SUMMARY OF TOXICOLOGY DATA  
Alachlor

Chemical Code # 678, Document Processing Number (DPN) 249  
SB 950 # 71  
November 10, 1986  
3/16/87, 6/5/87, 3/17/89, 3/23/90, 8/1/16

DATA GAP STATUS

Chronic toxicity, rat:          No data gap, possible adverse effect
Chronic toxicity, dog:        No data gap, no 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
Developmental toxicity, rat:  No data gap, no adverse effect
Developmental toxicity, rabbit: No data gap, no adverse effect
Gene mutation:                 No data gap, no adverse effect
Chromosome effects:           No data gap, no adverse effect
DNA damage:                   No data gap, no adverse effect
Neurotoxicity:                No studies have been submitted

Toxicology one-liners are attached.

All record numbers for the above study types through 67756 (Document No. 249-0132) were examined. This includes all relevant studies indexed by DPR as of 8/1/16.

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

File name: T160801  
Revised by T. Moore, 8/1/16
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

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

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METABOLISM AND PHARMACOKINETICS

Monkey Metabolism
249-0079; 17234; “Pharmacokinetic Study of Alachlor in Rhesus Monkeys Following Intravenous Administration”; (D.E. Johnson; International Research and Development Corporation, Mattawan, MI; Study No. 401-296; 12/22/84); Two rhesus monkeys/sex/group were dosed intravenously with 0.23 or 2.4 mg/kg of \(^{14}\)C-U-phenyl alachlor technical (radiochemical purity >99%, specific activity: 22.957 mCi/mM, chemical purity >98%). Urine and fecal samples were collected up to 10 days post-dose. Ninety three and 99% of the administered dose was recovered in the excreta by the end of the 10-day sampling period. For the 0.23 mg/kg treatment group (males and females), 82.07 and 11.19% of the administered dose was recovered in the urine and feces, respectively. For the 2.4 mg/kg treatment group, 91.42 and 8.13% of the administered dose was recovered in the urine and feces, respectively. Elimination of radiolabel from the blood and urine demonstrated a biphasic pattern for the 0.23 mg/kg treatment group. The T1/2 for the \(\alpha\) phase was 0.76 hours and for the \(\beta\) phase was 7.36 hours. For the 2.4 mg/kg group, only the rate for the \(\alpha\) phase could be ascertained which was 4.9 hours. Supplemental Study (Moore, 11/12/15)

249-0117; 59954, 59955, 59956; “Metabolism Study of Alachlor in Rhesus Monkeys following Intravenous Administration”; (K.A. Laughlin, D.E. Johnson; International Research and Developmental Corporation, Mattawan, MI; Study No. IR-85-204; 12/20/85); Three rhesus monkeys/sex/group were dosed by intravenous injection with 0.7 or 7.0 mg/kg of \(^{14}\)C-U-phenyl-Alachlor (radiochemical purity: at least 98.4%, specific activity: at least 19.6 mCi/mM; chemical purity: > 98%). Unlabeled alachlor technical (purity: >98%) was used to adjust the specific activity of the dosing preparations. Eighty eight to 89% of the administered dose was excreted in the urine (urine and rinsate) by 5 days post-dose. Eighty five to 89% of the administered dose was excreted within the first 24 hours post-dose. Isolation and identification of metabolites was performed on pooled 0 to 96 hour urine samples. Five metabolites were identified which comprised 51 to 52% of the total radiolabel recovery in the urine. The primary pathway of metabolism entailed conjugation of the test material with glutathione, followed by transformation to the mercapturic acid conjugate and further to the cysteine conjugate. An alternative pathway is hydroxylation of alachlor with secondary conjugation to glucuronide. This study did not comprehensively identify all of the metabolites, but provided an insight into the metabolic pathways and excretion profile of alachlor by primates. Study supplemental (Moore, 12/10/15)

Rat Metabolism
249-0120; 59966; “Pharmacokinetic Study of Alachlor Distribution and Elimination in the Long-Evans Rat, Part I: Absorption, Distribution and Excretion”; (A.G.E. Wilson, L.J. Hall; Monsanto Co., Environmental Health Laboratory, St. Louis, MO; Study No. 84027; 2/4/86); Thirty three Long Evans female rats/group were dosed orally by gavage with 7, 70 or 700 mg/kg of [phenyl-U-C\(^{14}\), 2-C\(^{13}\)] Alachlor technical (C\(^{14}\) labelling: chemical and radiochemical purity >98%, C\(^{13}\) labelling: chemical purity: >98%, radiochemical purity: 90%; no specific activity provided for the test material). Three animals/group/time point were euthanized at 2, 4, 6, 8 and 24 hours and 2, 5, 10, 20, 30, and 40 days post-dose. Urine and fecal samples were collected
up to 120 hours post-dose from the survivors. In another cohort, 21 females were dosed once daily with 700 mg/kg/day of the radiolabeled test material for 15 days. Three animals/group/time point were euthanized at 24 hours after the 3rd, 7th, 11th and 15th doses and at 2, 5 and 40 days post-final dose. Urine and fecal samples were collected at daily during the 15-day dosing period and at 1, 2, 3, 4, and 5 days post-final dose. In the single dosing regimen, radiolabel was relatively equally excreted via the urine and feces over the 100-fold range of treatment levels. At 7 mg/kg, 42.7 and 42.6% of the administered dose was recovered in the urine and feces, respectively. At 70 mg/kg, 47.5 and 41.0% of the administered dose was recovered in the urine and feces, respectively. At 700 mg/kg, 30.1 and 44.9% of the dose was recovered in the urine and feces, respectively. At the highest treatment level, the lower percentage of the administered dose in the urine was likely due to the limits of absorption having been achieved. For the multiple treatment regimen, the percentage of administered dose which was recovered in the urine and feces plateaued after 3 days with the percentage of dose recovered from the urine ranging from 25.3 to 36.4% and from the feces ranging from 45.8 to 54.9% over the 15-day treatment period. At the two lower treatment levels, 70 to 73% of the administered dose had been excreted by 24 hours post-dose (urine, feces and cage wash). At 700 mg/kg, 35% of the dose had been excreted at 24 hours. In the tissue distribution evaluation, the blood, especially the red blood cells, was the site of sequestration. The nasal epithelium demonstrated a relatively high concentration of radiolabel as well. A biphasic elimination pattern was evident for a number of the tissues. The T1/2 for the initial elimination phase for the three treatment levels ranged from 9.1 to 18.3 hours for the liver, 14.9 to 46.2 hours for plasma and 6.5 to 13.9 hours for the carcass. The T1/2 for the final elimination phase ranged from 328 to 573 hours for the liver, from 160 to 335 hours for the plasma and from 361 to 433 hours for the carcass. The T1/2 values for other tissues/organs were within these range of these values.

