1178 ±337 1.8= 1258 ±428 3.65= 1063 ±383 400= 1129 ±350
mean and SD *repeat bleed*	0= 909 ±410 1.8= 1075 ±621 3.65= 972 ±353 29.4= 1005 ±482	0=1136 ±554 1.8= 1468 ±977 3.65= 984 ±466 29.4= 1155 ±620	0= 2213 ±2562 1.8= 1603 ±682 3.65= 2277 ±1470 29.4= 850 ±352	0= 3336 ±3138 1.8= 3631 ±2732 3.65= 2500 ±1897 29.4= 858 ±416	0= 3388 ±3344 1.8= 2510 ±1138 3.65= 2409 ±1525 29.4= 1042 ±627	0= 1672 ±426 1.8= 1229 ±492 3.65= 1271 ±559 400= 953 ±549

Appendix Table 21: Group Mean Absolute Pituitary weights by Timepoints, Thakur, 1991a
Weights are in mg.

Absolute Pituitary Weights			
Dose (mg/kg/day) ▾	3 months	9 months	12 months
Control	$\bar{x}$= 23.0 SD= 4.2	$\bar{x}$= 24.0 SD= 6.4	$\bar{x}$= 37.0 SD= 19.9
4.23	$\bar{x}$= 21.2 (-8%)[1] SD= 3.0	$\bar{x}$= 29.9 (+25%) SD= 6.1	$\bar{x}$= 35.4 (-4%) SD= 26.4
26.23	$\bar{x}$= 20.5 (-11%) SD= 8.0	$\bar{x}$= 37.0 (+54%) SD= 7.9	$\bar{x}$= 41.8 (+13%) SD= 14.5

1 Values in parenthesis represent percent change relative to control

Appendix Table 22: Group Mean Pituitary Weights Relative to Body Weight, Thakur, 1991a

Values represent pituitary weight as a percentage of body weight

Relative Pituitary Weights			
Dose (mg/kg/day) ▾	3 months	9 months	12 months
Control	$\bar{x}$= 0.00697 SD= 0.0012	$\bar{x}$= 0.00607 SD= 0.00163	$\bar{x}$= 0.00985 SD= 0.0062
4.23	$\bar{x}$= 0.00668 (-4%)[1] SD= 0.00123	$\bar{x}$= 0.00765 (+26%) SD= 0.00187	$\bar{x}$= 0.00830 (-16%) SD= 0.00559
26.23	$\bar{x}$= 0.00677 (-3%) SD= 0.00249	$\bar{x}$= 0.00967 (+59%) SD= 0.00245	$\bar{x}$= 0.01239 (+26%) SD= 0.00572

1 Values in parenthesis represent percent change relative to control

Appendix Table 23: Group Mean Pituitary Weights: Absolute and Relative to Body Weight, Morseth, 1996b

Values represent pituitary weight as a percentage of body weight

Absolute and Relative Pituitary Weights				
Dose (mg/kg/day) ▸	Control	1.8	3.65	29.4
Absolute	$\bar{x}$= 23.0 SD= 5.0	$\bar{x}$= 24.0 (+4%) SD= 5.0	$\bar{x}$= 24.0 (+4%) SD= 5.0	$\bar{x}$= 28.0 (+22%) SD= 8.0
Relative	$\bar{x}$= 0.0075 SD= 0.0017	$\bar{x}$= 0.0078 (+4%) SD= 0.0015	$\bar{x}$= 0.0081(+8%) SD=0.0015	$\bar{x}$= 0.0096 (+28%) SD= 0.003

1 Values in parenthesis represent percent change relative to control

Appendix Table 24: Association of Pituitary Adenomas/Hyperplasia and Mammary Tumors

Study▸	Thakur, 1992a	Morseth, 1998
Animals *Without* Mammary Tumors	86% of the animals had either pituitary adenoma or hyperplasia	62% of the animals had either pituitary adenoma or hyperplasia
Animals *With* Mammary Tumors	86% of the animals had either pituitary adenoma or hyperplasia	93% of the animals had either pituitary adenoma or hyperplasia

Appendix Table 25a: Association of Absolute Pituitary Weight with Mammary Tumors

Absolute Pituitary Weight		
Study▸	Thakur, 1992a	Morseth, 1998
Animals *Without* Mammary Tumors	$\bar{x}$ = 0.0742 SD= 0.0823	$\bar{x}$ = 0.117 SD= 0.076
Animals *With* Mammary Tumors	$\bar{x}$ = 0.144 (94%)[1] SD= 0.109	$\bar{x}$ = 0.171 (46%) SD= 0.119

