8EHQ-0396-13600

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March 5, 1996

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TSCA Document Processing Center (TS-790)
Office of Toxic Substances
U.S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

Attention: Section 8(e) Coordinator

Dear Sir or Madam:

This information is submitted under the provisions of the Toxic Substances Control Act, 90 Stat. 2029, 15 USC 2607, Section 8(e). Attached are summary tables of a report currently being drafted which reflect low-level estrogenicity of low molecular weight polystyrene (LPS), CASRN 9003-53-6, a homopolymer of styrene. These data were provided by the performing laboratory, TNO, Zeist, The Netherlands, to Hercules regulatory office in Rijswijk, The Netherlands, on February 16, 1996, and forwarded to our Wilmington office on that date.

The data provided (see attachments) constitute summary tables and statistical analysis of uterine weights and body weights following dietary administration of LPS. The increase in the relative weight of the uterus of the immature rat is one of several possible tests for estrogenic effects. Data were collected following four days feeding of diets containing test material to groups of immature female Wistar rats. Dietary concentrations from 1 to 1,000 ppm were used in a range-finding study in parallel with untreated feed (negative control) and diethylsltilbestrol (DES; positive control). In the definitive study, dietary concentrations of 0, 10, 20, 40, 80, and 160 ppm of LPS were used and concentrations of 5, 10, and 20 ppb of DES.

The results show a dose-response relationship between dietary LPS concentration and the uterus weight/body weight ratio. The increase was statistically significant at 160 ppm LPS. The 80 ppm dosage level was a No-Effect Level (NOEL). The NOEL for the DES positive control was less than the minimum concentration used, 5 ppb, since that dosage gave a statistically significant uterine weight increase. The data indicate that the estrogenic activity of LPS is less than 1/20,000 of that of DES.

The full report of the estrogenicity study will be provided to EPA on receipt by this office.

88960000080

Sincerely,

Gary L. McCallister
Corporate Manager
Regulatory Affairs

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Attachments
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Table 1 - Oestrogenic activity (Tiecco test) of FZL5250 in rats; mean body weights, food consumed and absolute and relative uterus weights obtained in the range-finding study (assay no. 1794)

Treatment group	Animal No.	Day 0 Body Wgt g	Day 4 Body Wgt g	Day 4 ConsFood g	Day 4 Uterus g	Day 4 Uterus g/kg BW
Neg.Control	Mean	33.3	50.3	7.9	0.066	1.32
	sem	0.5	0.9	0.0	0.004	0.07
	n	5	5	5	5	5
1 PPM	Mean	33.3	49.4	7.1	0.068	1.38
	sem	0.5	0.4	0.0	0.005	0.10
	n	5	5	5	5	5
10 PPM	Mean	33.2	50.3	7.6	0.066	1.32
	sem	0.7	1.1	0.0	0.008	0.15
	n	5	5	5	5	5
100 PPM	Mean	33.2	49.9	7.4	0.086*	1.72**
	sem	0.5	1.0	0.0	0.005	0.08
	n	5	5	5	5	5
1000 PPM	Mean	33.6	47.3	6.6	0.231***	4.89***
	sem	0.7	1.2	0.0	0.026	0.55
	n	5	5	5	5	5

Statistics
Body weight: Covar + Dunnett's tests (two-sided): * P<0.05; ** P<0.01; *** P<0.001
Uterus weight: Mann/Whitney u-test (two-sided): * P<0.05; ** P<0.02; *** P<0.002
Food consumption: Anova + L.S.D. tests (two-sided): * P<0.05; ** P<0.01; *** P<0.001

Table 2 - Oestrogenic activity (Tiecco test) of F2LS250 in rats; individual and mean body weights, food consumed and absolute and relative uterus weights obtained in the main study (assay no. 1795)

Treatment group	Animal No.	Day 0 Body Wgt g	Day 4 Body Wgt g	Day 4 ConsFood g	Day 4 Uterus g	Day 4 Uterus g/kg BW
BASAL DIET	Mean	33.6	48.4	6.3	0.059	1.22
	sem	0.7	1.4	0.1	0.004	0.07
	n	10	10	10	10	10
10 PPM	Mean	31.8	47.3	6.4	0.056	1.18
	sem	0.8	1.1	0.0	0.003	0.06
	n	10	10	10	10	10
20 PPM	Mean	32.4	45.7	5.7	0.059	1.29
	sem	1.1	1.1	0.2	0.003	0.06
	n	10	9	9	9	9
40 PPM	Mean	33.1	48.9	7.0	0.063	1.29
	sem	0.8	1.1	0.1	0.002	0.05
	n	10	10	10	10	10
80 PPM	Mean	34.9	50.2	7.0	0.073	1.45
	sem	0.9	1.3	0.2	0.004	0.08
	n	10	10	10	10	10
160 PPM	Mean	33.8	48.9	7.0	0.101***	2.08***
	sem	0.6	1.7	0.1	0.007	0.18
	n	10	10	10	10	10
DES 5 ppb	Mean	33.6	49.9	7.4*	0.075*	1.52*
	sem	0.8	1.2	0.1	0.004	0.10
	n	10	10	10	10	10
DES 10 ppb	Mean	33.5	46.9	6.0	0.121***	2.57***
	sem	0.9	2.5	0.1	0.012	0.20
	n	10	10	10	10	10
DES 20 ppb	Mean	32.6	44.5	5.7	0.211***	4.63***
	sem	0.6	2.4	0.0	0.024	0.36
	n	10	10	10	10	10

