

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

Metribuzin

Chemical Code # 001692, Tolerance # 332
SB 950 # 216

NOVEMBER 19, 1986

Revised: 3/4/87, 12/10/87, 3/1/90, 4/29/91, 10/29/93, 2/16/00

I. DATA GAP STATUS

Combined, Rat	No data gap, possible adverse effect
Chronic dog:	No data gap, possible adverse effect
Oncogenicity mouse:	No data gap, no adverse effect
Reproduction, rat:	No data gap, no adverse effect
Teratogenicity rat:	No data gap, no adverse effect
Teratogenicity rabbit:	No data gap, no adverse effect
Gene mutation:	No data gap, no adverse effect
Chromosome:	No data gap, possible adverse effect
DNA damage:	No data gap, no adverse effect
Neurotox:	Data gap, no adverse effect indicated

Note, Toxicology one-liners are attached

** indicates acceptable study

Bold face indicates possible adverse effect

FILE NAME: T000216

Revised 3/1/90 by G. Chernoff; 4/29/91 by M. Silva; 10/29/93; M. Silva, 2/16/00

All record numbers through 167945 were examined.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

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

Combined, RAT

**** 211 120846** "Technical Grade Metribuzin (SENCOR®): A Combined Chronic Toxicity/Oncogenicity Feeding Toxicity Study in the Rat", (W.R. Christenson and B.S. Wahle, Miles Inc., Study Number 88-271-BM; Miles report #: 103970, 1/15/93). Metribuzin technical (purity = 92.1%-93.0%) was fed in diet to Fischer rats at 0 (ethanol), 30, 300 or 900 ppm for one (20/sex/group) or two years (50/sex/group). Chronic NOEL = 30 ppm (Body weights at 900 ppm and body weight gain at \geq 300 ppm were reduced. Clinical chemistry and hematology were affected--creatinine, globulin, calcium, cholesterol, phosphorous, AST, ALT, ALP, MCV and MCH in one or both sexes, primarily at \geq 300 ppm. Liver and thyroid weights were increased at \geq 300 ppm. Gross pathology was observed in liver and pancreas in males and in thyroid of females at 900 ppm. Thyroid gross pathology was observed in males at \geq 300 ppm.) **Possible adverse effect:** Follicular cell hyperplasia of the thyroid was observed in males at \geq 300 ppm and in females at 900 ppm. Oncogenicity NOEL: There was no compound-related oncogenicity at any dose. **ACCEPTABLE.** (Kishiyama & Silva, 10/25/93).

211 120846 Included in this volume containing the above combined study is an adverse effects disclosure statement. M. Silva, 10/25/93.

CHRONIC RAT

018 967343, "Bay 94337, Chronic Toxicity Studies on Rats (Two-year feeding experiment)", (Bayer AG, Institut fuer Toxikologie, report # 41816, 9/25/74), Metribuzin, 99.5%, fed in the diet for two years at 0, 25, 35, 100 or 300 ppm with 80 (control) or 40/sex/group. Slightly reduced bodyweights in both sexes reported at 300 ppm. No adverse effect reported. UNACCEPTABLE not upgradeable (inadequate high dose showing no signs of toxicity, no interim sacrifice, no analysis of diet presented, hematology/clinical chemistry on 5/sex/group at interim sampling times.) No adverse effect reported. (J. Gee, 6/19/85)

NOTE: The memo from EPA to DPR addressing differences in data gap status for this chemical (dated 1/23/89) notes EPA classification as "Core Minimum".

171 050571, Version (includes tumor survey and 033964) of 967343.

129 014639, Duplicate information to 967343 and 050751.

076 014501, 6-month interim report for 967343.

076 014642, Summary of 6 month interim report (014501) 967343.

145 033964, Appendix to 967343: Additional histopathology and reevaluation of slides.

146 033965, Appendix to 967343: Historical controls.

CHRONIC DOG

****017 967344**, "Bay 94 337, Chronic Toxicity Studies on Dogs (Two-year feeding experiment)", (Bayer AG, Institut fuer Toxikologie, report # 41814, 9/24/74). Metribuzin, 99.5%, fed in the diet to 4 Beagle dogs/sex/group for two years at 0, 25, 100 or 1500 ppm. Mortality at high dose with NOEL = 100 ppm (anemia, mortality). The report does not present analysis of the diet and no rationale for selecting the doses used. The high dose, however, was, if anything, too high. Other aspects of the report are adequate. **Adverse effects** on hematology, liver changes, kidney necrosis and testes at high dose. Because these effects occurred at a dose causing 75% mortality, they may reflect aspects of acute toxicity rather than chronic effects. ACCEPTABLE. (J. Gee, 6/19/85).
NOTE: The memo from EPA to DPR addressing differences in data gap status for this chemical (dated 1/23/89) notes EPA classification as "Core Minimum".

