

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

DICAMBA
Chemical Code # 000200, Tolerance # 00227
SB 950 # 070

August 8, 1986

Revised: 6/22/87; 5/4/88; 8/25/89; 12/8/89; 3/1/90; 9/17/90; 9/22/94; 11/3/95; 12/29/95; 2/29/96;
3/18/96

I. DATA GAP STATUS

Combined rat:	No data gap, possible adverse effect.
Chronic dog:	No data gap, no adverse effect ¹ .
Onco mouse:	No data gap, possible adverse effect.
Repro rat:	No data gap, possible adverse effect.
Terato rat:	No data gap, no adverse effect.
Terato rabbit:	No data gap, no adverse effect.
Gene mutation:	No data gap, no adverse effect.
Chromosome:	No data gap, no adverse effect.
DNA damage:	No data gap, possible adverse effect.
Neurotox:	Not required, adequate study on file, possible adverse effect.

1 - See one-liners in the chronic dog section.
Toxicology one-liners are attached.

** indicates an acceptable study.

Bold face indicates a possible adverse effect.

Rectified through Volume #: 277-088, record #: 145102 & 942838; volume 3: 50744-004, record #: 135247.

File name: 960318

Toxicology Summary revised by D. Shimer and J. Gee, 6/23/87; M. Silva, 5/4/88; S. Rinkus, 8/25/89; M. Silva, 12/8/89, 3/1/90 & 8/6/90; M. Silva, 9/22/94, 11/3/95, 12/29/95 & 3/18/96.

All one-liners on file are in the SUMMARY OF TOXICOLOGY DATA for the free acid, 2-methoxy-3,6-dichlorobenzoic acid, technical dicamba, SB950-070, tolerance # 227. The chemical grouping includes dicamba (SB950-070, tolerance # 227), dicamba diethanolamine (SB950-634, tolerance # 50744), dicamba dimethylamine (SB950-635, tolerance # 50745) and dicamba monoethanolamine (SB950-636, tolerance # 50746).

II. TOXICOLOGY SUMMARY

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

COMBINED (CHRONIC AND ONCO) RAT

**** 040-47 034309-034315, 034225** "Lifetime Dietary Toxicity and Oncogenicity Study in Rats With Technical Dicamba," (2/28/85, IRDC report #: 163-694). Technical Dicamba (86.8% pure, lot #: 52625110) was fed in diet to Albino rats (60/sex/group) at 0, 50, 250 or 2500 ppm in the diet for 115 to 118 weeks. Chronic (Systemic) NOEL = 50 ppm (Brain ventricular dilatation associated with pituitary anterior adenomas were observed in females at \geq 250 ppm. Adrenal enlargement was increased at \geq 250 ppm in both sexes. Increased macroscopic lesions in liver at \geq 250 ppm (males) and lesions in lymph nodes at 2500 ppm (males) were observed.) Oncogenicity NOEL = 50 ppm (There were increased malignant lymphomas in females at \geq 250 ppm, increased parafollicular cell carcinoma, and adenoma, as well as increased follicular adenoma and carcinomas in treated males, primarily at 2500 ppm, but could be extended down to the lower doses. **Possible adverse effect. Acceptable.** The study was previously considered to be unacceptable (JR, 4/4/85; CNA, 9/26/85 & M. Silva, 12/1/89--an MTD was not determined). After re-evaluation, the study is acceptable with a **possible adverse effect.** M. Silva, 8/14/95.

EPA 1-liner: NOEL \geq 2500 (HTD); Core Minimum, no adverse effect (1/13/89).

017 018630 (7-13-84, IRDC) Summary report of 034309-15. (4-4-85, Gee).

CHRONIC, RAT

017 018631, "Feeding for Two Years of the Herbicide 2-methoxy-3,6-Dichlorobenzoic Acid (Dicamba) to rats and Dogs (Rat Chronic feeding)" (3-11-62, Kettering). 90% 2-methoxy-3,6-dichlorobenzoic acid; 24-month study at 0, 5, 50, 100, 250 or 500 ppm in the diet, 32/sex/group. NOEL \geq 500 ppm. UNACCEPTABLE based on dose selection (too low), animal numbers, mortality from respiratory disease, inadequate histopathology and statement that tumors were removed periodically. No adverse effect could be identified. (Gee, 4-4-85).