Statistics
Body weight: CoVar + Dunnett's tests (two-sided): * P<0.05; ** P<0.01; *** P<0.001
Uterus weight: Mann/Whitney u-test (two-sided): * P<0.05; ** P<0.02; *** P<0.002
Food consumption: Anova + L.S.D. tests (two-sided): * P<0.05; ** P<0.01; *** P<0.001

Appendix 1 - Oestrogenic activity (Tiecco test) of F2LS250 in rats; individual and mean-body weights, food consumed and absolute and relative uterus weights obtained in the range-finding study (assay no. 1794)

Treatment group		Animal No.	Day 0 Body Wgt g	Day 4 Body Wgt g	Day 4 ConsFood g	Day 4 Uterus g	Day 4 Uterus g/kg BW
Neg.Control	A	1	33.3	49.3	7.9	0.067	1.28
	A	3	33.0	50.5	7.9	0.079	1.56
	A	5	35.2	53.4	7.9	0.072	1.35
	A	7	31.4	47.7	7.9	0.056	1.17
	A	9	33.8	50.6	7.9	0.062	1.22
Neg.Control		Mean	33.3	50.3	7.9	0.066	1.32
		sem	0.6	0.9	0.0	0.004	0.07
		n	5	5	5	5	5
1 PPM	B	11	33.4	49.9	7.1	0.058	1.16
	B	13	33.0	49.5	7.1	0.069	1.39
	B	15	34.6	48.6	7.1	0.055	1.13
	B	17	31.7	48.3	7.1	0.077	1.59
	B	19	33.7	50.6	7.1	0.082	1.62
1 PPM		Mean	33.3	49.4	7.1	0.068	1.38
		sem	0.5	0.4	0.0	0.005	0.10
		n	5	5	5	5	5
10 PPM	C	21	33.1	49.0	7.6	0.066	1.35
	C	23	32.7	49.5	7.6	0.053	1.07
	C	25	35.4	53.4	7.6	0.054	1.01
	C	27	31.0	47.4	7.6	0.063	1.33
	C	29	33.6	52.1	7.6	0.096	1.84
10 PPM		Mean	33.2	50.3	7.6	0.066	1.32
		sem	0.7	1.1	0.0	0.008	0.15
		n	5	5	5	5	5
100 PPM	D	31	33.5	49.1	7.4	0.095	1.93
	D	33	32.6	50.2	7.4	0.085	1.69
	D	35	34.2	52.2	7.4	0.096	1.84
	D	37	31.7	46.6	7.4	0.067	1.44
	D	39	34.2	51.5	7.4	0.088	1.71
100 PPM		Mean	33.2	49.9	7.4	0.086*	1.72**
		sem	0.5	1.0	0.0	0.005	0.08
		n	5	5	5	5	5
1000 PPM	E	41	33.3	49.7	6.6	0.247	4.97
	E	43	32.3	46.3	6.6	0.130	2.81
	E	45	35.9	50.0	6.6	0.266	5.32
	E	47	32.3	43.2	6.6	0.265	6.13
	E	49	34.1	47.3	6.6	0.247	5.22
1000 PPM		Mean	33.6	47.3	6.6	0.231***	4.89***
		sem	0.7	1.2	0.0	0.026	0.55
		n	5	5	5	5	5

Statistics
Body weight: Covar + Dunnett's tests (two-sided): * P<0.05; ** P<0.01; *** P<0.001
Uterus weight: Mann/Whitney u-test (two-sided): * P<0.05; ** P<0.02; *** P<0.002
Food consumption: Anova + L.S.D. tests (two-sided): * P<0.05; ** P<0.01; *** P<0.001

Appendix 1 - Oestrogenic activity (Tiecco test) of F2L5250 in rats; individual and mean body weights, food consumed and absolute and relative uterus weights obtained in the range-finding study (assay no. 1794)

