

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

ENDOTHALL

Chemical Code # 000260, Tolerance # 00293
SB 950 # 072

October 9, 1987
Revised 6/30/89, 1/16/92, 12/7/94, 10/25/95

I. DATA GAP STATUS

Chronic rat:	No data gap, no adverse effect
Chronic dog:	No data gap, possible adverse effect
Oncogenicity rat:	No data gap, possible adverse effect
Oncogenicity mouse:	No data gap, possible adverse effect
Reproduction rat:	No data gap, no adverse effect
Teratology rat:	No data gap, no adverse effect
Teratology mouse:	No data gap, no adverse effect
Gene mutation:	No data gap, no adverse effect
Chromosome effects:	No data gap, possible adverse effect indicated
DNA damage:	No data gap, no adverse effect
Neurotoxicity:	Not required at this time

-----**Note,**

Toxicology one-liners are attached

For the purpose of filling data gaps, Endothall (SB-072, tolerance #00293) has been grouped with endothall mono (N,N-dimethylalkylamine) salt (SB668, tolerance # 50755), endothall mono (N,N-diethylalkylamine) salt (SB667, tolerance # 50756) and endothall dipotassium salt (SB669, tolerance # 50757). The studies submitted to fill "SB-950" data requirements were conducted primarily with endothall free acid, or more commonly, with disodium or dipotassium salts. These submissions were submitted under tolerance numbers 00293 and 50755.

In "one-liner headings below:

** indicates acceptable study

Bold face indicates possible adverse effect

A one-liner is entered in the toxicology summary and more details will be present in individual worksheets.

File name: T951025

C. Aldous, 1/16/92; P. Iyer, 8/15/95, 10/25/95

Reconciled with library listing through volumes 293-059 (record number 126192, 293-060 135473), 50755-006 (record number 130115) and 50755-005 (record numbers 129866 and 129867).

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

COMBINED (chronic + oncogenicity), RAT

****293-049 073791** MacKenzie, K.M., "Combined Chronic Toxicity and Carcinogenicity Study in Rats", (Hazleton Laboratories America, Inc., report # HLA 6120-110 and HLA 6120-110A, 2/25/89), disodium endothall, 12.6% acid equivalent, lot numbers N.B. 136-88-1, N.B. 149-45-2, and N.B. 158-59-1. Study was performed in two phases, HLA 6120-110 and HLA 6120-110A. HLA 6120-110: fed in the diet for 104 weeks to 62 Crl:CD(SD)BR rats/sex/group at nominal concentrations of 0, 300, 900, and 1800 ppm with interim necropsies of 10/sex/group at 52 weeks. HLA 6120-110A: fed in the diet to 50 Crl:CD(SD)BR rats/sex/group at nominal concentrations of 0 and 150 ppm for 104 weeks. Actual concentrations were about 18% lower than nominal in both phases of the study. **Possible adverse effect:** (increase of endometrial stromal tumors in 900 and 1800 ppm females: see also review for 053:099091, below). Lesions of glandular and non-glandular stomach were common at higher doses, but were eventually determined to have NOELs of 150 ppm for females and 300 ppm for males. Initially it appeared that there was no NOEL for stomach lesions in males, based on the original pathologists' assessments. This and several other concerns of the 1989 CDFA review were addressed in 053:099091; see below. Nominal NOEL for other effects was 150 ppm in females (dose-related body weight decrements). There was no clear body weight effect NOEL in males (body weight decrements were dose-related at the higher two dosages, and there were small but statistically significant body weight decrements at 150 and 300 ppm, however 300 ppm is a defensible NOAEL for body weight reduction in males). ACCEPTABLE. (Green/Aldous, 6/21/89; Aldous, 1/16/92).

293-053 099091 Addendum to 293-049:073791. Addendum was completed Oct. 10, 1991 [Addendum is identified as HLA 6120-110B]. New data responded to each of the 5 principal concerns of the 1989 CDFA review. A re-evaluation of slides of glandular and non-glandular stomach identified NOELs of 150 ppm for females and 300 ppm for males for changes in these tissues. Historical control incidence data for endometrial stromal polyps plus endometrial stromal sarcomas were provided. Historical control incidence of the combined endometrial stromal tumors was sufficiently low (0 incidence in 10 of 12 studies) that the incidence in 900 and 1800 ppm females in this study (4/60 and 5/59, respectively) should be considered a possible treatment effect, therefore a "**possible adverse effect**". The study is upgraded to ACCEPTABLE status. Aldous, 1/16/92.