By 40 days post-dose, only trace amounts of radiolabel were still present in any of the tissues/organs. Study supplemental. (Moore, 11/12/15).

249-0123; 59972; “The Metabolism of Alachlor in the Laboratory Rat. Part II: Identification, Characterization, and Quantification of Alachlor and Its Metabolites after Oral Administration”; (S.J. Moran, M.C. Grabiak; Monsanto Co., Environmental Health Laboratory, St. Louis, MO; Project No. 7824, Report No. MSL-3016; 6/83); Radiolabeled compounds in the urine, feces, gut contents, and blood plasma which had been collected from female Long-Evans rats dosed orally by gavage with 7 or 700 mg/kg of radiolabeled alachlor or with 15 daily doses of 7 mg/kg/day of the radiolabeled test material (study report no. MSL-3098, ADE data were not submitted to DPR) were isolated and identified using HPLC, mass spectroscopy, high voltage electrophoresis, $^{13}$C-spectra nuclear magnetic resonance, liquid scintillation and chemical-derivatization methods. In a preliminary study, animals were dosed orally with 800 mg/kg of the radiolabeled test material and the presence of radiolabeled volatiles and/or carbon dioxide was monitored for 48 hours. As only 0.02% of the administered dose was recovered, excretion of the radiolabel via the inhalation route was not deemed to be an important path of excretion. Two approaches were employed to assay the metabolites, (1) use of pooled 96-hour urine samples for each animal and 72 or 96-hour samples for feces and (2) time course of pooled samples (i.e., 0 to 12, 12 to 24 hours, etc. up to 96 hour post-dose). In the excretion profile, the percentage of dose which was recovered in the urine across the treatment groups was slightly greater for the females ((M) 37.6 to 45.0% vs. (F) 42.5 to 53.2%). A significant fraction was also recovered in the fecal samples ((M) 47.7 to 51.6% vs. (F) 37.0 to 49.3%). Overall, there was no apparent difference in the spectrum of metabolites which were recovered based on dose or sex. Four main pathways of metabolism were defined by the metabolites which were recovered; (1) mercapturic acid conjugation, (2) methyl sulfoxides, methyl sulfones, (3) glucuronic acid conjugates and (4) aryl sulfate ester. Study supplemental. (Moore, 11/30/15)
Metabolism of Alachlor in Long-Evans Rats. Part II. Identification, Characterization, and Quantification of Alachlor and Its Metabolites after Oral Administration; (R.K. Howe, R.G. Nadeau, R.C. Chott, K.H. Carr, G. Yalamanchili; Monsanto Co., Environmental Health Laboratory, St. Louis, MO; Project ID No. 7824, Report No. MSL-5052; 5/86); Radiolabeled compounds in the urine, feces, gut contents, and blood plasma which had been collected from female Long-Evans rats dosed orally by gavage with 7, 70 or 700 mg/kg of radiolabeled alachlor or with 15 daily doses of 700 mg/kg/day of the radiolabeled test material (see rec. no. 59966, vol. no. 249-0120) were isolated and identified using HPLC, mass spectroscopy, high voltage electrophoresis and liquid scintillation. In order to identify and quantify the concentration of individual radiolabeled compounds, urine and feces samples collected up to 96 hours post-dose from 9 animals were pooled and analyzed. A total of 28 radiolabeled compounds were identified in either the urine and/or the feces. Any one compound constituted no more than 6.6% of the administered dose in either the urine or the feces. Among the more prominent metabolites, there were two metabolites of alachlor bound to cysteine (metabolite nos. 5, 15), a dithio-bis metabolite of alachlor (metabolite no. 22), two metabolites of alachlor hydroxylated on one of the ethyl chains and having a methyl sulfonyl moiety on the acetamide group (metabolite nos. 27, 35) and a glucuronidation product bound to one of the ethyl chains on the phenyl group (metabolite no. 7). The presence of these metabolites indicate the following pathways were incorporated in the metabolism of alachlor. Hydroxylation of one or both of the diethyl chains on the phenyl group followed by glucuronidation by a condensation reaction at the modified site was evident. Also, another site of modification was substitution of the chloride ion on the acetamide group for a bond with the cysteinyl sulfur of glutathione. Further metabolism resulted in the hydrolysis of the amide linkages of the glycine and glutamate moieties, leaving the cysteinyl moiety still bound to the alachlor metabolite. Ultimately oxidation of the sulfur resulted in the methyl sulfonyl acetamide metabolite and the formation of the dithio-bis acetamide. Phase 2 conjugation reaction with glucuronide at the phase 1 hydroxylation sites constituted the 3rd pathway of metabolism. Despite the extensive effort to identify the metabolites, a significant fraction of the radiolabeled compounds were not identified. For the urine, 30.1, 47.5 and 42.7% of the administered dose was recovered in the urine by 120 hours post-dose of the 700, 70 and 7 mg/kg groups, respectively. The 96 to 120 hour portion constituted a small part of the overall recovery so these percentages are a reasonable approximation of the recovery between 0 and 96 hours post-dose. The identified metabolites were only 17.2, 31.4 and 27.9% of the administered dose, respectively. Likewise, radiolabel recovered in the feces constituted 44.9, 41.0 and 42.6% of the administered dose by 120 hours post-dose for the 700, 70 and 7 mg/kg groups, respectively. The identified metabolites were 17.8, 21.6 and 15.2% of the administered dose, respectively. For the feces, extraction from the solid material was problematic. The distribution of metabolites in the urine of the 700 mg/kg/day treatment group was largely similar to that of the other treatment groups. Additional analyses were performed in which radiolabeled moieties recovered from the gastrointestinal tract content and the plasma were identified. As these efforts did not necessarily elucidate the overall metabolic profile of alachlor, the data were not included in this evaluation. Supplemental Study. (Moore, 11/17/15)
radiochemical purity: 90%). At a treatment level of 700 mg/kg, the primary route of excretion was via the feces (males: 67%, females: 54%). Eighteen and 24% of the radiolabel was recovered in the urine of the males and females, respectively. Up to 7 days post-dose, for the males and females, respectively, 15 and 21% of the administered radiolabel was not accounted for. The residual radioactivity may have in been in the body, although analysis of the blood at the conclusion of the sample collection period did not result in the recovery of much radioactivity. Sixty three and 51% of the administered dose was excreted in the first 24 hours post-dose for the males and females, respectively. **Supplemental Study.** (Moore, 12/16/15)