1 Value in parenthesis represents percent increase over pituitary weight of animals without tumors

Appendix Table 25b: Association of Relative Pituitary Weight with Mammary Tumors

Relative Pituitary Weight		
Study▸	Thakur, 1992a	Morseth, 1998
Animals *Without* Mammary Tumors	$\bar{x}$ = 0.021 SD= 0.024	$\bar{x}$ = 0.0321 SD= 0.029
Animals *With* Mammary Tumors	$\bar{x}$ = 0.0379 (80%)[1] SD= 0.0307	$\bar{x}$ = 0.053 (65%) SD= 0.068

1 Value in parenthesis represents percent increase over pituitary weight of animals without tumors

Appendix Table 26: Pituitary Tumor and Focal Hyperplasia Incidenes and Piutiatry Weights In OVX *vs* Intact Animals, Morseth, 1998

Pituitary Tumor and Enlarged Pituitary Incidence and Pituitary Weight[1]		
	OVX	Intact
â-Adenoma (12 months)	= 6%	= 17%
â-Adenoma (24 months)	= 50.2%	= 69.8%
Absolute Pituitary Wt. in grams (12 months)	= 0.020	= 0.0314
Absolute Pituitary Wt. in grams (24 months)	= 0.051	= 0.184
Relative Pituitary Wt. as a % of body wt. (12 months)	= 0.0037	= 0.00832
Relative Pituitary Wt. as a % of body wt. (24 months)	= 0.0116	= 0.0331
Enlarged Pituitary	= 34%	= 86%

1 Values shown represent means for all the OVX or intact animals combined, regardless of dose group. Mean values between dose groups were very similar.

Appendix Table 27: Control individual animal data from the nine month timepoint of the two-year serial sacrifice study,Thakur 1991a

Control animals at 9 months							
Animal#	**Mammary tumor**	**Pituitary Alteration**	**Pituitary wt. (abs. in mg)**	**Galactocele**	**Acinar/lobular Development**	**Secretory Activity**	**Dilated Duct with Secretion**
B94752	none	Foc. Hy. - slight	26	none	1	1	-
B94753	none	none	30	none	2	2	1
B94754	none	none	24	none	-	1	-
B94755	none	none	27	none	1	2	1
B94756	none	none	25	none	1	1	-
B94757	none	none	16	none	2	-	-
B94758	none	none	19	none	2	2	1
B94759	none	none	33	slight	2	3	4
B94760	none	none	26	none	2	2	-
B94761	none	none	14	none	-	-	-

Appendix Table 28: Low dose (70 ppm, 4.23 mg/kg/day) individual animal data from the nine month timepoint of the two-year serial sacrifice study, Thakur 1991a.

70 ppm animals at 9 months							
Animal#	**Mammary tumor**	**Pituitary Alteration**	**Pituitary wt. (abs. in mg)**	**Galactocele**	**Acinar/lobular Development**	**Secretory Activity**	**Dilated Duct with Secretion**
B94822	none	none	28	none	2	2	1
B94823	none	Foc. Hy. - slight	28	minimal	1	1	-
B94824	none	none	41	moderate	3	4	4
B94825	none	none	29	none	1	2	-
B94826	none	none	21	none	2	-	-
B94827	none	none	27	none	2	2	2
B94828	none	none	37	minimal	2	2	3
B94829	none	none	35	none	2	2	2
B94830	none	Foc. Hy. - slight	29	slight	3	3	2
B94831	none	none	24	none	-	-	-

Appendix Table 29: High dose (400 ppm, 26.23 mg/kg/day) individual animal data from the nine month timepoint of the two-year serial sacrifice study, Thakur 1991a.

400 ppm animals at 9 months							
Animal#	**Mammary tumor**	**Pituitary Alteration**	**Pituitary wt. (abs. in mg)**	**Galactocele**	**Acinar/lobular Development**	**Secretory Activity**	**Dilated Duct with Secretion**
B94892	carcinoma	none	36	moderate	2	3	4
B94893	none	none	36	moderately severe	4	4	4
B94894	fibroadenoma	none	38	moderately severe	3	4	4
B94895	none	none	23	none	4	4	4
B94896	none	none	37	severe	4	4	4
B94897	carcinoma	Focal hy. -mimimal	36	moderately severe	4	4	4
B94898	carcinoma	adenoma	55	minimal	2	3	2
B94899	none	Focal hy.- slight	41	moderately severe	4	4	4
B94900	none	none	33	moderately severe	4	4	4
B94901	fibroadenoma	adenoma	35	none	1	2	1

Appendix Figure 1: Mean plasma LH levels from the repeat bleed group of the 6-month study (Morseth, 1996b)