076, 129 014502, 014641, 6-month interim report for 967344.

ONCOGENICITY, MOUSE

**** 024 967345** "Metribuzin (Sencor) Oncogenicity Study in Mice." Mobay-Stanley Research Center, report # 80050, 10/30/81), Metribuzin, 92.9%, fed to 50/sex/group at 0, 200, 800 or 3200 ppm for two years; maximum dose estimated as 450 - 600 mg/kg. Initially reviewed as having a possible adverse effect based on hematology changes in females only at 800 and 3200 ppm at termination - decreased mean hematocrit and hemoglobin. Study was evaluated as acceptable. (J. Gee, 6/20/85) Reconsideration of the data notes that, although statistically significant, the results are of equivocal toxicological significance with individual data affecting the mean values. The systemic NOEL = 200 ppm (hematology, liver and kidney organ weights increased). The onco NOEL \geq 3200 ppm with no evidence for oncogenicity. ACCEPTABLE. (J. Gee, 3/14/90)
NOTE: The memo from EPA to DPR addressing differences in data gap status for this chemical (dated 1/23/89) notes EPA classification as "Core Minimum".

017 967346 Invalid IBT study.

REPRODUCTION, RAT

018 025219, "Bay 94337, Multigeneration Study on Rats", (Bayer AG, Institut fuer Toxikologie, report # 41818, 9/24/74), Metribuzin, 99.5%, fed in the diet to 10 males and 20 females at 0, 35, 100 or 300 ppm, three generations, 2 litters each; dosed 8 weeks before mating. No adverse effect reported. UNACCEPTABLE, not upgradeable (inadequate necropsy - on F3b only, dose selection not justified and no signs of toxicity are reported at the high dose, no analysis of diet). (J. Gee, 6/19/85)
NOTE: The memo from EPA to DPR addressing differences in data gap status for this chemical (dated 1/23/89) notes EPA classification as "Core Supplementary".

**** 189, 196 070525, 091196**, "A Two-Generation Reproduction Study in Rats with Sencor Technical (Metribuzin)", (Porter, M.C., Jasty, V., and Hartnagel, R.E. Jr., Miles Inc., Report # 98295, 9/23/88). Metribuzin (92.6% pure; batch # 77-297-50) was fed in the diet to groups of 30 Crl:CD*BR rats for 2 generations (1 litter/generation) at 0, 30, 150, and 750 ppm. Parental NOEL = 30 ppm (At 750 ppm, pre-mating food consumption and weight gain was reduced in both sexes in each generation. At 150

and 750 ppm, mild hypertrophy of centrilobular and midzonal hepatocytes was observed in F-0 and F-1 females. Decreased gestational weight gain was noted in F-1 females. Reduced pup weight was reported at weaning for all treated offspring from the F-1 generation.) Reproductive NOEL \geq 750 ppm (No significant effects at any dose). Initially the study was reviewed as unacceptable with a possible adverse effect (decreased implantations and litter size in F1 generation, Green & Chernoff, 2/28/90). Upon submission of requested information and re-review of the study, it has been upgraded to ACCEPTABLE with no adverse effect. M. Silva, 4/23/91

TERATOGENICITY, RAT

**168 048961, "A Teratology Study with Sencor Technical (Metribuzin) in the Rat", (Miles Laboratories, Inc., report # 91330, 10/3/86), Metribuzin (92.6%) tested at 0, 25, 70 and 200 mg/kg/day in Emulphor by gastric intubation of female Charles River Cr1:CD BR rats from Day 5 to Day 16 of gestation; Two termination phases: Phase I included 5 dams/dose terminated on Day 17 and Phase II 28 dams/dose terminated on Day 20. Findings: decrease in body weight, actual body weight (dam body weight less uterus weight), weight gain and actual weight gain at 25 mg/kg on Day 15 and at 70 and 200 mg/kg starting on Day 8; decrease in food consumption at all dose levels starting on Day 8; decrease in thyroxine at 70 and 200 mg/kg on Day 16 followed by an increase on Day 20; increase in thyroid weight at 200 mg/kg on Days 16 and 20; decrease in fetus body weight at all dose levels; decrease in placental weight and increase in fetal thyroid weight at 200 mg/kg; increase in skeletal variations at 200 mg/kg. No adverse effect. Maternal NOEL < 25 mg/kg (clinical signs). Developmental NOEL = 70 mg/kg (skeletal and thyroid changes). ACCEPTABLE. (W. Choy, 11/3/86)

NOTE: The memo from EPA to DPR addressing differences in data gap status for this chemical (dated 1/23/89) notes that EPA had not completed review on this study at that time.