Supplemental Study (Moore, 12/18/15)

**GUIDELINE ACUTE STUDIES ON ACTIVE INGREDIENT**

**Acute oral toxicity, rat**

249-063; 6456; “Acute Oral Toxicity Study in Rats”; (P.R. Heenehan; Bio/dynamics Inc., East Millstone, NJ; Project No. 4899-77; 6/28/78, revised, 5/8/79 and 8/6/79); Five Wistar rats/sex/group were dosed orally by gavage with 0.46, 0.66, 0.93, 1.31 or 1.86 g/kg of Alachlor Technical (purity: 92.8%). The resulting mortality was as follows: 0.46 ((M) 1/5, (F) 2/5), 0.66 ((M) 1/5, (F) 0/5), 0.93 ((M) 4/5, (F) 1/5), 1.31 ((M) 4/5, (F) 5/5), 1.86 ((M/F) 5/5). The clinical signs included ataxia, red and/or clear nasal and oral discharge, urinary staining, piloerection, lethargy, dyspnea, unergroomed appearance, soft stool and prostration. In the necropsy examination, for the animals which died, mottling of the liver and/or spleen, pale kidneys, and air-filled stomach were noted. LD50 (95% confidence limits) (M/F) 0.93 (0.81 to 1.05) g/kg; Toxicity Category III; **Study acceptable.** (Moore, 8/2/04)

**Acute dermal toxicity**

249-063; 6455; “Acute Dermal Toxicity Study in Rabbits”; (C.S. Auletta; Bio/dynamics Inc., East Millstone, NJ; Project No. 4900-77; 4/30/79, revised 8/6/79); The skin of two New Zealand White rabbits/sex/group was treated with 5.6, 8.0, 11.3, 16.0, or 20.0 g/kg of Alachlor Technical (purity: 92.8%) for 24 hours under an occlusive wrap. Treatment-related mortality was as follows: 5.6 (M: 1/2, F: 0/2), 8.0 (M/F: 0/2), 11.3 (M: 2/2, F: 1/2), 16.0 (M: 0/2, F: 1/2), 20 (M/F: 2/2). Time to death was within 4 days of dosing except for the female in the 16.0 g/kg group which died on day 11. Clinical signs included ataxia, nasal discharge, decreased activity, and fine and/or coarse tremors. Grade 1 or 2 erythema and/or edema was noted at the site of application for some of the rabbits. In the necropsy examination, among the animals which died, mottling of the liver, pale kidneys and spleen and dark red lungs were noted. Reported
LD50 (M/F) 13.3 g/kg; Toxicity Category not established; **Study unacceptable**, not upgradeable (number of animal/sex/group were too few to establish an adequate dose-response). (Moore, 8/2/04)

**Acute inhalation toxicity, rat**

249-028; 963623; “An Acute Inhalation Toxicity Study of Alachlor Technical in the Rat”; (J.C. Eschbach; Bio/dynamics Inc., East Millstone, NJ; Project No. 81-7502; 12/22/81); Five Sprague-Dawley rats/sex were exposed whole-body to 5.1 mg/l (gravimetric) of a mixture of Alachlor Technical (purity: 95.3%) and chlorobenzene (80% Alachlor) for 4 hours. The test material was diluted with the chlorobenzene in order to obtain a sprayable consistency. The mean MMAD (GSD) was 2.93 (4.63) um. No deaths resulted from the exposure. Clinical signs included lacrimation, nasal discharge, chromodacryorrhea, dry or moist rales, reduced righting reflex, swollen eyelids and anogenital staining. In the necropsy examination, the scattered gray foci were noted in the lungs. LC50 (M/F) > 5.1 mg/l (80% alachlor mixture); Toxicity Category IV; **Study acceptable**. (Moore, 8/3/04)

**Primary eye irritation, rabbit**

249-063; 6449; “Rabbit Eye Irritation Study”; (P.R. Heenehan; Bio/dynamics Inc., East Millstone, NJ; Project No. 4901-77; 5/25/78, revised: 8/6/79); The eyes of 6 New Zealand rabbits were dosed by ocular instillation with 0.1 ml/eye of Alachlor Technical (purity: 92.8%). No corneal opacity nor iritis were evident during the 4 day observation period. Conjunctival irritation, grade 1 (3/6), was noted at 24 hours post-dose, persisting in one animal at 48 hours and clearing by 72 hours. No chemosis nor discharge were noted at 24 hours. Toxicity Category IV; **Study acceptable**. (Moore, 8/3/04)

