CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
HUMAN HEALTH ASSESSMENT BRANCH

SUMMARY OF TOXICOLOGY DATA

Terbutryn

Chemical Code #1691**, Document Processing Number (DPN)** 265
SB 950 # 205
8/19/15
12/2/15

DATA GAP STATUS

Chronic toxicity, rat:	No data gap, no adverse effect indicated
Chronic toxicity, dog:	Data gap, no study submitted
Oncogenicity, rat:	No data gap, possible adverse effect indicated
Oncogenicity, mouse:	Data gap, no study submitted
Reproduction, rat:	No data gap, no adverse effect indicated
Developmental toxicity, rat:	No data gap, no adverse effect indicated
Developmental toxicity, rabbit:	Data gap, no study submitted
Gene mutation:	No data gap, no adverse effect indicated
Chromosome effects:	No data gap, no adverse effect indicated
DNA damage:	No data gap, no adverse effect indicated
Neurotoxicity:	No study submitted nor required at this time.

Toxicology one-liners are attached.

All record numbers for the above study types through 287510 (Document No. 265-0054) were examined. This includes all relevant studies indexed by DPR as of 12/2/15.

In the 1-liners below:
indicates an acceptable study.
Bold face indicates a possible adverse effect.
indicates a study on file but not yet reviewed.

File name: T151202
Revised by T. Moore, 12/2/15

NOTE: The following symbols may be used in the Table of Contents which follows:
* = data adequately address FIFRA requirement
† = study(ies) flagged as "possible adverse effect"
N/A = study type not currently required

The active ingredient has been submitted for registration as an antimicrobial for use in paints and other sealants. Toxicity data requirements are based upon those set forth in 40 CFR, section 158.2230 (2014).

This record contains summaries of studies. Individual worksheets may be useful for detailed assessment.

Table of Contents

METABOLISM AND PHARMACOKINETICS 3
GUIDELINE ACUTE STUDIES ON ACTIVE INGREDIENT 3
Acute oral toxicity, rat 3
Acute dermal toxicity 3
Acute inhalation toxicity, rat 3
Primary eye irritation, rabbit 4
Primary dermal irritation 4
Dermal sensitization 4
SUBCHRONIC STUDIES (units of mg/kg/day unless specified) 5
Oral toxicity, rat: 5
Oral toxicity, non-rodent: 5
Dermal toxicity, 21/28-day or 90-day: 5
CHRONIC STUDIES 6
Chronic, rat 6
Chronic, dog 6
Oncogenicity, rat 7
Oncogenicity, mouse 7
GENOTOXICITY 7
Gene mutation 7
Chromosome damage 7
DNA damage or miscellaneous effects 8
REPRODUCTIVE TOXICITY, RAT 8
DEVELOPMENTAL TOXICITY 9
Rat 9
Rabbit 9
NEUROTOXICITY 9

Acute, rat 9
90-day, rat 9
Developmental neurotoxicity, rat 9
Delayed neurotoxicity, hen 9
IMMUNOTOXICITY 9
ENDOCRINE DISRUPTOR STUDIES 9
SUPPLEMENTAL STUDIES 9

METABOLISM AND PHARMACOKINETICS

Study not submitted nor required at this time.

GUIDELINE ACUTE STUDIES ON ACTIVE INGREDIENT

Acute oral toxicity, rat

265-0033; 281578; "Acute Oral Toxicity Study on GS-13529 Technical and GS-14260 Technical in Male and Female Albino Rats"; (C. Mastri; Industrial Bio-Test Laboratories, Inc., Northbrook, IL; Study ID. No. A8087; 1/23/70); Five Charles River albino rats/sex/group were dosed orally by gavage with 1.4, 2.0, 3.0 or 4.6 g/kg of GS-14260 Technical (lot no. FL-8369; purity: 98.3%). The following mortality resulted from the treatment: 1.4 (M: 1/5, F: 0/5), 2.0 (M: 3/5, F: 2/5), 3.0 (M:4/5, F: 5/5), 4.6 (M/F: 5/5). Clinical signs included hypoactivity, muscular weakness, diarrhea, ruffled fur and emaciation. Necropsy examination results were not included in the report. LD50 (95% confidence limits): (M) 1.9 (1.5 to 2.4) g/kg, (F) approximately 2.1 g/kg; Toxicity Category III; **Study acceptable.** (Moore, 5/5/15)