EPA 1-LINER: SUPPLEMENTARY, oncogenic NOEL = > 500 ppm (HDT), systemic NOEL > 500 ppm (HDT)

039 034223. Histopathology report for 18631.

017 018628. Brief summary of 018631.

009 942829. Analytical Methods.

CHRONIC, DOG**The following one-liner contains an explanation on the current chronic dog data gap status:**

060 54480 "One Year Dietary Toxicity Study in Dogs," (IRDC, 12/19/86, Report no: 163-696). Technical Dicamba (lot 52625110, 86.6% pure) was fed in diet to beagle dogs (4/sex/dose) at 0, 100, 500 or 2500 ppm for 1 year (9 months of age at start of feeding). NOEL > 2500 ppm (No effect observed at any dose). Reviewed as unacceptable (J.Gee, 6/8/87), the study was reevaluated upon receipt of a pilot study (DPR Volume/record #: 227-063/061043) which did not provide sufficient justification for dose selection (M. Silva, 5/4/88). Further submissions were letters between the Velsicol Chemical Corporation and EPA regarding EPA agreement to the protocol for the chronic dog study and a letter from EPA to the Sponsor stating that a MTD was not considered tested, but the study was accepted as Core Minimum data (Rinkus, 8/25/89). The complete chronic data base for dicamba has been re-evaluated. DPR now considers the chronic dog data gap to be filled, in light of the fact that a chronic (systemic) NOEL/target organ has been identified in both mice and rats (50 ppm) and that risk assessment for chronic effects of dicamba will likely be based on that value. The chronic dog study will not be considered acceptable by DPR, however, since effects were not elicited at any dose. While it is true that an MTD was not achieved in the definitive study, the high dose was 2500 ppm, which is high, when compared to doses eliciting effects in rodents. Therefore, at this time, there is no need to repeat the chronic dog study, since the NOEL may exceed 2500 ppm without contributing more information than already obtained from the rodent studies. **CONCLUSION:** When evaluating the entire chronic data base as a whole, DPR considers there is sufficient information to fill the data gap, although the chronic dog study remains unacceptable. M. Silva, 2/16/96.

EPA 1-liner: NOEL \geq 2500 (HTD); Core Minimum; no adverse effect.

Subchronic (8-Week) Rangefinding Study:

227-060 & 063 054480 & 061043 "4-Week (Extended to 8 Week) Dietary Toxicity Study in Dogs" and "One Year Dietary Toxicity Study in Dogs" (Blair, M.-Pilot & Full Study; International Research and Development Corp., Mattawan, MI; 9/7/84 (Pilot), 12/19/86 (Full Study). Both the pilot and the definitive studies were re-evaluated for consideration of acceptability. There were no new findings which could upgrade the 52 week chronic dog study. Although there was decreased food consumption early on, this "inappetence" effect was transitional in both the preliminary study (high dose = 5000 ppm) and in the definitive study (high dose = 2500 ppm). No other effects related to treatment were observed. The full report for the 52 week chronic dog study stated: "In conclusion, administration of technical reference standard dicamba in the diet in concentrations of up to 2500 ppm to beagle dogs for one year resulted in no toxic or pathological effects though some dogs did not consume the diet during the very early part of the study." Therefore, the study remains unacceptable and not upgradeable (No MTD). M. Silva, 12/29/95.

009 942829 Very brief reference to analytical methods.

017 038275, 018629 (path report). "Feeding for two Years of the Herbicide 2-Methoxy-3,6-Dichlorobenzoic Acid (Dicamba) to Rats and Dogs", (3-11-62, Kettering). 24-month study, animals fed test compound at 0, 5, 25 or 50 ppm, 3/sex/group. UNACCEPTABLE on dose selection, animal number (especially after an interim sac of 1/sex/group at 12 months), no diet analysis, missing individual data on weights, limited histopathology. No adverse effect could be identified. (Gee, 4-4-85).