**Primary dermal irritation**

249-063; 6464; “Primary Dermal Irritation Study in Rabbits”; (P.R. Heenehan; Bio/dynamics Inc., East Millstone, NJ; Project No. 4902-77; 3/22/78, revised, 8/6/79); The skin of 6 New Zealand White rabbits was exposed to 0.5 ml/site, 2 sites/animal (one intact, one abraded) of Alachlor Technical (purity: 92.8%) for 24 hours under an occlusive wrap. Erythema (intact skin), grade 1 (6/6), was noted at 24 hours post-application, persisting with grades 2 (1/6) and 1 (4/6) at 72 hours. Edema (intact skin), grade 1 (6/6), was evident at 24 hours post-application, persisting with scores of grade 1 (3/6) at 72 hours. Toxicity Category not assigned; **Study unacceptable**, not upgradeable (reversibility of irritation was not demonstrated before the study was terminated). (Moore, 8/3/04)

**Dermal sensitization**

249-0055; 6439; “A Dermal Sensitization Study in Guinea Pigs”; (C.S. Auletta; Bio/dynamics Inc., East Millstone, NJ; Study No. BD-82-206; 4/13/83); The skin of 5 Hartley albino guinea pigs/sex was exposed to 0.2 ml of Alachlor technical (lot no. MCLT 0914B; purity: 94.5%), undiluted, for 6 hours/day, 3 days/week for 3 weeks in the induction phase. After a 2-week interlude, the skin of these animals was exposed to 0.2 ml of the test material for 6 hours in the challenge treatment. The skin of a naïve control group of 3 animals/sex was exposed in the same manner at this time. In the challenge treatment, 4 of the 10 animals in the induced group demonstrated a positive response at 24 hours post-application, increasing to 7 animals at 48 hours. None of the naïve control demonstrated a response to the treatment at either 24 or 48 hours. The test material is a positive dermal sensitizer as assessed in the Buehler assay. **Study acceptable**. (Moore, 11/3/15)

**SUBCHRONIC STUDIES**

Rat and dog subchronic dietary toxicity studies have been previously submitted to CDPR. These studies were submitted in volume 249-0037 under record numbers 963630 and 963632
and were performed at Industrial Biotest in 1966. They have not been reviewed at this time. Two other rat and dog subchronic dietary toxicity studies on a metabolite of alachlor (rec. nos. 963628 and 963629) were also performed at Industrial Biotest in 1968. A rabbit 21-day repeated dosing dermal toxicity study (rec. no. 963634) using a 4 lb/gal formulation as the test material was also submitted in this volume. This study was performed at Industrial Biotest in 1968.

CHRONIC STUDIES

**021 - 025 029655-56, 031965-67, (old record No. on J. Christopher's review was 963637). "A chronic feeding study of Alachlor in rats." Bio/dynamics, 11/3/81, (study designation BDN-77-421). Alachlor, 92.6%. Test article used during the first year was stabilized with 0.5% epichlorohydrin (see Vol. 20, part 3, p. 8). Epichlorohydrin was subsequently removed from tech. alachlor used in this study and from all alachlor produced by the Monsanto, or used by Monsanto for subsequent studies. Monsanto studies in CDFA Vols. 056-057 and 059-060 were considered in chronic toxicity/oncogenicity evaluation. Study 021:029655 used 0, 14, 42, and 126 mg/kg/day in diet, 50/sex/group. No definitive NOEL was found in study 021:029655 (mild degree of uveal degeneration syndrome in eyes of 2 males at 14 mg/kg/day: apparent mild periportal hepatocyte hypertrophy and centrilobular hepatocyte necrosis at 14 mg/kg/day). A "non-neoplasia effects" NOEL of 2.5 mg/kg/day derives from study 059:006445. Possible adverse effects include: malignant stomach tumors (carcinomas, sarcomas, and "mixed"; marked incidence in M and F at 126 mg/kg/day, plus one in F at 42 mg/kg/day); nasal turbinate tumors (generally adenomas; dose-related in M and F at 42 to 126 mg/kg/day); thyroid follicular tumors (generally adenomas, definitive in 126 mg/kg/day M, weak indications in 42-126 mg/kg/day F); uveal degeneration syndrome (M and F, definitive and dose-related at 42 and 126 mg/kg/day). In addition, possible treatment effects include low incidence of rare brain tumors (ependymoma at 42-126 mg/kg/day in F and 126 mg/kg/day in M; one oligodendroglioma in a 126 mg/kg/day M); also non-statistically significant increases in "nodular hyperplasia" or hepatocellular adenomas in 126 mg/kg/day M and F, respectively. These and other major findings are tabulated and discussed in 3/10/89 review. Acceptable. J. Christopher, 4/12/85, C. Aldous, 3/10/89.

097 048630 Monsanto response to the 4/12/85 CDFA review of the 11/3/81 Bio/dynamics study (Vol. 21-25). Statistical data were provided on major oncogenicity and chronic effects in the study. The new information indicates that there is no NOEL for chronic effects in this study due to liver necrosis at all treatment levels, statistically significant even at the lowest level. The discussion in the CDFA Supplementary Worksheet for this response indicates that follow-up studies allow establishment of an LEL for chronic effects of 15 mg/kg/day, and a NOEL of 2.5 mg/kg/day. [Note: the 3/16/87 Summary of Toxicology Data incorrectly considered the overall NOEL for rat chronic toxicity to be 15 mg/kg/day. This could not be correct, considering that in study 059:006445, 15 mg/kg/day was clearly an effect level: there were non-neoplastic and neoplastic lesions in the nasal turbinates in that study]. C. Aldous, 10/28/86, 3/10/89.

Summary of in-life physical observations for rat combined study: Vols. 021 - 025.

Final ophthalmological exam reports for rat combined study: Vols. 021 - 025.