Acute dermal toxicity

265-0033; 281582; "Acute Toxicity Studies in Albino Rabbits"; (W.P. Dean; International Research and Development Corporation, Mattawan, MI; Study No. 382-021; 7/16/77); The skin of 3 New Zealand White rabbits/sex was exposed to 20000 mg/kg of Terbutryn Technical (batch no. FL-761552; purity not reported) for 24 hour under an occlusive wrap. The test material was moistened with physiological saline. No deaths resulted from the treatment. No treatmentrelated clinical signs were evident. One animal demonstrated barely perceptible erythema between days 2 and 3. No necropsy examination was performed. LD50 (M/F) > 20000 mg/kg; Toxicity Category IV; **Study acceptable.** (Moore, 5/6/15)

Acute inhalation toxicity, rat

265-0044; 281487; "Terbutryn Technical: Acute Inhalation Toxicity Study in Rats-Limit Test"; (D. Merrill; Product Safety Labs, Dayton, NJ; Study No. 36822; 8/14/13); Five Sprague-Dawley rats/sex were exposed nose-only to 2.10 mg/l (gravimetric) of Terbutryn Technical (batch no. 20130428; purity: 98.46%) for 4 hours. The mean MMAD (GSD) was 3.52 (2.46) µm. No deaths resulted from the exposure. Abnormal respiration and/or hypoactivity were noted up to 5 days post-exposure, resolving thereafter. No treatment-related lesions were evident in the necropsy examination. LC50 (M/F) > 2.10 mg/l; Toxicity Category IV; **Study acceptable.** (Moore, 6/10/15)

Primary eye irritation, rabbit

265-0044; 281486; "Primary Eye Irritation Study in Rabbits"; (A. McKenzie; Product Safety Labs, Dayton, NJ; Study No. 34194; 4/19/12); The eyes of 3 New Zealand albino rabbits were treated by ocular instillation with 0.1 ml (0.05 g)/eye of Troy EX AA (lot no. D1280D; purity: >96%). No corneal opacity nor iritis were noted during the 72-hour observation period. Conjunctival redness, grade 2 (1/3), was noted at 24 hours post-dose, diminishing to grade 1 (1/3) at 48 hours and clearing by 72 hours. No chemosis nor discharge were evident at 24 hours post-dose. Toxicity Category III; **Study acceptable.** (Moore, 6/10/15)

265-0033; 281582; "Acute Toxicity Studies in Albino Rabbits"; (W.P. Dean; International Research and Development Corporation, Mattawan, MI; Study No. 382-021; 7/16/77); The eyes of 6 New Zealand White rabbits were treated by ocular instillation with 100 mg/eye of Terbutryn Technical (batch no. FL-761552; purity not reported). The treated eyes of 3 animals were washed 30 seconds after treatment. For the unwashed eyes, no corneal opacity nor iritis were noted (there was a slight dulling of the cornea of the three animals through 48 hours). Conjunctival redness, grades 2 (1/3) and 1 (1/3), was evident at 24 hours, diminishing to grade 1 (2/3) at 48 hours, grade 1 (1/3) at 72 hours and clearing by 7 days. Chemosis, grade 1 (2/3), was noted at 24 hours, persisting with grade 1 (3/3) at 48 hours, and clearing by 72 hours. Discharge, grade 1 (2/3), was evident at 24 hours, diminishing to grade 1 (1/3) at 48 hours and clearing by 72 hours. For the washed eyes, no corneal opacity nor iritis were noted (there was a slight dulling of the cornea of two animals through 24 hours). Conjunctival redness, grade 2 (1/3), was evident at 24 hours, persisting with grades 2 (1/3) and 1 (1/3), at 48 hours, and clearing by 72 hours. Chemosis, grade 1 (2/3), was noted at 24 and 48 hours, and clearing by 72 hours. No discharge was evident. Toxicity Category III; **Study acceptable.** (Moore, 5/6/15)