EPA 1-liner: SUPPLEMENTARY, NOEL = 5.0 ppm (males)(decreased body wt. in males), NOEL = 25 ppm (female body weight, hematology and urinalysis)

017 038273. Brief summary of 038275.

ONCOGENICITY, MOUSE

**** 075 075245**, "Potential Tumorigenic Effects in Prolonged Dietary Administration to Mice", (Huntingdon Research Center, HRC Report No. VCL 72/871205, 10/11/88). Dicamba (purity = 86.8%) was administered in the feed at concentrations of 0, 50, 150, 1000, or 3000 ppm/day to 52 CD-1 mice/sex/group. Males received dicamba treated diets for 89 weeks and females 104 weeks. Systemic NOEL = 50 ppm (Increased mortality at ≥ 150 ppm was observed. Females at ≥ 150 ppm showed decreased neutrophils and eosinophils and increased lymphocytes. Female kidney weights at ≥ 1000 ppm were increased. Males showed enlarged spleens and pale kidneys at ≥ 150 ppm. Females at ≥ 150 ppm showed increased liver masses, enlarged spleen, kidney scarring and uterine distension.) Oncogenicity NOEL = 50 ppm (There was an increase in lymphoid leukemias and lymphoid sarcomas, in addition to hemangiosarcomas and hemangiomas at ≥ 150 ppm.) **Possible adverse effect.** Previously evaluated as unacceptable (Silva, 2/26/90), upon re-review, the study is now considered to be acceptable. M. Silva, 8/21/95.

077 088548 This volume contains a letter with information regarding the rationale for dose selection for 075 075245 (provided by Sandoz Crop Protection Corporation, June 19, 1990). It included:

1. Body weight and feeding data from a 4-week pilot study, using 0, 30, 100, 300, 1000, 3000 and 10000 ppm of Dicamba (summary data only--IBT, 1976). No bodyweight or feeding effects were observed at any dose.
2. A brief summary of a 4-week pilot study, using doses of 0, 10000, 15000, 20000, 25000, 30000 and 50000 ppm of Dicamba (IBT, 1976). According to the summary (no data were presented), bodyweights decreased at ≥ 30000 ppm, food intake decreased at ≥ 15000 ppm, 3 deaths occurred at 50000 ppm. In week 4 of the study, slight muscular rigidity was observed at 15000 ppm and at ≥ 20000 ppm, rigidity of limb muscle, in-coordination, impaired locomotion, partial paralysis of the hind legs and ruffled fur was seen and was considered to be dose related. The report recommended a dose range up to 10000 ppm for the definitive study.
3. Letters regarding opinions of EPA about the rationale for selecting 0, 50, 150 and 3000 ppm were included (supposedly in appendices 3-5, however nothing was in appendix 3). (no worksheet) M. Silva, 8/6/90.

076 075612 Supplement to 075245. A letter from EPA dated August 25, 1989 accepting 075245 as core minimum and EPA's reviewer comments addressing study 075245. EPA considers the (equivocal) LEL for systemic toxicity (increased mortalities in males and decreased body weight gain in females) to be 3,000 ppm (approximately 360 mg/kg/day) with a NOEL of 1,000 ppm (approximately 115 mg/kg/day). M. Silva, 2/22/90.

048-49 034558-034561, "Twenty-four Month Chronic Oral Toxicity and Carcinogenicity Study with Technical Banvel-Dicamba in Charles River CD-1 Mice-Final Pathology Report", (6-4-80, IBT judged invalid by EPA). 19 month study with 60/sex/group fed 0, 100, 1000 or 10,000 ppm.

UNACCEPTABLE on basis of EPA evaluation plus high dose exceeded m.t.d. and inadequate mid-dose histopathology. Possible oncogenic effect of marginal increase in angiosarcomas in males at mid-dose. (CNA, 8-30-85).