171 050573, Partial duplicate (missing page 2) of 048961.

017 967348, "Sencor (Bay 94337), Studies for Possible Embryotoxic and Teratogenic Effects on Rats after Oral Administration", (Bayer AG, Institut fuer Toxikologie, report # 35073, 9/29/72), Metribuzin, 99.5%, given by oral gavage to 21 - 22 female rats, days 6 - 15 of gestation, at 0, 5, 15, 50 or 100 mg/kg and sacrificed on day 20; females in high dose group gained 14% less weight and the average placental weight was 7 % less; maternal NOEL = 50 mg/kg (weight gain); no evidence of fetotoxicity reported; initially reviewed as acceptable with a possible adverse reproductive effect, reconsideration (11/19/86) finds the study UNACCEPTABLE (missing clinical observations, marginal maternal toxicity) with no adverse effect. The data gap, however, is filled with the 1986 Miles Laboratory study, which demonstrated a similar NOEL (70 mg/kg) -- see # 048961 above. (J. Gee, 6/19/85 and 11/19/86)

NOTE: The memo from EPA to DPR addressing differences in data gap status for this chemical (dated 1/23/89) notes EPA classification as "Core Supplementary".

TERATOGENICITY, RABBIT

**155 090002, "Teratology Study in the Rabbit with Sencor Technical (Metribuzin)" (Toxicology Department, Miles Inc., Laboratory ID 99654, 8/2/89). Sencor Technical (Metribuzin 92.7%), Batch No. 77-297-50, was administered by oral gavage to groups of 17 inseminated American Dutch Belted rabbits at doses of 0 (0.5% carboxymethyl cellulose, 0.4% Tween 80), 10, 30 or 85 mg/kg/day on

days 6-18 of gestation. Decreased maternal weight gain and food consumption during the treatment period was observed at the high dose, and decreased amounts of stool were noted in both the 30 and 85 mg/kg/day dose groups. Decreased fetal weight and delayed ossification noted only at 30 mg/kg/day was not considered treatment related. Maternal NOEL = 30 mg/kg/day (decreased food consumption, weight gain, and stool production); Developmental NOEL = 85 mg/kg/day (HDT). The study is ACCEPTABLE and no adverse effects are noted (D. Shimer, 10-27-89; G. Chernoff, 2/22/90).

200 096716, This volume is a supplement to 090002 and contains information requested by the EPA:

1. Litter incidence data for fetal skeletal abnormalities listed in Table VI of the report.
2. Historical control data for the skeletal abnormalities listed in Table VI of the report.
3. Necropsy findings on does not listed in Appendix D.
4. Results of histological examinations of maternal tissues, if any.
5. Times and dates of sacrifice for all maternal rabbits.
6. A discussion to clarify the findings presented in Table VI of the original report.

No worksheet was done for this volume. (M. Silva, 4/22/91).

171 050572, "A Teratological Evaluation of Sencor® in Mated Female Rabbits", (Midwest Research Institute, report # 80051, 10/30/82), Metribuzin, 93.0%, given to 17/group at 0, 15, 45 or 135 mg/kg on days 6 through 18 of gestation by oral gavage; 17 deaths, some from pneumonia; maternal NOEL = 45 mg/kg (body weight, increased abortions, reduced food intake); report states no teratogenic effect. Developmental NOEL \geq 135 g/kg. UNACCEPTABLE (no analysis of dosing solution, not all fetuses for both visceral and skeletal exam). (J. Gee, 6/20/85 and 3/4/87)

NOTE: The memo from EPA to DPR addressing differences in data gap status for this chemical (dated 1/23/89) notes EPA classification as "Core Guideline Data".

024 967349 Part of record # 50572 (contains pages missing in the original submission).

017 967354 Invalid IBT study.

017 967350 Invalid IBT study.