Primary dermal irritation

265-0033; 281582; "Acute Toxicity Studies in Albino Rabbits"; (W.P. Dean; International Research and Development Corporation, Mattawan, MI; Study No. 382-021; 7/16/77); The skin of 6 New Zealand white rabbits was exposed to 500 mg/site, 2 sites/animal (one intact, one abraded) of Terbutryn Technical (batch no. FL-761552; purity not reported) for 24 hours under an occlusive wrap. The test material was moistened with physiological saline. At the intact sites, no erythema nor edema were evident for the 72-hour observation period. At the abraded sites, erythema, grade 1 (1/6), was noted at 24 hours, clearing by 72 hours. No edema was evident. Toxicity Category IV; **Study acceptable.** (Moore, 5/6/15)

Dermal sensitization

265-0033; 281583; "Final Report: GS 14260 Tech. Skin Sensitization Test in the Guinea Pig"; (M. Schoch; Giba-Geigy Limited, Basle, Switzerland; Study ID No. 860616; 4/13/87); Ten Pirbright White guinea pigs/sex received ten 0.1 ml intracutaneous injections of a 0.1% solution of GS 14260 Technical (batch no. P. 506001; purity: 97.4%) in an aqueous 20% solution of propylene glycol every other day. During the 2nd and 3rd week of these injections (5th through 10th injection), the injection preparation was prepared 1:1 with complete Bacto adjuvant. Fourteen days after the last induction injection, 0.1 ml of the 0.1% test material preparation in 20% propylene glycol was injected intracutaneously for the challenge treatment. Twenty four hours after each of the first four induction injections and the challenge injection, the volume of the weal at the site of injection was determined. A naïve control group of 10 animals/sex was treated in the same manner except the test material was not included in the injection preparations. The reaction threshold was ascertained by adding the mean of the weal volume and the standard deviation of the four measurements. If the weal volume for the challenge treatment was greater than that value, then it was deemed to be a positive response. Ten days after the intracutaneous injection challenge, an epicutaneous challenge was performed in which

a 5% preparation of the test material in vaseline was applied to the skin of the induced animals for 24 hours. The naïve control group was treated in the same manner. The skin of each animal was examined for irritation at 24 and 48 hours post-exposure. In the intracutaneous injection challenge, all of the induced animals demonstrated a positive response. The naïve control animals were free of any significant reaction. In the epicutaneous challenge, 5 of the 20 animals in the induced group demonstrated a positive response at either 24 or 48 hours post-exposure. None of the naïve control animals exhibited a positive response. The test material is a positive dermal sensitizer. **Study acceptable.** (Moore, 5/7/15)