Treatment group		Animal No.	Day 0 Body Wgt g	Day 4 Body Wgt g	Day 4 Food Consumed g	Day 4 Uterus g	Day 4 Uterus g/kg BW
BASAL DIET	A	1	33.4	48.6	6.6	0.047	0.97
	A	3	35.3	49.2	6.6	0.055	1.12
	A	5	36.7	52.1	6.6	0.068	1.31
	A	7	35.2	52.9	6.6	0.072	1.36
	A	9	31.4	43.4	6.6	0.060	1.38
	A	11	33.2	40.8	6.0	0.057	1.17
	A	13	31.0	41.1	6.0	0.034	0.83
	A	15	32.0	48.4	6.0	0.073	1.51
	A	17	36.2	54.6	6.0	0.075	1.37
	A	19	31.0	44.6	6.0	0.051	1.14
BASAL DIET		Mean	33.6	48.4	6.3	0.059	1.22
		sem	0.7	1.4	0.1	0.004	0.07
		n	10	10	10	10	10
10 PPM	B	21	35.9	51.7	6.3	0.052	1.02
	B	23	30.9	45.9	6.3	0.053	1.15
	B	25	33.3	50.3	6.3	0.055	1.09
	B	27	26.6	40.5	6.3	0.058	1.43
	B	29	32.3	48.9	6.3	0.066	1.35
	B	31	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	B	33	30.5	43.8	6.4	0.039	0.89
	B	35	32.0	48.4	6.4	0.066	1.36
	B	37	34.0	45.7	6.4	0.049	1.07
	B	39	29.0	48.7	6.4	0.048	0.99
10 PPM		Mean	31.8	47.3	6.4	0.056	1.18
		sem	0.8	1.1	0.0	0.003	0.06
		n	10	10	10	10	10
20 PPM	C	41	33.4	48.2	6.1	0.054	1.12
	C	43	32.0	47.7	6.1	0.079	1.66
	C	45	30.7	41.5	6.1	0.054	1.29
	C	47	28.3	41.9	6.1	0.057	1.36
	C	49	30.3	44.8	6.1	0.056	1.25
	C	51	36.7	49.8	5.1	0.052	1.04
	C	53	36.2	49.1	5.1	0.064	1.30
	C	55	32.5	41.3	5.1	0.051	1.23
	C	57	27.2	7 12 February 1996			
	C	59	36.2	46.6	5.1	0.064	1.37
20 PPM		Mean	32.4	45.7	5.7	0.059	1.29
		sem	1.1	1.1	0.2	0.003	0.06
		n	10	9	9	9	9
40 PPM	D	61	32.5	48.1	7.4	0.061	1.27
	D	63	36.8	52.9	7.4	0.079	1.49
	D	65	34.5	51.0	7.4	0.057	1.12
	D	67	32.8	48.7	7.4	0.058	1.19
	D	69	36.0	52.8	7.4	0.071	1.35
	D	71	30.2	42.9	6.6	0.056	1.31
	D	73	29.9	45.8	6.6	0.054	1.18
	D	75	32.6	48.6	6.6	0.077	1.58
	D	77	34.8	52.3	6.6	0.062	1.19
	D	79	30.6	45.9	6.6	0.054	1.18
40 PPM		Mean	33.1	48.8	7.0	0.060	1.29
		sem	0.8	1.1	0.1	0.003	0.05
		n	10	10	10	10	10

Statistics
Body weight: Covar + Dunnett's tests (two-sided): * P<0.05; ** P<0.01; *** P<0.001
Uterus weight: Mann/Whitney u-test (two-sided): * P<0.05; ** P<0.02; *** P<0.002
Food consumption: Anova + L.S.D. tests (two-sided): * P<0.05; ** P<0.01; *** P<0.001

Appendix 1 - Oestrogenic activity (Tiecco test) of PZL5250 in rats; individual and mean body weights, food consumed and absolute and relative uterus weights obtained in the main study (assay no. 1795); continued