293-018, 029, 030, 031, 032, 033, 034, 035, 036, 037 014332, 014371 through 014382, "Two-Year Chronic Oral Toxicity and Carcinogenic Study with Dipotassium Endothall Monohydrate or Disodium Endothall in Albino Rats." (IBT, 6/3/75) Invalid IBT study. Changed from dipotassium salt to disodium salt at week 20. (J. Remsen (Gee), 4/26/85)

CHRONIC, RAT

293-015 019204 "Endothall, Long-Term Oral Toxicity Test on Rats." (Jefferson Medical College, 5/6/53) Endothall (no purity stated, not described) fed to Wistar rats in the diet at levels equal to 0, 2, 6, 20 or 50 mg/day, 10/sex/group. NOEL estimated as 1000 ppm (slightly decreased weight gain) Study terminated at 27 months. No adverse effect indicated. UNACCEPTABLE. - Too few animals to do meaningful statistics on tumor formation, high dose showed little toxicity, test material not described. Not upgradeable. (J. Remsen (Gee), 4/22/85)

293-004, 007 031710 Brief summary of 015 019204.

293-010 031715 Summary statement of 015 019204.

293-015 019203 Summary of 015 019204.

293-017 014226 Summary of a 15 month rat study (endothall in the drinking water).

CHRONIC, DOG

****293-046 068571**, "Disodium Endothall, 52 Week Oral (Dietary) Toxicity Study in Dogs", (Inveresk Research International (IRI) Limited, Project ID IRI 632934, 6/4/87). Disodium endothall, 16.1% acid equivalent, lot # 144-77-II, fed in the diet to 4 Beagle dogs/sex/group 7 days/week for 52 weeks at 0, 150, 450, and 1350/1000 ppm (reduced from 1350 ppm to 1000 ppm from week 7 due to anorexia and bodyweight loss). No NOEL was achieved: stomach epithelial hyperplasia was observed in mild or very mild degree down to the lowest dosage of 150 ppm. At 450 ppm and above, other alimentary epithelial tissues were affected (especially esophagus), and effects on liver parenchymal and bile ductule cells were seen at 450 ppm and above. The 1000 ppm dose was not tolerated: five of 8 of these dogs were killed in extremis. The stomach lesions constitute a **"possible adverse effect"** because there was no NOEL, however meaningful risk assessment is possible with existing data. The study is ACCEPTABLE. (H. Green and C. Aldous, 6/29/89)

293-045 068570 Dose range finding study for 046:068571, above. A summary of this study, prepared by H. Green, is included in background section of the CDFA review of 046:068571.

293-015 019205 "Two-Year Chronic Feeding of Disodium Endothall to Beagle Dogs." (Scientific Associates, 6/4/65) Disodium endothall, 19.3% in water, was mixed in the diet and fed to beagles, 3/sex/group, for 2 years at 0, 100, 300 or 800 ppm. NOEL estimated as 800 ppm. No adverse effect indicated. UNACCEPTABLE. -High dose too low but was increased in several increments to 2000 ppm (50 mg/kg) from months 20 - 23 with a decrease in weight; histology reported is minimal at best except in high dose and control, no ophthalmological exam, no justification of dose selection. Not upgradeable. (J. Remsen (Gee), 4/22/85)

293-004, 007 031711 Brief summary of 015 019205.

293-010 031716 Short summary of 015 019205.

ONCOGENICITY, MOUSE

293-019 to 027 014342, 014346, 013115, 013116, 013117, 013125 through 013131, "24-Month Feeding Study of Disodium Endothall (15.8% active) in CD1 Mice." (Cannon Laboratories, 6/22/79) Disodium endothall, 15.8%, was fed in the diet to CD1 mice for 72 weeks at 0, 300, 600 or 1200 ppm, 50/sex/group for 24 months. Possible **adverse effect** indicated: internal masses present in tissues including stomach and liver. Nominal systemic NOEL = 600 ppm. UNACCEPTABLE. Major problem is lack of analysis of diet and statement of composition. (J. Remsen (Gee), 4/25/85)

293-015 019196 Summary of 019 to 027 014342, 014346, 013115, 013116, 013117, 013125 through 013131.