SUBCHRONIC STUDIES

Rat Subchronic Dietary Toxicity Study

265-0034; 281584; "3-Month Oral Toxicity Study in Rats (Administration in Food); (R. Gerspach; Giba-Geigy Limited, Short/Long-term Toxicology, 4332 Stein, Switzerland; Test No. 931124; 4/11/95). Ten Tif: RAif rats/sex/group received 0, 30, 1000 or 3000 ppm of GS 14260 Technical (terbutryn technical) (batch no. P.506001; purity: 97.4%) in the diet for 3 months. A recovery cohort of 10 animals/sex/group received 0 or 3000 ppm of the test material in the diet for 3 months and then were maintained for an additional 4 weeks on a maintenance diet ((M) 0, 1.91, 68.80, 208.2 mg/kg/day, (F) 0, 2.00, 70.57, 231.0 mg/kg/day). No animals died during the study. The mean body weights and food consumption of both sexes in the 1000 and 3000 ppm treatment groups were less than the control values (NS, $p<0.01$, 0.05). The mean body weights of both sexes in the 3000 ppm were still lower than those of the control group at the end of the recovery period ($p<0.01$). In the hematology evaluation, the mean red blood cell count, hemoglobin concentration and hematocrit percentage of the females in the 3000 ppm group were less than the control group values ($p<0.01$). The percentage of reticulocytes was increased for the females in the 3000 ppm group ($p<0.01$). The effects were no longer evident at the end of the recovery period. In the clinical chemistry evaluation, the serum cholesterol levels were increased for both sexes in the 3000 ppm group in comparison to the control values ($p<0.01$). The level of alkaline phosphatase activity in the serum of both sexes in the 3000 ppm group was elevated in comparison that of the control group ($p<0.01$). These effects were no longer evident at the end of the recovery period. No treatment-related effects were evident in the urinalysis or ophthalmology. The mean absolute weights of the organs of both sexes in the 3000 ppm animals were less than those of the control group as a consequence of the lower mean body weights of these animals. The mean relative weights of these organs were greater than the control group as these organs were conserved due to the severe weight loss. When the tissues/organs were examined microscopically, no treatment-related lesions were evident. **No adverse effects were evident. Rat Subchronic Dietary NOEL:** (M/F) 30 ppm ((M) 1.91 mg/kg/day, (F) 2.00 mg/kg/day) (based upon the reduced mean body weights and food consumption of both sexes in the 1000 ppm treatment group); **Study acceptable.** (Moore, 5/12/15)

Oral toxicity, non-rodent:

Study not submitted nor required at this time.

Rabbit 21-Day Repeated Dosing Dermal Toxicity Study

265-0035; 281585; "21-Day Dermal Toxicity Study in Rabbits"; (D.M. Schiavo, J.R. Hazelette, J.D. Green; Research Department, Pharmaceuticals Division, Ciba-Geigy Corporation, Summit, NJ; Study No. 87040; 6/30/87); The skin of five New Zealand white rabbits/sex/group was exposed to 0, 10, 100 or 1000 mg/kg/day of Terbutryn technical (lot no. FL 870004; purity: 97.3%) for 6 hours/day for at least 22 days. The test material was moistened into a paste with purified water. No deaths resulted from the treatment. There was no treatment-

related effect upon the mean body weight gain. Although the females in the 100 and 1000 mg/kg treatment groups demonstrated a lower mean food consumption on study day 7, this reduced food consumption was not an apparent consequence of the treatment. There was no treatment-related effect on any of the hematology or clinical chemistry parameters. The ophthalmological examination did not reveal any treatment-related ocular lesions. There was no treatment-related effect upon the mean absolute and/or relative organ weights. No treatment-related lesions were evident in the microscopic examination of the tissues/organs. **No adverse effect indicated. Rabbit Repeated Dose 21-Day Dermal NOEL:** (M/F) > 1000 mg/kg/day (based upon the lack of a treatment-related effect noted for either sex in the 1000 mg/kg treatment group); Previously the study was deemed to be unacceptable, possibly upgradeable with the submission of the test material's purity. The information provided in the cover letter of 9/28/15 documented the purity of the test material. (Moore,5/13/15, revised, Moore, 10/29/15)