EPA 1-liner: Invalid IBT study.

REPRODUCTION, RAT

**** 086, 088 127243, 145101-145102**, "Technical Dicamba, A Study of the Effect on reproductive Function of Two Generations in the Rat", (Robert E. Masters, Huntingdon Research Centre Ltd, Huntingdon, Cambridgeshire, England, Report # SNC 140/921437, 20 October 1993). Technical dicamba (86.9% pure) was fed in diet to CrI:CD*(SD) BR VAF/Plus rats (28 or 32/sex/dose) at 0 (Biosure Laboratory Animal Diet No. 2), 500, 1500, and 5000 ppm through 2 generations (with one litter in the first and two in the second). Treatment began 10 weeks prior to F0 mating. **Parental NOEL = 1500 ppm** (An increased (tense/stiff) body tone and slow righting reflex in F1 females was observed at 5000 ppm. Females in both generations and males in F1 generation showed increased liver weights at 5000 ppm.) **Reproductive NOEL = 500 ppm** (There was an indication of dose-related decrease in sperm motility in the F1 generation at ≥ 1500 ppm.) **Pup NOEL = 500 ppm Possible adverse effect:** Both sexes of F1 weanlings at ≥ 1500 ppm and F2a & F2b weanlings at 5000 ppm showed increased liver weights. There was a significant ($p < 0.01$) delay in balanopreputial skinfold cleavage formation in males at 5000 ppm and growth development (body weight) in all generations at ≥ 1500 ppm was delayed. **Note:** Reduced mating success was noted across all groups, including controls, in both F1 pairings. Previously reviewed as not acceptable (Silva, 9/20/94), however after evaluation of requested information, the study status is upgraded to acceptable. (Silva, 3/15/96).

087 136117, 136118 This volume contains supplementary data for the rat reproduction study (086 127243). In addition, a USEPA review of the study was included. No worksheet. M. Silva, 9/15/95.

The unacceptable rat reproduction study: 086 127243, "Technical Dicamba, A Study of the Effect on reproductive Function of Two Generations in the Rat", (Robert E. Masters, Huntingdon Research Centre Ltd, Huntingdon, Cambridgeshire, England, Report # SNC 140/921437, 20 October 1993) was independently re-evaluated at DPR. The reviewer reached the following conclusions (worksheet included):

227--86 127243; "Technical Dicamba, A Study of the Effect on reproductive Function of Two Generations in the Rat", (R.E. Masters, Huntingdon Research Centre Ltd., Huntingdon, Cambridgeshire, UK, 10/20/93); Dicamba Technical (Batch # 52103810, 86.9% purity) administered to 4 groups 28 to 32 Sprague Dawley rats/sex/group at concentrations of 0, 500, 1500 and 5000 ppm for 2 generations; reduced male fertility was noted in the F1a and F1b generations in the control and treated groups; histopathological examination of the reproductive organs in both sexes as well as semen analysis did not reveal evidence of any abnormal findings; growth retardation was detected in the offsprings from both generations at doses as low as 1500 ppm; developmental NOEL = 500 ppm (reduced pup size); reproductive NOEL not determined; study **unacceptable** due to reduction of fertility in control and treated males; (Leung, 12/28/95). [See 1-liner, above].

018 018634, "Effects Exerted Upon the Fertility of Rats and Upon the Viability of Their Offspring by the Introduction of Banvel D into Their Diets" (12-6-66, Kettering). Banvel-D, 87.2% C-64184, 2-methoxy-3,6-dichlorobenzoic acid; three generation study with 10 males/20 females per group fed 0, 50, 125, 250, or 500 ppm. NOEL ≥ 500 ppm. UNACCEPTABLE. Age (11 weeks at start of dosing), dose selection (no sign of toxicity), short dosing of three weeks before first mating, inadequate pathology, others. No adverse effect on reproduction reported. Reproductive NOEL $>$

500 ppm (HDT). (Gee, 4-3-85).