293-047 068594, "18-Month Oncogenicity Study in Mice with Disodium Endothall", (WIL Research Laboratories, Inc., project # WIL-75009, 5/31/88). Endothall Disodium Salt, nominally 15.6% a.i., N.B. 136-88-1, fed in the diet at nominal concentrations of 0, 50, 100, and 300 ppm to 50 CrI:CD-1(ICR)BR mice/sex/group for 92 weeks (an additional 10/sex/dose were designated for 12-month interim sacrifice). Systemic NOEL = 100 ppm (Decreased mean body weight in 300 ppm males; 6% maximum decrease compared to control values; minimal to mild multifocal mineralization in kidneys of males at 300 ppm). **Possible adverse effect indicated** (slight increase in

hepatocellular tumor incidence in 300 ppm males). UNACCEPTABLE, unlikely to be upgradeable (dosage levels were not justified, and appeared to be below the MTD: see discussion section of 6/23/89 review for other concerns). (Green/C. Aldous 6/23/89).

060 135473: J.A. Trutter, "18-Month Dietary Oncogenicity Study in Mice with Disodium Salt of Endothal", Hazleton Washington, Inc., HWA 153-151, (3/2/95). Disodium Salt of Endothal, purity 19.0 to 23.1%, was admixed with the feed at concentrations of 0, 750 and 1500 ppm and fed to 60 CrI:CD-1* (ICR)BR albino mice/sex/group for at least 78 weeks. Endothal targets the gastrointestinal tract. Effects include **mucosal hyperplasia and glandular dilatation in the glandular stomach at 750 ppm and 1500 ppm; mucosal hyperplasia in the duodenum** and proplases of the rectum at 1500 ppm. **Increased incidence of tumors (in duodenum and jejunum)** for the high dose group. Survival decreased for the high dose group (46-49 % at 60 weeks). NOEL < 750 ppm in this study. Acceptable as supplemental study. Not upgradeable (too few dose levels, low dose not low enough). This study by itself does not fill the data gap, however, since this study satisfies the MTD requirement, collective data from previous studies (293 047 068594) support a NOEL = 100 ppm (Kishiyama, J and P. Iyer 9/27/95).

REPRODUCTION, RAT

** 293-059 126192, 50757 138412, 138416, "Two-Generation Reproductive Study in Rats with Disodium Salt of Endothall", (J.A. Trutter, Hazleton Washington, Inc., HWA Study No. 153-142, 9/15/93, 6/5/95). Disodium salt of endothall, 19.9% a.i (16.1% endothall acid equivalent) was admixed with the feed at concentrations of 0, 30, 150 or 900 ppm and fed to two generations of 26 Charles river rats/sex/group. The F1 generation was bred twice (number of litters/group was lower in control and low-dose groups in both matings) with a rest phase (approximately 6 weeks) between matings. A reduction in body weight was noted at the high dose for both the F0 and F1 parental generations as well as in the F1-2a and F1-2b pups. NOAEL = 150 ppm/day. Initially reviewed as UNACCEPTABLE. Upgraded upon submission of certificate of analysis identifying ingredients of test article formulation. Technical grade of the test article was probably not used because the dietary concentrations prepared were adjusted to 100% using a factor of 19.2% for the active ingredient of the disodium salt of Endothall. Individual data for pairing and results submitted demonstrate that the reduced number of pregnancies in the control and 30 ppm group for both the F1 matings (F2a and F2b generation) were probably linked to specific animals. ACCEPTABLE. No adverse effects (P. Iyer, 8/16/95).

293-015 019189 "Final Report for Three-Generation Reproduction Study in Rats on Disodium Endothall." (Biological Research Service, 12/15/65). Disodium endothall, 19.2% in water, was fed in diet to Sprague Dawley rats at 0, 100, 300 or 2500 ppm for 3 generations, 2 litters/ generation. Ten males and 20 females per dose level, mated 2 males with 4 females per cage. Maternal NOEL = 300 ppm (numerous effects); Developmental Toxicity = 100 ppm (decreased litter size at 2500 ppm in F1A, F1B, F2A and F2B generations and increased mortality in F3A and F3B litters at 300 ppm.) **Possible adverse effects indicated:** increased mortality in F3A and F3B litters at 300 ppm. Other adverse effects in adults include kidney discoloration, P1, at 2500 ppm, pale colored adrenals in P1 at 2500 ppm. UNACCEPTABLE. No analysis of diets, no individual data, housed two males and four females per cage for mating, necropsy on 10 randomly chosen animals. Not upgradeable. (J. Remsen (Gee), 4/22/85. A CDFA response of 10/09/87 by Parker and Gee to a rebuttal dated January 13, 1987, in package SBCS 102054-E., confirmed that the study was not upgradeable.)