Supplement to rat combined study above (Vols. 021 - 025, report located in Tab 3, p. 5). Brief summary relating to tumor findings, as part of Monsanto's assessment of oncogenic risk.

"Special Chronic Study of Alachlor Administered in Feed to Long-Evans rats". Monsanto Project No. ML-80-224, 4/16/84. (A follow-up to primary Biodynamics study BDN-77-421, 021:029655). A single-dose study with technical alachlor (94.1%) administered at 126 mg/kg/day in diet to Long-Evans rats, 100/sex. Design involved three treatment groups: a 25-month continuous dosing group; a recovery group involving 5-6 month dosing, followed by control diet up to 25-month sacrifice; and a group given continuous treatment up to sacrifice at 8 months. Possible adverse effects, previously identified in study 021:029655, were confirmed in this study. These included uveal degeneration syndrome, which was found to be irreversible, and discontinuance of treatment did not necessarily arrest progression of symptoms. Nasal turbinate adenomas or adenocarcinomas were found in M and F lifetime treated rats, and in the recovery study. Gastric carcinomas, sarcomas, or mixed tumors were found in 3/68 M and in 19/30 F in lifetime exposure groups, but not in recovery rats. Lifetime treatment elicited thyroid follicular tumors in males only; however in the recovery group, these tumors were not demonstrably elevated in either sex. Bone marrow myelocytic hyperplasia and urinary bladder epithelial hyperplasia also appeared to be increased due to treatment. J. Christopher, 4/15/85; C. Aldous 3/14/89 (see also March 1989 "Supplemental Information Worksheet" on collective rat studies related to 021:029655).

Response to "UNACCEPTABLE" classification of study: 056:006442, Monsanto, 4/12/84. The study is so classified because it cannot independently fill a data gap, and not as an indication of failure to fulfill its intended function. This study contributes meaningfully toward filling the data gap for rat chronic and oncogenicity data requirements, which are now considered filled. C. Aldous, 10/27/86).

Addendum to 4/16/84 Monsanto study (ML-80-224). Clarification regarding tumors in or adjacent to and affecting the brain in study described above: Vols. 056 and 057.

"Chronic Study of Alachlor Administered in Feed to Long-Evans rats". Monsanto, St. Louis, MO. 2/27/84. (Supplemental to primary study by Biodynamics, 021:029655). Alachlor, tech., (no epichlorohydrin in this tech.). 50/sex given 0, 0.5, 2.5, or 15 mg/kg/day in diet: NOEL for chronic tox = 2.5 mg/kg/day (nasal submucosal gland hyperplasia at 15 mg/kg/day (M & F). Significant increases in nasal epithelial adenomas in M and F at 15 mg/kg/day. One stomach adenocarcinoma (rare tumor) in 2.5 mg/kg/day male attributed by investigators to test article, considering results of other studies. ACCEPTABLE, useful data. J. Christopher, 4/15/85.

Response to two issues noted by John P. Christopher in his 4/15/85 review of above study (059:006445, Monsanto, 2/27/84). Registrant noted reason for selection of Long-Evans strain is because the 1981 Biodynamics study (Vols. 021-025) used the same strain. Registrant acknowledged that hematology/clinical chemistry assays were not as frequent as suggested in current guidelines, however that the 1981 study had already adequately assessed these parameters. This reviewer considers John P. Christopher's concerns to be adequately
addressed, and the report should be considered ACCEPTABLE and a significant contribution toward filling the rat chronic/oncogenicity data gap. (C. Aldous, 10/27/86).

011 046912 "Herbicide, Chronic and Delayed Effects Studies: two-year chronic oral toxicity study with Lasso Technical in albino rats". (Rec. # 963611 given on worksheet. The latter "Rec. #" was not applied uniquely to this study, but was used repeatedly for various types of studies within this review. This study is reported on pp. 14-16 of section C.) IBT, 9/16/77 (BTL-72-7 study ruled invalid by EPA.). Summary only. Lasso, tech. 0, 100, 300, and 1000 ppm in diet of "albino" rats. No tumorigenicity nor other significant effects on microscopic evaluation. UNACCEPTABLE, NOT upgradeable. (EPA invalid, dose levels clearly too low.) J. Christopher, 4/4/85.

020 029648 (another summary of 011:046912; see above).

105 050238 Information submitted by Monsanto to FIFRA Science Advisory Panel in response to EPA classification of alachlor as a "B2" oncogen. This is not a study, but rather a risk assessment document, and has been examined as such by CDFA Health Assessment Group. No review is necessary by Data Review Group (C. Aldous, 3/16/89).

112 055472 "Statement of Thomas W. Fuhremann" [Toxicology - Alachlor Review Board]. An interpretative summary of alachlor data representing several study types. No new data presented. This statement is primarily of interest in risk assessment. Representative topics include apparent strain specificity of uveal degeneration syndrome, and apparent thresholds for thyroid and other tumors. No Data Review Group review is appropriate. C. Aldous, 3/16/89.

**103 049227 "Chronic study of alachlor administered by gelatin capsule to dogs"**
Environmental Health Lab (Monsanto), 11/16/84. Alachlor, tech. 0, 1.0, 3.0, and 10.0 mg/kg/day. NOEL = 1.0 mg/kg/day (based primarily on slight, dose-related incidence of hemosiderosis or excess hemosiderin in kidney, liver, and spleen; also on modest increases in gastro-intestinal findings such as diarrhea, mucus stool, and other stool abnormalities: all of these findings predominantly in males). Mild anemia and mild liver toxicity indicated at 10 mg/kg/day, particularly in males. Acceptable. Study was previously considered to represent "possible adverse effects", to flag a comparatively low NOEL (even though there was not remarkable toxicity at the LEL). The "possible adverse effects" flag is no longer used to advise Health Assessment Group of low NOELs, hence the flag is removed as of 3/16/89. (C. Aldous, 11/3/86, 6/5/87, 3/16/89).