EPA 1-liner: Core Supplementary, downgraded from Core Minimum as of 2/27/89.

50745-003, 046841. Supplementary to 018634. EPA review of study. (Kettering Laboratory, 12-6-66); "technical Banvel D", 87.2% AI; 500, 250, 125, 50, or 0 ppm in the feed (2 control groups); No adverse effects and no change in conclusions or status from previous review (Gee, 4/3/85). UNACCEPTABLE and not upgradeable due to major flaws. [The tolerance number assigned is for the dimethylamine salt although the free acid was used.] (Martz, 8-15-86).

009 942829 Brief one paragraph summary. EPA has no record of having received this document as of 2/27/89.

017 018631 (3-11-62, Kettering). No useful information -- part of the rat chronic study. (Gee, 4-4-85).

EPA 1-liner: Supplementary.

TERATOLOGY, RAT

** 018 018632 "Teratology Study in Albino Rats with Technical Dicamba", (8-24-81, Toxigenics study 450-460). Technical Dicamba; 20-24 females given 0, 64, 160 or 400 mg/kg by oral gavage. 15% mortality at high dose. Maternal NOEL = 160 mg/kg/day (body weight gain, clinical signs); Fetotoxic NOEL \geq 400 mg/kg/day ACCEPTABLE No adverse effect reported. (Gee 4-3-85).

The slight increase in the number of fetuses at 400 mg/kg/day with reduced ossification of one or more bones is not a malformation but may reflect slightly lower fetal weight. (JAP, 6/24/87).

EPA 1-liner: MINIMUM, maternal NOEL = 160 mg/kg (ataxia, salivation, decreased motor activity, mortality, decreased body wts.), fetotoxic NOEL = $>$ 400 mg/kg (HDT), teratogenic NOEL requires clarification due to occurrence of skeletal malformations at all dosage levels which are not statistically significant.

015 942839 Very brief summary, refers to 018632.

TERATOLOGY, RABBIT

** 003, 004 114740, 135244 & 135247 "Developmental Toxicity (Embryo-Fetal Toxicity and Teratogenic Potential) Study of Technical Dicamba Administered Orally Via Capsule to New Zealand White Rabbits", (A.M. Hoberman, Argus Research Laboratories, Inc., Protocol Number 1819-004, 1/27/92). Technical Dicamba, purity 90.4% was administered orally via capsule at concentrations of 0 (size 1 gelatin capsule), 30, 150, or 300 mg/kg/day to 19-20 artificially inseminated female New Zealand White rabbits/group on days 6 through 18 of gestation.

Maternal NOEL = 30 mg/kg/day (There was a decreased bodyweight gain and a decrease in food consumption at 300 mg/kg. At \geq 150 mg/kg, there was an increase in ataxia. Rales, decreased motor activity, labored breathing, perinasal substance, dried feces/no feces, impaired righting reflex and red substance in cage pan were observed to increase at 300 mg/kg. There was an increase in abortions at 300 mg/kg.) **Developmental NOEL** = 150 mg/kg/day (Irregular nasal & internasal ossification occurred at 300 mg/kg.) No adverse effect indicated. Previously unacceptable (Silva, 7/29/94), however, upon receipt and review of the requested information, the study is now acceptable. M. Silva, 10/30/95.

018 018633, "Teratology Study in Rabbits (Banvel D)", (10-24-78, IRDC study 163-436).

Technical Banvel-D, 87.7%, lot A5-S-3-4; 21-22 rabbits were given 0, 1.0, 3.0 or 10.0 mg/kg/day by oral gavage on days 6-18. Inadequate number of pregnancies necessitated repeat 5 months later with 11-14/group. Data are combined. Developmental NOEL \geq 10 mg/kg/day; Maternal NOEL = 3.0 mg/kg (marginal body wt. effect). UNACCEPTABLE -- combining of data, no individual fetal/litter data, pulmonary involvement in first study, no analysis of dosing solutions. No teratogenic effect reported. (Gee, 4-3-85).