293-010 031717 Brief summary of 015 019189.

293-015 019201 Summary of 015 019189.

TERATOLOGY, RAT

** 293-038 014383 "Teratology and Postnatal Behavioral A study of Endothall Technical in Albino Rats." (Science Applications Inc., 11/11/82) Endothall technical, 89.5% acid equivalent, lot 84-33, was given by gavage to pregnant Sprague Dawley rats on days 6-19 of gestation at 0 (water), 10, 20 or 30 mg/kg/day, 25/group. Maternal NOEL = 20 mg/kg (mortality but no cause of death), Developmental NOEL > 30 mg/kg. Additional dams were allowed to deliver and the physical development and behavior of the offspring observed. There were inconsistent results in pivoting locomotion at 20 and 30 mg/kg. No other effects were noted for development. No adverse effect. ACCEPTABLE. (J. Remsen (Gee), 4/29/85 and J. Parker, 7/29/86)

293-038 014384 Range finding study for 038 014383 at doses of 10 - 50 mg/kg.

293-019 014341, 014349 "Report: Teratologic Evaluation of Endothall Technical in Rats." (Food and Drug Research Labs, 11/11/76) Endothall technical, 89.5% acid equivalent, was given to pregnant Wistar rats by gavage on day 6-15 of gestation at 0 (water), .01, .15 or 2.0 mg/kg/day, 20/group. Maternal NOEL > 2 mg/kg (HDT), Developmental NOEL > 2 mg/kg (HDT). No adverse effect indicated. UNACCEPTABLE. No evidence MTD was reached. Not upgradeable. (J. Remsen (Gee) and J. Parker, 4/25/85 and 7/29/86)

TERATOLOGY, MICE

** 293-020 013122, 013124, "Teratology Study in Mice (Endothall)." (International Research and Development Corp, 7/2/81) Endothall technical, 89.5% mixed at 75% active with 25% vehicle of blended whole egg and deionized water, dosing solutions were prepared every 4 days; given to CD-1 mice by gavage on days 6 to 16 of gestation at dose levels of 0 (water), 5, 20 or 40 mg/kg/day, 25/group. Maternal NOEL = 5 mg/kg (mortality from unknown cause in 7 of 8 deaths at 40 mg/kg and 2 of 2 at 20 mg/kg), Developmental NOEL = 20 mg/kg. The number of malformations in the high dose group (total of 16 - 9.1% in 6 litters) was increased over the controls (4 - 1.8% in 3 litters) but was attributed to the severe maternal toxicity as shown by mortality and were stated not to be statistically significant. Initially reviewed as having a possible adverse developmental effect but reconsideration of the data as discussed above indicates the effects were noted in the presence of maternal toxicity. No adverse effect. ACCEPTABLE. (J. Remsen (Gee), 4/26/85 and 10/8/87)

293-020 013123 Range finding study for 020 013122, 013124 at 5, 10, 20 and 60 mg/kg to pregnant mice.

293-020 013121 Range finding study for 020 013123.

TERATOLOGY, RABBIT

Addendum II of 13122 contains a memorandum dated August 25, 1980, from Obren Keckemet of Pennwalt in which it is stated that EPA requested a teratology study in a second species. In the range-finding study at IRDC, it was established that rabbits were extremely susceptible to endothall with deaths occurring at < 20 mg/kg. Changing vehicles from water/methocel to propylene glycol/corn oil did not result in improvement. Mice were selected as the animal of choice. (J. Gee, 10/9/87)

GENE MUTATION

Microbial systems

293-019 014339 "Evaluation of Herbicides for Possible Mutagenic Properties." (publication in J. Agr. Food Chem. 20: 649 - 656 (1972), Columbus Laboratories, Battelle Memorial Institute) Endothall, not described but apparently free acid, was spread into the top agar on a plate to test S. typhimurium

(strains not identified) and E.coli B T4 bacteriophage for mutagenicity. Tested 110 compounds. No increase in mutation indicated. UNACCEPTABLE. No activation, very limited information - data presented as (-). (J. Remsen (Gee), 4/25/85)

** 293-020 013118 "Activity of YT1604 (Endothall) in the Salmonella/ Microsome Assay for Bacterial Mutagenicity." (Microbiological Assoc., 4/29/80) Endothall, 89.5%, was tested with S. typhimurium strains TA1535, TA1537, TA1538, TA98 and TA100 at 0, 0.05, 0.15, 0.5, 1.5 or 5.0 mg/plate in the direct plate assay done in triplicate, with and without activation. No increase in reversion indicated. ACCEPTABLE. (J. Remsen (Gee), 4/25/85)