Oncogenicity, rat
See Chronic rat, above.
Oncogenicity, mouse

"014, 015 963643 and 046246 "Eighteen Month Chronic Feeding Study of Alachlor in mice". Bio/dynamics, 6/18/81 (Study No. BD-77-423). Alachlor tech., 92.6% (with 0.5% epichlorohydrin as stabilizer for first 11 months, final 7 months without epichlorohydrin. 0, 26, 78, and 260 mg/kg/day in diet, 50/sex/group. Apparent chronic toxicity NOEL = 26 mg/kg/day (increased liver/BW and kidney/BW ratios in males at 78 mg/kg/day and above. Slight decrease F survival at 260 mg/kg/day.) Increases in lung adenomas and carcinomas of F at 260 mg/kg/day and increases in liver adenomas and carcinomas of M at 260 mg/kg/day. Originally classified as UNACCEPTABLE (confounding effect of epichlorohydrin, lack of stability of test article during the time period following removal of epichlorohydrin from the technical, many missing tissues in animals dying on study, missing BW and food consumption individual data, inadequate mortality data evaluation [needs K-M curves]). A rebuttal (see 098:048633, below) allowed an upgrade to ACCEPTABLE status for this study. A subsequent rebuttal plus new information (114:060100 and 125:061246, see one-liners below) prompted removal of liver tumors as an apparent treatment effect, however there is insufficient information to change CDFA conclusion that lung tumors constitute a "possible adverse effect". J. Christopher, 4/12/85, C. Aldous, 10/28/86, 3/16/89 (worksheets bear record numbers 060100 and 061246).

098 048633 Monsanto response to John P. Christopher review of study: 014:963643, Bio/dynamics, 6/18/81 (Study No. BD-77-423). Some additional data have been provided in this submission. Some rebuttals were submitted in response to concerns that Dr. Christopher had indicated as reasons for not accepting the study. Some items for which additional information could have been provided were not further elucidated, the registrant citing adequacy of data as previously provided. This reviewer (CNA) recommends considering this study as ACCEPTABLE for the mouse oncogenicity data requirement. C. Aldous, 10/28/86.

114 060100 (relates to primary study, 014:963643). "Witness statement of R. Harold Grice" (representing Monsanto Canada at Alachlor cancellation hearings). No date, but prior to 7/23/87. Statement addresses the lung tumor (alveologenic adenoma and carcinoma) potential of alachlor with respect to the above 18-month mouse study. Arguments were (1) These are common tumor types with unusually low incidence in concurrent control females. (2) A true treatment effect should have shown a typical distribution pattern over time, with increasing incidence over the last months of the study. (3) True treatment effects should include multiplicity of tumors, which was not observed here. (4) Compounds which cause lung tumors generally are not sex-specific. (5) There were no associated increases in tumor incidence, and particularly, no increase in tumor progression, such as from adenomas to carcinomas. (6) General provisions used by regulatory agencies to evaluate oncogenicity studies were not applied to this study. In addition to these major points, Bio/dynamics laboratory historical control data were provided. CDFA acknowledged the usefulness of this evaluation and requests additional information about the historical data (see review for details). C. Aldous, 3/16/89.

125 061246 (Rebuttal to mouse oncogenicity study review for record 014:963643, study by Bio/dynamics, dated 6/18/81). Date of this rebuttal: 8/26/87. Registrant presented a case that there is insufficient evidence to conclude that liver tumors were treatment-related in males. All other commentary related to female lung tumor data. A statement by Haseman (1984) was quoted, indicating that common tumors should be considered treatment-related only if significant at the p < 0.01 level. The EPA Science Advisory Panel concluded that the mouse was negative for oncogenicity. BIBRA reviewers concluded similarly; they noted, among other things, that more lung tumors should have been observed in high dose female survivors to term if alachlor were oncogenic in lungs of females. CDFA Action: re-examination of the data finds insufficient
reason to consider liver tumors a treatment effect. There is insufficient information to make a final decision about lung tumors: CDFA will consider the above comments when re-examining the mouse lung tumor data, on receipt of the historical control data requested in the CDFA review of Dr. Grice’s comments (Record 114:060100). C. Aldous, 3/16/89.

020 029647 Summary of 014:963643, see one-liner, above.

029 963644 Summary of in-life physical observations for 014:963643.

075 017656 Addendum to pathology report of study 014:963643.

017 963638 Summary of 014:963643, see one-liner, above.

011 29619 "Summary of Toxicology Studies Conducted on Lasso Herbicide, Chronic and Delayed Effects Studies: Eighteen month mouse carcinogenic study with Lasso Technical in albino mice". (Rec. # 963611 given on worksheet. The latter "Rec. #" was not applied uniquely to this study, but was used repeatedly for various types of studies within this review. This study is reported on p. 13 of section C.) IBT, 7/17/74 (BTL-72-9A) Summary only. Lasso, tech. An IBT study ruled invalid by EPA. 0, 100, 300, and 1000 ppm in diet of "albino" mice. No significant adverse effects noted. UNACCEPTABLE, NOT UPGRADEABLE. (IBT invalid, dose levels apparently too low.) J. Christopher, 4/4/85.

020 029649 1-page summary of 011:029619.

008 029591 (Original Rec. No. was 963641). 7/8/80. Appendix to invalid IBT mouse oncogenicity study (IBT 621 1182) with histological evaluation of eyes. No adverse effects noted. J. Christopher, 4/11/85.

GENOTOXICITY

There is one acceptable gene mutation study in mammalian cells on file for technical alachlor with no mutagenicity reported. The studies in bacteria which have been reviewed do not suggest a high potential for gene mutation, although one of several representative metabolites of alachlor is mutagenic in the Ames test, as indicated below (Study 076:17661). CDFA requires mutagenicity studies on the technical material to meet the respective data category requirements, thus study 028:963650 (below) does not fill the gene mutation "data gap", although it is a well-executed study on the analytical grade material. A supplementary information worksheet has been included respecting the change of status.