Treatment group		Animal No.	Day 0 Body Wgt g	Day 4 Body Wgt g	Day 4 ConsFood g	Day 4 Uterus g	Day 4 Uterus g/kg BW
80 PPM	E	81	37.8	53.2	7.5	0.087	1.64
	E	83	36.9	53.3	7.8	0.065	1.22
	E	85	38.4	54.7	7.5	0.087	1.59
	E	87	33.0	46.6	7.5	0.090	1.93
	E	89	36.4	50.8	7.5	0.067	1.32
	E	91	32.6	46.7	6.6	0.056	1.20
	E	93	34.0	49.5	6.6	0.079	1.60
	E	95	31.8	47.2	6.6	0.077	1.63
	E	97	37.9	55.9	6.6	0.069	1.23
	E	99	29.9	44.3	6.6	0.051	1.15
80 PPM		Mean	34.9	50.2	7.0	0.073	1.45
		sem	0.9	1.3	0.2	0.004	0.08
		n	10	10	10	10	10
160 PPM	F	101	34.2	51.1	6.8	0.108	2.11
	F	103	32.9	49.2	6.8	0.101	2.05
	F	105	35.5	54.0	6.8	0.132	2.44
	F	107	30.6	38.1	6.8	0.088	2.31
	F	109	31.9	46.4	6.8	0.112	2.41
	F	111	38.2	56.1	7.2	0.080	1.43
	F	113	34.3	46.9	7.2	0.097	2.07
	F	115	33.4	49.1	7.2	0.068	1.38
	F	117	36.4	54.0	7.2	0.081	1.49
	F	119	30.5	44.1	7.2	0.142	3.22
160 PPM		Mean	33.8	48.9	7.0	0.101***	2.08***
		sem	0.8	1.7	0.1	0.007	0.18
		n	10	10	10	10	10

Statistics
Body weight: Covar + Dunnett's tests (two-sided): * P<0.05; ** P<0.01; *** P<0.001
Uterus weight: Mann/Whitney u-test (two-sided): * P<0.05; ** P<0.02; *** P<0.002
Food consumption: Anova + L.S.D. tests (two-sided): * P<0.05; ** P<0.01; *** P<0.001

Appendix 1 - Oestrogenic activity (Tiecco test) of DES in rats; individual and mean body weights, food consumed and absolute and relative uterus weights obtained in the main study (assay no. 1795); continued

Treatment group		Animal No.	Day 0 Body Wgt g	Day 4 Body Wgt g	Day 4 ConsFood g	Day 4 Uterus g	Day 4 Uterus g/kg BW
DES -5 ppb	G	121	36.1	58.0	7.1	0.073	1.40
	G	123	32.3	46.4	7.1	0.094	2.03
	G	125	32.8	46.1	7.1	0.081	1.76
	G	127	34.0	50.3	7.1	0.070	1.39
	G	129	30.9	46.2	7.1	0.069	1.49
	G	131	35.1	51.9	7.6	0.073	1.41
	G	133	30.5	46.7	7.6	0.056	1.20
	G	135	27.0	55.0	7.6	0.075	1.36
	G	137	36.4	56.1	7.6	0.062	1.11
	G	139	30.4	48.1	7.6	0.100	2.08
DES 5 ppb		Mean	33.6	49.9	7.4*	0.075*	1.52*
		sem	0.8	1.2	0.1	0.004	0.10
		n	10	10	10	10	10
DES 10 ppb	M	141	33.1	49.4	6.2	0.120	2.43
	M	143	37.8	55.3	6.2	0.120	2.17
	M	145	33.6	50.0	6.2	0.175	3.50
	M	147	33.0	49.4	6.2	0.145	2.94
	M	149	32.4	27.7	6.2	0.070	2.53
	M	151	33.8	48.4	5.8	0.073	1.51
	M	153	33.2	48.3	5.8	0.089	1.84
	M	155	36.8	54.9	5.8	0.185	3.37
	M	157	31.5	44.1	5.8	0.105	2.38
	M	159	27.9	41.3	5.8	0.126	3.05
DES 10 ppb		Mean	33.5	46.9	6.0	0.121***	2.57***
		sem	0.9	2.5	0.1	0.012	0.20
		n	10	10	10	10	10
DES 20 ppb	I	161	28.4	37.8	5.6	0.090	2.38
	I	163	32.3	41.8	5.6	0.134	3.21
	I	165	31.7	47.4	5.6	0.283	5.97
	I	167	32.9	49.2	5.6	0.288	5.85
	I	169	38.4	47.3	5.7	0.223	4.74
	I	171	33.8	48.5	5.7	0.230	4.74
	I	173	32.9	45.7	5.7	0.222	4.86
	I	175	35.0	50.9	5.7	0.250	4.91
	I	177	34.4	49.9	5.7	0.282	5.65
	I	179	31.2	26.5	5.7	0.106	4.00
DES 20 ppb		Mean	32.6	44.5	5.7	0.211***	4.63***
		sem	0.6	2.4	0.0	0.024	0.36
		n	10	10	10	10	10

Statistics
Body weight: Cavar + Dunnett's tests (two-sided): * P<0.05; ** P<0.01; *** P<0.001
Uterus weight: Mann/Whitney u-test (two-sided): * P<0.05; ** P<0.02; *** P<0.002
Food consumption: Anova + L.S.D. tests (two-sided): * P<0.05; ** P<0.01; *** P<0.001

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