GENE MUTATION

073 031095, "Metribuzin, Mutagenicity Test on Bacterial Systems", (Institute of Environmental Toxicology, Japan, Report # 66748, 8/17/78), Metribuzin, 93.3%, in Salmonella strains TA1535, TA1537, TA1538, TA98 and TA100, with and without activation; tested at 0, 10, 50, 100, 200, 500, 1000 or 5000 ug/plate, in duplicate. No increase in reversion reported. UNACCEPTABLE, not upgradeable (no repeat trial). (J. Gee, 6/20/85)

NOTE: The memo from EPA to DPR addressing differences in data gap status for this chemical (dated 1/23/89) notes EPA classification as "Acceptable".

073 031093, "Bay 94337, Mutagenicity Test on Bacterial Systems", (Nitokuno, Agricultural Chemicals Institute, Japan, Report # 54127, 12/19/77), Metribuzin, 93.7%, tested with Salmonella strains TA1535, TA1537, TA98 and TA100, with and without activation with S9 from mouse and rat, at 0, 2, 20 or 500 ug/plate, single plate, no top agar - the bacteria, S9 and test article were spread onto agar with a spreader in a total volume of 0.5 ml. No increase in reversion reported. UNACCEPTABLE, not upgradeable (no justification for high concentration, single plate only). (J. Gee, 6/20/85)

NOTE: The memo from EPA to DPR addressing differences in data gap status for this chemical (dated 1/23/89) notes EPA classification as "Acceptable".

****179 060685**, "S. cerevisiae D7 test for determination of point mutations", (Bayer AG, Wuppertal-Elberfeld, Report # 94786, 5/5/87). In 2 separate tests, Metribuzin (94.7-8%) in DMSO at concentrations of 0, 625, 1250, 2500, 5000 and 10,000 ug/ml was added to suspension cultures (1/conc.) of S. cerevisiae for 16 hrs. The cells were then plated in nutrient and selective media to test for viability and revertants, respectively. No increase in revertants. ACCEPTABLE. (Harnois, 12/4/87)

197 091443 This volume is an addendum to 179 060685 and contains a response to EPA's review of the study, "S. cerevisiae D7 test for determination of point mutations." EPA requested an analysis of dosing material, which was provided in this supplement. The analysis confirmed the intended concentrations and showed the test substance was stable in DMSO for 4 hours at room temperature. It was not stated in this addendum whether the study was acceptable at EPA. (No worksheet for this volume. M. Silva, 4/22/91).

157 042943, "CHO/HGPRT Mutation Assay in the Presence and Absence of Exogenous Metabolic Activation", (Microbiological Associates, Inc., Report # 91760, 3/26/86), Metribuzin (92.6%); \pm rat liver S9 activation; 0, 600, 700, 800, 900, 1000 ug/ml -S9; 0, 50, 100, 150, 175, 200 ug/ml +S9. No increase in mutation frequency reported. UNACCEPTABLE, not upgradeable (no repeated trials, insufficient cytotoxicity in the nonactivated trial). (W. Choy, 9/19/86)

NOTE: The memo from EPA to DPR addressing differences in data gap status for this chemical (dated 1/23/89) notes EPA classification as "Acceptable".

CHROMOSOME EFFECTS

**** 195 090985**, "Sencor Technical: In an In Vitro Cytogenetic Assay Measuring Chromosomal Aberration Frequencies in Chinese Hamster Ovary (CHO) Cells", (H. Murli, Hazleton Laboratories America, Inc., Mobay #: 100042; HLA study no. 10857-0-437, 3/30/90). Sencor technical (purity = 93.0%) was used on Chinese hamster ovary (CHO) cells at concentrations of 199, 299, 399, 499, or 598 ug/ml (10 hour harvest) or 25, 37.5, and 50 ug/ml (10 hour harvest) and 50.1, 100, 150, and 200 ug/ml (20 hour harvest) with S9 from Aroclor induced rat livers. Exposure time was 17.25 and 2 hours for sencor treatments without and with metabolic activation, respectively (duplicate cultures; 100 consecutive metaphases assessed/culture). Sencor doses without S9 mixture did not induce chromosome aberrations. However, at 150 ug/ml with S9 (20 hour incubation), an increase in the number of chromosomally aberrant cells was observed. The highest dose (200 ug/ml) was toxic to cells and could not be evaluated. ACCEPTABLE. (Kishiyama & Silva, 4/18/91).