CHRONIC STUDIES

Chronic, rat

**** 265-0037; 281587**; "24-Month Carcinogenicity and Chronic Toxicity Study in Rats"; (H. Frankhauser; Syngenta Crop Protection AG, Health Assessment, 4332 Stein, Switzerland; Test No. 951040; 5/8/01); Seventy Tif: Raif rats/sex/group were fed GS 14260 Technical (terbutryn technical) (batch no. P 506001; purity: 97.4%) in the diet at concentrations of 0, 30, 100, 300 or 600 ppm for 2 years ((M) 0, 1.19, 4.03, 12.1, 24.8 mg/kg/day, (F) 0, 1.40, 4.69, 14.0, 29.8 mg/kg/day). An additional 10 animals/sex/group were included in an interim sacrifice after 53 weeks of treatment. There was no treatment-related effect upon the survival of the study animals. The mean body weights of both sexes in the 600 ppm treatment group and the males in the 300 ppm group were lower than those of the control group over the course of the study ($p<0.01$). Food consumption was reduced for the 600 ppm females ($p<0.01$). The ophthalmological examination did not reveal any treatment-related effect on the eyes of either sex in the 600 ppm treatment group. Although some of the hematological parameters demonstrated a statistical difference between the control and the 600 ppm treatment group, there was no apparent treatment-related effect. In the clinical chemistry, the only parameter which demonstrated a treatment-related effect was the increase of inorganic phosphate in the serum of the females in the 300 and 600 ppm treatment groups. However this effect was not accompanied by signs of renal failure (elevated serum urea and creatinine levels) or concomitant low calcium levels and thereby did not signify a significant physiological effect. No treatment-related effect was evident in the urinanlysis. Although the relative liver, kidney and ovary weights were significantly increased, the increases were largely due to the decreased body weights observed for the animals in the 600 ppm group. No treatment-related lesions were evident in these organs. In the histopathological evaluation, there were increased incidences of acinar adenomas in the pancreas, foam cells in the lungs and follicular hyperplasia and hypertrophy in the thyroids of the 600 ppm males. There was an increased incidence of hemosiderosis in the spleens and stromal polyps in the urteri of the 600 ppm females. **Possible adverse effect:** increased incidence of acinar adenomas in the pancreas. **Rat Chronic Dietary NOEL:** (M) 100 ppm (4.03 mg/kg/day) (based upon the lower mean body weights of the 300 ppm males) (F) 300 ppm (14.0 mg/kg/day) (based upon the lower mean body weights and food consumption and the increased incidence of lesions in the spleen and uterus of the 600 ppm females); **Oncogenicity:** acinar adenomas in the pancreas; **Study acceptable.** Moore, 5/20/15)

Chronic, dog

Study not submitted nor required at this time.

Oncogenicity, rat

See chronic, rat above.

Oncogenicity, mouse

Study not submitted nor required at this time.

GENOTOXICITY

Gene mutation

** 265-0038; 281588; "Terbutryn Technical: Gene Mutations Test"; (E.R. Lasinski, J.C. Kapeghian, J.D. Green; Research Department, Pharmaceuticals Division, Ciba-Geigy Corporation, Summit, NJ; Study No. MIN 872186; 6/18/87); Terbutryn technical (batch no. FL870004; purity not reported) was added to the cultures of *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 at concentrations of 0, 10, 50, 150, 300 and 600 µg/plate by the plate incorporation assay method and incubated at 37° C for 48 hours under conditions of activation and non-activation. Two trials were performed with 3 replicates for each concentration (data were combined for one analysis). An Aroclor 1254-induced rat liver S9 fraction was used to activate the test material. There was no apparent treatment-related increase in the incidence of reverse mutation. **No adverse effect indicated.** The positive controls were functional. **Study acceptable.** (Moore, 5/22/15)

265-0038; 281589; "*Salmonella/*Mammalian-Microsome Mutagenicity Test"; (E. Deparade; Ciba-Geigy Limited, Experimental Pathology Laboratories, Basle, Switzerland; Study No. 860706; 3/4/87); GS 14260 (terbutryn technical) (batch no. P.506001; purity: 97.4%) was added to the cultures of *S. typhimurium* strains TA98, TA100, TA1535, and TA1537 in 0.1 ml aliquots at concentrations of 20 to 5000 µg/0.1 ml by both plate incorporation and preincubation assay (20 minutes of preincubation) methods and incubated at 37° C for 48 hours under conditions of activation. Both trials were performed with 3 replicates for each concentration. There was no apparent treatment-related increase in the incidence of reverse mutation. **No adverse effect indicated.** The positive controls were functional except for the TA1537 assay with preincubation. **Study unacceptable**, not upgradeable (non-activation assay was not performed). (Moore, 5/22/15)