Earlier versions of the Summary of Toxicology Data indicated a "possible adverse effect" on page 1 for gene mutation based on the study with a metabolite (076:017661). In this study, the mutation frequency was increased greater than 3-fold at 10 mg/plate and also increased at 3.0 mg/plate with Salmonella strain TA100. The other 3 strains tested (TA1535, TA1537, and TA98) were clearly negative at these concentrations. Based on the negative results with technical alachlor in mammalian cells (108:053748) and the negative results in the other reports with bacteria, the positive result with a metabolite in one strain only of Salmonella is of questionable biological significance. Therefore, the weight of evidence is for a lack of activity for gene mutation. C. Aldous and J. Gee, 3/17/89.

Gene mutation

028 963650 (worksheet incorrectly lists as Rec. # 096350). Institute of Environmental Toxicology (ET 80-0101), Jan., 1980. Alachlor, analytical grade. Ames test with strains TA1538,
TA98, TA100, TA1535, and TA1537. Duplicate plates at 10, 50, 100, 500, 1000, and 5000
ug/plate, w/ and w/o S9. Also E. coli WP2 hcr at same treatment levels. All responses
negative. Classified as ACCEPTABLE by John P. Christopher, despite use of analytical grade
alachlor and despite test apparently having been run only once with duplicate plates. Study
now re-classified as UNACCEPTABLE because of the inappropriate grade of test article. See
statement at beginning of this section of the summary. Note: EPA One-liner lists this study as
ACCEPTABLE for both the rec-assay and the reverse mutation portions of the report. J.
Christopher, 4/5/86.

076 017660  Monsanto, 2/22/85. Introduction to the several gene mutation studies of of
compounds representative of major alachlor metabolites: Reports contained in same volume:
see above one-liners.

028 963653  Publ., Northern Illinois Univ., 1981. Alachlor mixed with other pesticides in
various combinations. Ames test. No data. No adverse effects indicated. UNACCEPTABLE
(not tech. material, no data). J. Christopher, 4/5/85.
028 963652  (worksheet incorrectly lists as Rec. # of 96352). (Inst. of Environmental
Toxicology, Japan; Mut. Res. 40:19-30, 1976) Alachlor, grade not specified. Reversion assays
with E. coli (WP2) and S. typhimurium (Ames series). No activation. No data presented. No
adverse effects reported. UNACCEPTABLE (test article not characterized, no data). J.
Christopher, 4/5/86.

028 963651  Publ., Lilly Research Labs, 1981. Alachlor, grade not specified. Tested for both
modified Ames test (with and without activation) and in vitro rat hepatocyte UDS assay. No
adverse effects reported. UNACCEPTABLE (no data, no detail of experimental methods, etc.).
J. Christopher, 4/5/85.

011 033212  (Rec. # 963611 given on worksheet. The latter "Rec. #" was not applied uniquely
to this study, but was used repeatedly for various types of studies within this review. This study
is on pp. 19-20 of section C.) IBT (BTL-75-144A). Study validated by EPA. Summary only.
Presume tech. alachlor (CP-50144, 92.6%). Host-mediated mutation assay with S. typhimurium
(strain G 46) in rats. No mutagenicity observed. UNACCEPTABLE. NOT upgradeable.
Summary only. Insufficient data for independent evaluation. Unlikely that investigators could
demonstrate that treatment was performed to the limits of toxicity of test organism (i.e., the

011 029617  An invalid IBT bacterial reverse mutation study.

011 029616  An valid IBT host-mediated assay with S. typhimurium strain G 46 injected into
mice. No data presented, no adverse effects reported.

** 108 053748  "CHO/HGPRT Mammalian Cell Forward Gene Mutation Assay".  (Pharmakon,
7/30/84, PK-83-249, Study No. 314-MO-006-83) Alachlor technical, 95.4%; CHO/HGPRT
assay, tested with and without rat liver activation; S9 at 2% or 5%, 0, 15, 30, 60, 100, 150, 200
or 330 ug/ml, 5 hour incubation; 8-day expression for thioguanine resistance; no increase in
mutation frequency reported; acceptable. J. Gee, 3/12/87.

Chromosome damage
** 054 006437  Hazleton Labs, 3/1/84. "In vivo bone marrow chromosome study in rats".
Rats dosed with tech. alachlor by gavage in corn oil: 0, 100, 330, and 1000 mg/kg in a single
administration. Rats killed at 6, 12, 24, and 48 hr after dosing (48-hr specimens not read as
there was no evidence of mitotic delay). No increase in aberrations noted. Study classified as unacceptable by J. Christopher, due principally to lack of evidence that the high dose was maximized. (see rebuttal response, below). Reconsideration by Gee, in light of the submission of study on absorption in rats following oral dosing (109:054066, see under supplemental studies), found that the high dose of 1000 mg/kg was reasonable based on efficient absorption and on closeness of dose levels to the LD50 in rats. Report is now acceptable. J. Christopher, 4/5/86, C. Aldous, 10/29/86, J. Gee, 3/13/87.

DNA damage or miscellaneous effects

**054 006438** SRI, 4/5/84. In vivo rat hepatocyte UDS assay. Alachlor, tech. 6 rats/dose gavaged with 50, 200, and 1000 mg/kg; 3 rats sacrificed at 2 hr, 3 at 12 hr in each group. Two rats each for pos. and neg. controls, killed at 12 hr. Alachlor found to be weakly genotoxic in this assay (significant increase in UDS in 1000 mg/kg group sacrificed after 12 hr). ACCEPTABLE. J. Christopher, 4/5/86.

028 000995 (worksheet incorrectly lists as Rec. # of 96350; part of report in Vol. -028, part C. Balance of report is under GNMU, 028/963650). (Inst. of Environmental Toxicology, Japan; 1/80) Alachlor, analytical grade. B. subtilis rec assay. 20, 100, 200, 500, 1000, and 2000 ug/disk. Single rep only. No apparent DNA damage. UNACCEPTABLE to fill DNA damage data gap, NOT upgradeable: Single rep not acceptable, technical material not used. EPA One-liner lists this study as acceptable. J. Christopher, 4/5/86.