****191 085178**, "Chromosome Aberrations in Chinese Hamster Ovary (CHO) Cells." (Microbiological Assoc., Mobay No. 99658, 8/30/89) Sencor technical, 93%, tested with CHO-K1 cells in the presence and absence of rat liver S9 activation for induction of chromosome aberrations. Duplicate cultures were treated with 0 (DMSO), 100, 200, 400, 800 or 1600 ug/ml. Exposure was for 18 or 2 hours in the absence or presence of activation, respectively. Harvest time was 20 hours after beginning of treatment. A confirmatory trial was conducted with activation at dose levels of 1024, 1280, 1600, 2000, 2500 or 3125 ug/ml. Fifty cells were scored per flask, 500 cells were scored for mitotic index. All activated concentrations above 1000 ug/ml produced an increase in aberrations (p

≤ 0.01) **Possible adverse effect.** (Shimer/J. Gee, 1/10/90)

073 014479, "Micronucleus Test on the Mouse to Evaluate for Mutagenic Effect", (Bayer AG, Institute of Toxicology, Report # 82361, 3/10/82), Metribuzin, 93.3%, in mouse micronucleus test, given by oral gavage at 24 hour interval to 5/sex at 0, 200 or 400 mg/kg; sacrificed at 6 hours after the second dosing; scored 1000 PCE's per animal. No adverse effect reported. UNACCEPTABLE, not upgradeable (protocol with single sampling time -- multiple times including 24 hours should be used, two doses only with no justification of those selected.) (J. Gee, 6/20/85)

NOTE: The memo from EPA to DPR addressing differences in data gap status for this chemical (dated 1/23/89) notes EPA classification as "unacceptable".

073 014482, "Evaluation of the Mutagenic Potential of @Sencor in an In Vivo Cytogenetic Study on Spermatogonia of Chinese Hamster", (Bayer AG, Institut fuer Toxikologie, Report # 43067, 10/7/74). Metribuzin, 99.5%, tested at 0 and 100 mg/kg given by oral gavage twice at 24 hour intervals and sacrificed 48 hours after second dosing; 8 males per group with thiotepa as positive control; counted 100 spermatogonial metaphases/animal. No effect on spermatogonia was reported. Supplemental information. (J. Gee, 6/20/85)

NOTE: The memo from EPA to DPR addressing differences in data gap status for this chemical (dated 1/23/89) notes EPA classification as "acceptable".

024 967357, "@Sencor, Additional Dominant Lethal Study on Male Mice to Test for Mutagenic Effects by an Improved Method", (Bayer AG, Institut fuer Toxikologie, Report # 49068, 5/19/76). Metribuzin, 99.5%, given by oral gavage to 50 male mice per group at 0 or 300 mg/kg in a single dose; mated 1:1 for 4 days for 5 mating periods -- inadequate length for dominant lethal test. No effect is reported. UNACCEPTABLE, not upgradeable (time interval, no concurrent positive control or acceptable historical data presented). (J. Gee, 6/20/85)

NOTE: The memo from EPA to DPR addressing differences in data gap status for this chemical (dated 1/23/89) notes EPA classification as "acceptable".

024 967356, "@Sencor, Dominant Lethal Study on Male Mice to Test for Mutagenic Effects", (Bayer AG, Institut fuer Toxikologie, Report # 45023, 7/10/75), Metribuzin, 99.5%, 20 males per group were given 0 or 300 mg/kg, single oral gavage, and mated 1:3 females per week for 8 weeks; dose selection based on an acute study in which 2/5 died at 400 mg/kg. No effect reported. UNACCEPTABLE (no concurrent control or acceptable historical data), upgradeable. (J. Gee, 6/20/85)

NOTE: The memo from EPA to DPR addressing differences in data gap status for this chemical (dated 1/23/89) notes EPA classification as "acceptable".

024 967355, "Evaluation of @Sencor for Mutagenic Effects on the Mouse (Dominant lethal test with the treatment of female mice)", (Bayer AG, Institut fuer Toxikologie, Report # 43068, 10/5/74), Metribuzin, 99.5%, given to 37 control and 38 test group females at 0 and 300 mg/kg in a single dose by oral gavage; dosed females in pre-ovulatory oocyte stage, then mated. No adverse effect reported. UNACCEPTABLE, not upgradeable (no positive control, not usual guideline protocol.) (J. Gee, 6/19/85)

NOTE: The memo from EPA to DPR addressing differences in data gap status for this chemical (dated 1/23/89) notes EPA classification as "acceptable".