** 265-0038; 281590; "Gene Mutation Test with Chinese Hamster Cells V79 *In Vitro*"; (D. Geleick; Genetic Toxicology, Ciba-Geigy Limited, Basle, Switzerland; Test No. 931116; 1/13/94); Chinese hamster V79 cells were exposed to GS 14260 technical (batch no. P 506001; purity: 97.4%) at concentrations ranging from 1.85 to 50.0 µg/ml (activated) or 2.96 to 80.00 µg/ml (non-activated) for 5 hours (activated) or 21 hours (non-activated) at 37° C in the first trial. In the 2nd trial, the cells were exposed to concentrations ranging from 1.48 to 40.00 µg/ml (activated) or from 4.44 to 120 µg/ml (non-activated) under the same conditions as the first trial. There were duplicate cultures for each treatment level. An Aroclor 1254-induced rat liver S9 fraction was used to metabolize the test material. There was no treatment-related effect upon the forward mutation frequency. **No potential adverse effect evident**. The positive controls were functional. **Study acceptable.** (Moore, 5/26/15)

Chromosome damage

** 265-0038; 281591; "Micronucleus Test'; (F. Strasser; Ciba-Geigy Limited, Protection of Health and Environment, Genetic Toxicology, , Basle, Switzerland; Test No. 871235; 12/11/87); In Part 1 of the study, 8 Tif:RAI rats/sex/group/time point were dosed orally by gavage with a dose of 0 (vehicle: aqueous 0.5% sodium carboxymethyl cellulose) or 1800 mg/kg of GS 14260 technical (batch no. P. 506001; purity: 97.4%) and sacrificed at 16, 24 and 48 hours after

dosing. Eight animals/sex were dosed with a positive control of cyclophosphamide (64 mg/kg) and sacrificed 24 hours after dosing. In Part 2, eight animals/sex/group were dosed with 0, 450, 900 or 1800 mg/kg of the test material or 64 mg/kg of cyclophosphamide and euthanized at 24 hours post-dose. In both parts, bone marrow samples from the femur were examined and the ratio of polychromatic (PCE) to normochromatic erythrocytes and the percentages of PCEs and oxyphilic erythrocytes with micronuclei were determined. No treatment-related increase in the number of polychromatic erythrocytes with micronuclei was noted. **No adverse effect indicated. Study acceptable.** (Moore, 5/27/15)

DNA damage or miscellaneous effects

** 265-0038; 281592; "Autoradiographic DNA Repair Test on Rat Hepatocytes"; (E. Puri; Ciba-Geigy Limited, Protection of Health and Environment, Experimental Pathology, Basle, Switzerland; Test No. 850909; 7/24/86); Primary rat hepatocyte cultures were exposed to GS 14260 technical (batch no. P. 506001; purity: 97.4%) at concentrations ranging from 0.25 to 31.3 µg/ml for 5 hours at 37° C. Vehicle and positive (4-ABP, 50 µM) controls were included in the assay. There were 4 cultures/treatment level. There was no treatment-related increase in unscheduled DNA synthesis. **No adverse effect indicated.** The positive control was functional. **Study acceptable.** (Moore, 5/27/15)