** 50755 005 129867, "Ames/Salmonella Plate Incorporation Assay on Technical Endothal Amine Salt Solution", (Leon F. Stankowski, Jr., Pharmakon Research International, Inc., PA., Report # PH 301-ANA-001-92, 10 December 1993). The test article is identified as technical endothal amine salt solution mono(N,N-dimethylalkylamine) salt (1.5:1 amine:salt ratio) with acid equivalence purity of 11.6%. Salmonella typhimurium strains TA98, TA100, TA1535, TA1537, and TA1538 were exposed in the presence and absence of activation, in triplicate, at 0 (DMSO), 0.580, 1.93, 5.80, 19.3, 58.0, 116.0, or 193.0 acid equivalent $\mu\text{g}/\text{plate}$ for 48 hours. A slight increase in the reversion rate (less than 3 fold over negative control values), was noted for strains TA1537 and TA1538. However, the increase in revertant frequencies were within historical control ranges in all except one case (2.2 fold control value for TA 1538 without S9). Results were considered equivocal and not indicative of mutagenicity in this assay. **Acceptable** (H. Green and P. Iyer 3/28/94).

Mammalian systems

293-020 013120 "Activity of T1604 (Endothall) in the in vitro Mammalian Cell Point Mutation Assay in the Presence of Exogenous Metabolic Activation." (Microbiological Associates, 6/26/80) Endothall, 89.5%, was tested with BALB 3T3 clone A31 cells with exogenous activation at 0.01, 0.1 or 1 $\mu\text{g}/\text{ml}$, plated in triplicate. No mutagenicity to ouabain resistance was found. UNACCEPTABLE. No repeat trial and by guidelines, survival should have been reduced much more at highest concentration used. (J. Remsen (Gee), 4/26/85)

293-020 013119 "Activity of T1604 (Endothall) in the in vitro Mammalian Cell Point Mutation Assay in the Absence of Exogenous Metabolic Activation." (Microbiological Associates, 6/26/80) Endothall, 89.5%, was tested with BALB 3T3 clone A31 cells in the absence of exogenous activation at 0.5, 1, 3 or 10 $\mu\text{g}/\text{ml}$, plated in triplicate. No increase in mutation frequency for ouabain resistance. UNACCEPTABLE. High concentration did not decrease survival sufficiently, no repeat trial. See 013120 for assay with activation. (J. Remsen (Gee), 4/25/85)

** 50755 005 129866, "AS52/XPRT Mammalian Cell Forward Gene Mutation Assay on Technical Endothal Amine Salt Solution", (Leon F. Stankowski, Jr., Pharmakon Research International, Inc., PA., Report # PH 314-ANA-001-92, 12/10/93). The test article is identified as technical endothal amine salt solution (mono(N,N-dimethylalkylamine) salt of endothal (1.5:1 amine:salt ratio) as 11.6% acid equivalent. AS52 (clone -1.3) Chinese hamster ovary cells were exposed (5 hours) in duplicate without activation at 0 (untreated), 0 (DMSO), 0.0116, 0.0580, 0.116, 0.580, 1.160, 2.320, 2.900, 3.480, 4.060, and 4.640 $\mu\text{g}/\text{ml}$ and with activation at 0 (untreated), 0 (DMSO), 0.116, 0.580, 1.160, 5.800, 11.600, 17.400, 20.300, 21.800, 23.200, 26.100, and 29.000 $\mu\text{g}/\text{ml}$. Evidence of cytotoxicity was seen at 5.80 $\mu\text{g}/\text{ml}$ and above without activation and at 26.10 $\mu\text{g}/\text{ml}$ and above with activation. **Increased forward gene mutation is not indicated. Acceptable.** (H. Green and P. Iyer, 3/23/95).

SUMMARY: Collectively, the data with endothall do not indicate it causes gene mutations in Salmonella or in mammalian cells.