EPA 1-liner: Core Supplementary (downgraded from Core Minimum as of 2/27/89), teratogenic NOEL \geq 10 mg/kg/day (HDT); fetotoxic NOEL = 3.0 mg/kg/day (reduced body wts., increased post implantation loss); maternal NOEL = 3.0 mg/kg/day (slightly lower net wt. gain)

50745-003 046842. An EPA review of 018633. (IRDC, 10/4/78). Banvel technical, 87.7%; 10, 3, 1, or 0 mg/kg/day by gavage, days 6-18 (mating=day0). Low pregnancy accompanied by excessive mortality from disease necessitated repeat study 5 months later. Results of both were combined. No effects, no useful data, no change in conclusions or status from previous review (4/3/85, Gee). UNACCEPTABLE and not upgradeable due to major flaws. (Martz, 8-15-86).

057 058111, "Pilot Teratology Study in Rabbits ", (9-13-77, IRDC, 163- 436). Technical Dicamba, 87.7%, Lot A5-S-3-4; Given by oral gavage at 0, 0.5, 1.0, 3.0, 10.0 or 20.0 mg/kg/day, days 6 through 18, 10 New Zealand White rabbits per group; NOEL = 10.0 mg/kg/day (slight weight loss at 20.0 mg/kg/day, some reduced activity on some days at 20.0 mg/kg/day; slight increase in postimplantation loss); UNACCEPTABLE (fetuses not examined). [No review sheet.] (JG, 6/22/87).

GENE MUTATION

015 942840. Summary of various mutagenicity assays with dicamba.

** 019 and 050 036137 "In Vitro Microbiological Mutagenicity and Unscheduled DNA Synthesis Studies of Eighteen Pesticides (Reverse Mutation in *Salmonella typhimurium* strains and in *Escherichia coli*)" (10-79, SRI) *Salmonella*, 5 strains, TA1535, TA1537, TA1538, TA98 and TA100, 0-5000 ug/plate, with and without S-9, three trials. Also, *E. coli* WP2 at 0 to 1000 ug/plate (trial 1) and 0 to 5000 ug/plate (trial 2) with and without S9 activation. ACCEPTABLE. No mutagenic effect reported. (Gee, 1-21-86).

EPA 1-liner: ACCEPTABLE, the number of tryptophan revertants [*E. coli*] per plate did not differ from the negative control with or without metabolic activation using 1 to 1000 ug of dicamba per plate. Not mutagenic to any of the strains of *Salmonella typhimurium*.

50745-002 046840. Summary of EPA review of study 036137, agreed with CDFA review. (Martz, 8-15-86).

050 036141 "Mutagenesis Screening of Pesticides Using *Drosophila* (Sex-Linked Recessive Lethal Test)" (2-81, Warf Institute) Males were fed 3 or 2000 ppm and mated for four broods. UNACCEPTABLE-- missing pages, also purity of test material. Upgradeable. No adverse effect reported. (Gee, 1-21-86).

No EPA 1-liner.

CHROMOSOME EFFECTS

**059 054479, "Chromosome Aberrations in Chinese Hamster Ovary (CHO) Cells", (Microbiological Associates, Inc. 12-29-86). Technical Dicamba lot 52625110; assay conducted

with and without Aroclor-induced S-9 activation system at dose levels of 2330, 1170, 590, 300 and 0 ug/ml; incubation for 8 hours without activation and for 2 hours with activation; no evidence for an increase in chromosomal aberrations is reported; Acceptable. (JG, 6/8/87).

EPA 1-liner: Unacceptable (no stability or solubility of test material).

DNA DAMAGE

015 942838. Summary of various mutagenicity assays with dicamba

019 and 050 036138, "In vitro Microbiological Mutagenicity and Unscheduled DNA Synthesis Studies of Eighteen Pesticides (Induction of Mitotic Recombination in the Yeast *Saccharomyces cerevisiae* D3)", (10-79, SRI). *Saccharomyces* mitotic recombination, technical Dicamba, 0, 0.1, 0.5, 1.0 or 5.0% (w/v), 4 hour treatment with and without activation. UNACCEPTABLE -- no purity, no positive controls with S-9, DMSO used as solvent. No adverse effect reported. (Gee, 1-21-86).