DNA DAMAGE

**157 042942, "Unscheduled DNA Synthesis in Rat Primary Hepatocytes", (Microbiological Associates, Inc., Report # 91759, 3/26/86), *in vitro* exposure; Metribuzin (92.6%); 0, 0.07, 0.7, 6.7, 20, 100, 200 ug/ml. No increase in UDS. ACCEPTABLE. (W. Choy, 9/22/86)

NOTE: The memo from EPA to DPR addressing differences in data gap status for this chemical (dated 1/23/89) notes EPA classification as "acceptable".

073 031096, "Metribuzin, Mutagenicity Test on Bacterial Systems", (Institute of Environmental Toxicology, Japan, Report # 66748, 8/17/78), Metribuzin, 93.3% in Bacillus subtilis strains H17 and M45 testing for differential growth; filter paper disks at 0, 20, 100, 200, 500, 1000 or 2000 ug/disk applied to streaks of the bacteria; single plate at each concentration; kanamycin and mitomycin C as positive controls. No effect reported. UNACCEPTABLE, not upgradeable (no repeat trial, no activation included). (J. Gee, 6/20/85)

NOTE: The memo from EPA to DPR addressing differences in data gap status for this chemical (dated 1/23/89) notes EPA classification as "acceptable".

073 031094, "Bay 94337, Mutagenicity Test on Bacterial Systems", (Nitokuno, Agricultural Chemicals Institute, Japan, Report # 54127, 12/19/77), Metribuzin, 93.7%, tested with Bacillus subtilis strains NIG17 (rec+) and NIG45 (rec-) at 0, 3, 30 or 300 ug/disc, no activation only, apparently a single plate for each concentration. No effect reported. UNACCEPTABLE, not upgradeable (no activation included, no justification for concentrations used, no repeat trial). (Gee, 6/20/85)

NOTE: The memo from EPA to DPR addressing differences in data gap status for this chemical (dated 1/23/89) notes EPA classification as "acceptable".

NEUROTOXICITY

332-253 167944, "A Subchronic Dietary Neurotoxicity Screening Study with Technical Grade Metribuzin (Sencor®) in Fischer 344 Rats", (L.P. Sheets and R.G. Gilmore, Bayer Corporation, Agriculture Division, Toxicology, 17745 South Metcalf, Stilwell, KS, Report # 108661, Study # 97-472-KU, 12 March 1999). 12 Fischer 344 CDF(F-344) rats per sex per group received technical grade metribuzin (94.2% purity, Batch #: 414-5356) in the diet at nominal concentrations of 0, 30, 300, and 900 ppm for 13 weeks. The mean analytical concentrations were: 0, 27, 297 and 861 ppm. 12 animals per sex per group were used for neurobehavioral evaluation; 6 per sex per group were used for micropathology. Group mean food consumption was reduced 5% to 10% for females at the mid and high dose levels. Subchronic NOEL = 30 ppm (2.19 mg/kg/day). **Neurotoxicity is not indicated.** Neurotoxicity NOEL = 900 ppm (70.1 mg/kg/day) **Not acceptable** but possibly upgradeable with the appropriate positive control. (H. Green & M. Silva, 2/16/00).

332-254 167945 "An Acute Oral Neurotoxicity Screening Study with Technical Grade Metribuzin (Sencor®) in Fischer 344 Rats", (L.P. Sheets, B.F. Hamilton; Bayer Corporation, Agriculture Division, Toxicology, Stilwell, KS, Report # 108660, Study # 96-412-KP, 11 March 1999). Fischer 344 CDF(F-344)/BR rats (12/sex/dose) were gavaged with a single dose of technical metribuzin (94.2% pure) at 0 (0.5% methylcellulose/0.4% Tween 80 in deionized water), 2, 5, 20, and 100 mg/kg. Neurobehavioral tests (Functional Observational Battery--FOB; Motor Activity) were performed 7 days pre-test, then, 1 hour, 7 and 14 days post dosing. The incidence of ataxia, salivation, and decreased activity were increased at 100 mg/kg, relative to controls. At 20 and 100 mg/kg, eye ptosis (at 20 mg/kg only females), oral stain, red nasal stain, and clear lacrimation (females only) were noted for both sexes. All signs were resolved by day 6. Decreases on day 0 in motor and

locomotor activity are noted for both sexes at 5, 20, and 100 mg/kg. Decreases in activity were still noted at day 7 for males at 20 and 100 mg/kg and persisted to day 14 for high dose males while females were comparable to controls by day 7. Neurobehavioral NOEL = 2 mg/kg.

Neuropathology was not indicated. Neuropathology NOEL = 100 mg/kg. **Not acceptable** (Appropriate positive control data need to be confirmed.) (H. Green & M. Silva, 2/16/00).