50755-006 130115, "In Vivo Micronucleus Test on Technical Endothal Amine Salt Solution in Mouse Marrow Erythropoietic Cells" J.R. SanSebastian, Pharmacon Research International., Waverly, PA. Report No: 309-ANA-001-92 (7 Jan 1994). was used. CD-1 mice (15/sex/group) received a single treatment of 0 (deionized water), 0.464, 0.928 and 1.86 mg/kg bodyweight of technical endothal amine salt solution (amine:salt ratio of 1.5:1; Batch #B46-44-1) via intraperitoneal injection in a volume of 10 ml/kg. The positive control group (5/sex/group) was given triethylenemelamine - TEM (0.5 mg/kg) and sampled at 24 hours after treatment. The animals were killed (5 per sex/group) and samples collected 24, 48 and 72 hours after treatment. **No increase in micronuclei in the polychromatic erythrocytes was observed. Acceptable. (P. Iyer, 12/7/94).

50755-002 112419, "In Vitro Assessment of the Clastogenic Activity of Endothall Technical in Cultured Human Lymphocytes", (J. Bootman, et al., Life Science Research Limited, U.K., Report # 88/0666, 3/28/89). Endothall Technical purity, 89.4% (lot B14-37). The *in vitro* cytogenetics assay was performed in triplicate with human male peripheral blood lymphocytes at concentrations of 0 (DMSO and untreated), 2.5, 10.0, 20.0 and 40.0 ug/ml without activation and at 0 (DMSO and untreated), 15.0, 60.0, 120.0 and 240.0 ug/ml in the presence of activation. **An increase in chromosomal aberrations was not observed, but an increase in polyploidy was noted at the high exposure levels both in the presence and absence of bioactivation).** Unacceptable, but upgradeable with identification of test material (H. Green, and P. Iyer, 2/17/94).

50755-002 112418, "Endothall Technical: Assessment of Clastogenic Action on Bone Marrow Erythrocytes in the Micronucleus Test", (J.M. Mackay, Life Science Research, U.K., Report # 89/PSV034/0044, 11 May 1989). Endothall Technical (lot B14-37), 89.4% unverified purity, was used. CD-1 mice received a single treatment of 0 (0.9% saline), 2, 10, or 50 mg/kg orally by gavage. The low and mid-dose groups (5 per sex per group) were killed at 24 hours after treatment and sampled; the control and high dose groups (15 per sex per group) were killed (5 per sex/group) and samples collected 24, 48 and 72 hours after treatment. The positive control group was given chlorambucil (30 mg/kg) and sampled at 24 hours after treatment. **No increase in micronuclei in the polychromatic erythrocytes was observed. Unacceptable,** upgradeable with submission of test article identification (H. Green, and P. Iyer, 2/15/94).

293-019 014347 "Rat Bone Marrow Cytogenetic Analysis Disodium Endothall." (Litton Bionetics Inc, 1/77) Endothall, 15.8% acid equivalent, was given to Sprague Dawley rats in their feed on five consecutive days at 0, 150, 300 or 600 ppm, 5 males/group. No increase in micronuclei indicated. UNACCEPTABLE. An additional time point should have been included, no females in study without justification, inadequate number of animals, doses too low. Not upgradeable. (J. Remsen (Gee), 4/25/85)

293-019 014348 "Mutagenicity Evaluation of Rat Dominant Lethal Assay Disodium Endothall." (Litton Bionetics Inc., 1/77) Disodium Endothall, 15.8% acid equivalent was given to Sprague Dawley rats in their diet for 5 consecutive days at 0, 150, 300 or 600 ppm, 10 males/group, mated to 2 females per week for 7 weeks. Triethylene melamine as positive control. No dominant lethal effect indicated. UNACCEPTABLE. High dose showed no toxicity, therefore too low. Too few females per group for evaluation. Not upgradeable. (J. Remsen (Gee), 4/25/85)

DNA DAMAGE

**293-048 073540, "Endothall Technical: Assessment of Its Ability to Cause Lethal DNA Damage in Strains of *Escherichia coli*", (Life Science Research Limited, report # 88/0656, 12/9/88), Endothall technical, batch no. B14-37, 89.4% purity, liquid suspension assay in duplicate with and without S9 activation (Aroclor 1254-induced male CD rat liver fraction) using *Escherichia coli* WP2, WP67 (uvrA and polA repair deficient), and CM871 (uvrA, recA and lexA repair deficient) at concentrations of 0 (DMSO), 100, 316, 1000, 3160, and 10000 µg/ml with 2 and 18 hour incubation periods. No

evidence of DNA damage. ACCEPTABLE (Green/J. Gee, 6/30/89)

293-050 086133 Exact duplicate of 048:073540, above.

NEUROTOXICITY

Not required at this time.