EPA 1-liner: UNACCEPTABLE, the absolute number or relative number of mitotic recombinations in *S. cerevisiae* at 0 to 5% concentration of dicamba were not increased. However, no positive control was used.

50745-002 046840. Summary of EPA review of study 36318, agreed with CDFA review. (Martz, 8-1-86).

019 and 050 036139, "In vitro Microbiological Mutagenicity and Unscheduled DNA Synthesis Studies of Eighteen Pesticides (Relative Toxicity Assays in DNA Repair-Proficient and -Deficient strains of *E. coli* and of *B. subtilis*)" (10-79, SRI). Technical Dicamba; *E. coli* W3110 and p3478, *B. subtilis* H17 and M45; 0, 0.01, 0.1, 1.0 or 5.0 mg/disk, no activation only. UNACCEPTABLE (activation not included, no purity of test article.) Increased zone of inhibition of growth with both repair deficient strains compared with their comparable proficient strains. **Adverse effect** on bacterial growth at highest concentration only with zone also increased for proficient strains. Considering the other 844 tests and the small difference between strains (3-4 mm) in diameter or 1.5 to 2 mm greater from the disk edge, the finding is of questionable biological significance. Initially reviewed without noting the growth differential. (Gee, 1-21-86 and 6-22-87).

EPA 1-liner: EPA has not received this document for review as of 2/27/89.

** 019 and 050 036140, "In vitro Microbiological Mutagenicity and Unscheduled DNA Synthesis Studies of Eighteen Pesticides (Unscheduled DNA Synthesis in Human Fibroblasts)" (10-79, SRI) WI-38. Technical material, unscheduled DNA synthesis at 0-3000 ug/ml with and without mouse liver activation, two or three trials. ACCEPTABLE. No increase in UDS. (Gee, 1-21-86).

EPA 1-liner: ACCEPTABLE, levels of 0.1 to 3000 ug/ml did not induce UDS with or without metabolic activation.

50745-002 046840 Summary of EPA review of study 036140, agreed with CDFA review. (Martz, 8-15-86).

Summary: A possible adverse was noted in one study with *E. coli* and *B. subtilis* measuring DNA repair study with differential growth between the repair deficient strain and the repair effective strain in both species. No evidence, however, was noted in an unscheduled DNA synthesis assay in mammalian cells. No other genotoxic effect was reported in other test types. The significance of the finding in study 36139 is, therefore, not clear but does provide evidence for interaction of dicamba with bacterial DNA followed by repair involving both polymerase A (*E. coli*) and

recombination *B. subtilis*). (JG, 6/22/87).

NEUROTOXICITY, HEN

Note: Acute delayed neurotoxicity studies are not required at this time for Dicamba.

051 036142, "Acute Oral Toxicity (LD 50) and Neurotoxic Effects of Dicamba in the Domestic Hen", (8-1-83, Huntingdon). Test article 86.82% pure, lot 52625110; Hens were dosed with 79, 158 or 316 mg/kg. The high dose was the estimated LD50. The test agent is not an organophosphate or carbamate. The study is evaluated as "ACCEPTABLE" but is NOT REQUIRED. **A possible adverse effect** was noted in pathology of the sciatic nerve which was correlated with recumbancy due to acute toxicity at the high dose. A compound-related effect could not be positively excluded. (Gee, 1-21-86).

EPA 1-liner: MINIMUM, neurotoxic NOEL > 316 mg/kg (HDT); no classical ataxia was noted.

SUPPLEMENTAL INFORMATION

084 124546 This volume contains a risk assessment performed on dicamba using hypothetical data. It was submitted to show that the studies currently unacceptable for dicamba would not make a difference in the ultimate risk assessment for dicamba. No worksheet. M. Silva, 9/15/95.