REPRODUCTIVE TOXICITY, RAT

** 265-0054; 287510; "GB 14260 Technical: Rat Dietary Two-Generation Reproduction Study"; (S. Khalil; Novartis Crop Protection AG, Human Safety Assessment, 4002 Basel, Switzerland; Study No. 951041; 12/2/98); Thirty Tif: RAI f rats/sex/group were treated in the diet with 0, 30, 100, 300 or 600 ppm of GB 14260 Technical (Terbutryn) (batch no. P. 506001; purity: 97.4%) for two generations. The treatment period for the F0 generation adults included 10 weeks prior to mating, mating, 3 weeks of gestation and 3 weeks of lactation. At that time, 30 F1 animals/sex/group were selected as parents and treated for an additional 10 weeks, followed by mating and 3 weeks each for gestation and lactation of the F2 generation. There were no apparent treatment-related parental mortalities. Both sexes in the 300 and 600 ppm groups and the females in the 100 ppm group of the F0 generation had lower mean body weights than the control group by the end of the premating period ($p<0.01$ or 0.05). In the F1 generation, both sexes in the 600 ppm group and the males in the 300 ppm group had lower mean body weights than did the control group by the end of the premating group ($p<0.01$). Lower food consumption was also noted for these respective groups over both generations. Although some of the mean relative organ weights of both sexes in the 300 and 600 ppm group of both generations were significantly greater than the control values, this result was largely due to the lower mean body weights of the animals in these groups. The lack of treatment-related lesions in the histopathological evaluation confirmed that was the case. There were no treatment-related effects upon the mating, fertility, or litter size. The mean pup weights on day 0 were comparable for all groups. However, by weaning, the mean weights of both sexes of F2 pups in the 600 ppm group were lower than those of the control ($p<0.01$). **No adverse effect indicated**. **Parental NOEL:** 30 ppm ((M) 2.67, (F) 2.74 mg/k/day) (based upon lower mean body weight of the F0 females in the 100 ppm treatment group); **Reproductive NOEL:** 600 ppm (53.2 mg/kg/day) (based upon the lack of treatment-related effects upon reproductive parameters for both generations in the 600 ppm treatment group); **Developmental NOEL:** 300 ppm (43.0 mg/kg/day) (based upon the lower mean body weights of both sexes of F2 pups in the 600 ppm treatment group after 21 days of lactation). **Study acceptable.** (Moore, 11/20/15)

DEVELOPMENTAL TOXICITY

Rat

** 265-0036; 281586; “Terbutryn Technical: A Teratology Study in Rats”; (R.N. Infurna, K.V. Wimbert, J. Mainiero, A.T. Arthur; Research Department, Pharmaceuticals Division, Ciba-Geigy Corporation, Summit, NJ; Report No. 85111; 10/25/85); Twenty five mated Crl: CD(SD) BR female rats/group were dosed orally by gavage to 0, 10, 50 or 500 mg/kg/day of Terbutryn Technical (batch no. FL-840054; purity: 98.2%) from gestation day 6 through gestation day 15. Two dams in the 500 mg/kg group were found dead on gestation day 20. The mean body weights and food consumption of the dams in the 500 mg/kg group were less than the control values (NS, $p<0.05$ or 0.01). There was no increase in the incidence of fetal resorptions or malformations. The mean body weight of the fetuses in the 500 mg/kg group was less than that of the control group ($p<0.01$). Lack of ossification was noted for numerous bones of the fetuses in the 500 mg/kg treatment group as a consequence of delayed development. **No adverse effect indicated. Maternal NOEL:** 50 mg/kg/day (based upon the lower mean body weights and reduced food consumption noted for the dams in the 500 mg/kg treatment group); **Developmental NOEL:** 50 mg/kg/day (based upon the lower mean body weights and the lack of ossification of numerous bones of the fetuses in the 500 mg/kg treatment group). **Study acceptable.** (Moore, 5/18/15)

Rabbit

Study not submitted.

NEUROTOXICITY

Acute neurotoxicity, rat

Study not submitted nor required at this time.

90-day neurotoxicity, rat

Study not submitted nor required at this time.

Developmental neurotoxicity, rat

Study not submitted nor required at this time.

Delayed neurotoxicity, hen

Study not submitted nor required at this time.

IMMUNOTOXICITY

Waiver granted from study requirement.

ENDOCRINE DISRUPTOR STUDIES

Study not submitted nor required at this time.

SUPPLEMENTAL STUDIES

Studies not submitted nor required.