011 033210 IBT-invalid recombination assay (BTL-75-142, 4/20/76). No adverse effects indicated.


REPRODUCTIVE TOXICITY, RAT

**016 963648 "Three Generation Reproduction Study in Rats with Alachlor, Final Report (Lasso Technical)". Bio/dynamics, 2/20/81. [BDN-77-422] Alachlor, tech. 0, 3, 10, and 30 mg/kg/day in feed. Originally classified as unacceptable (Dosages not justified and appear to be below the MTD on comparison with dosages tolerated in other long-term studies. Histopathology was not performed on animals which were not successfully bred. Other deficiencies noted.) The 10/29/86 re-examination and rebuttal response led to a re-classification as "acceptable". Dosage selection was determined to be adequate, however range was lower than currently recommended. The NOEL for parental toxicity is 10 mg/kg/day, based on chronic nephritis in F2b males at 30 mg/kg/day. No apparent reproductive toxicity. The randomization procedure for selection of parental animals, or for the selection of animals to be examined microscopically, was adequate under circumstances of this study. J. Christopher, 4/8/85, C. Aldous, 10/29/86.

099 048634 Monsanto rebuttal to CDFA review of study: 016:963648. Response review and re-evaluation of data by C. Aldous, 10/29/86. See above.

017 963649 Summary of 016:963648.

020 029653 (Previously designated as 963612 or 963612-2). Brief summary of 016:963648.
011 029620 "Summary of Toxicology Studies Conducted on Lasso Herbicide, Chronic and Delayed effects studies: Three-Generation reproduction study with Lasso Technical in albino rats". (Rec. # 963611 given on worksheet. The latter "Rec. #" was not applied uniquely to this study, but was used repeatedly for various types of studies within this review. This study is reported on pp. 12-13 of section C.) IBT, 4/22/74 (BTL-72-12). Summary only. Lasso, tech. An IBT study ruled invalid by EPA. 0, 30, 100, and 300 ppm in diets of "albino" rats. No significant adverse effects noted. UNACCEPTABLE, NOT UPGRADEABLE. (EPA invalid, dose levels apparently too low.) J. Christopher, 4/4/85.

DEVELOPMENTAL TOXICITY

**Rat

**009 963647 "Teratology Study in rats". (IRDC No. 401-058) 3/21/80. Alachlor, tech. (92.2%). 25 dams/group gavaged with 0, 50, 150, or 400 mg/kg/day. Maternal toxicity NOEL = 150 mg/kg/day (decreased BW gain of pregnant dams, days 6-20, 4 deaths in 400 mg/kg/day group). Developmental toxicity NOEL = 400 mg/kg/day (no apparent effects at HDT). Originally UNACCEPTABLE, now ACCEPTABLE (see response to rebuttal in 102: 048853, 048854, below). J. Christopher, 4/10/85. Rebuttal review by C. Aldous, 10/30/86.

102 048853, 048854 Monsanto rebuttal to J. Christopher review (4/10/85) of 009:963647.

New submissions: analysis of test material, surrogate analysis of dosing solution and original dose prep sheets, fetal individual body weight data, necropsy data on dams, reference to a pilot study to determine dosages, clinical observation data, source of male rats given. Additional data is sufficient to warrant upgrade to ACCEPTABLE status. C. Aldous, 10/30/86.

011 029621 (summary of 009:963647, above).

**Rabbit

**132 067756, "A teratogenicity study in rabbits with Alachlor", (Bio/dynamics, Inc., Study no. BD-87-83, 3/28/88). Alachlor, purity 94.7%, administered by gavage at dose levels of 0 (corn oil), 50, 100 and 150 mg/kg/day from gestation days 7 through 19. There were 18 mated female New Zealand White rabbits/dose. Some reduction in food consumption was observed during the treatment period at each dose level, but body weights were not markedly affected by treatment. Maternal NOEL = 100 mg/kg/day, based on small but statistically significant body weight loss during early treatment period (days 7-10) at 150 mg/kg/day. Developmental NOEL = 150 mg/kg/day (HDT), thus there were no adverse effects. ACCEPTABLE (information missing from original CDFA copy of report was provided: see next "one-liner"). (Aldous, 3/17/89 and 3/23/90).

249-132 [missing pages added to original record number = 067756]. Submission contains the pages which were missing from the copy of the report previously submitted to CDFA. These are the Title Page (prepared by Monsanto), Data Confidentiality page, and the GLP Compliance Statement. The original copy evaluated by CDFA contained p. 290 of the report, indicating dates of QA inspections: nevertheless that page did not indicate whether or not there were significant deviations from GLP guidelines. The new submission provided the signed GLP compliance statement, indicating that the study did conform to essential GLP standards. This submission makes the study fully acceptable. C. Aldous, 3/23/90.

131 067755 Pilot study for 132:067756, above.
062 006448 "Teratology Study in Rabbits-Technical Alachlor". IRDC, 12/29/83. Alachlor, 94%, administered by gavage to 18 pregnant rabbits/group at 0, 10, 30, and 60 mg/kg/day in mineral oil vehicle. No developmental toxicity nor maternal toxicity observed. UNACCEPTABLE (insufficient dosages, inappropriate vehicle, administration of dosage began 1 day too late) apparently not upgradable. Rebuttal response below clarified some concerns of original CDFA review, but study is still classified as "unacceptable" (see 101:048851 below). J. Christopher, 4/10/85, C. Aldous, 10/30/85.

101 048851 (with addendum, 101:048852) Monsanto rebuttal to J. Christopher review (4/10/85) of 1983 IRDC rabbit teratogenicity study (062 006448). Registrant provided satisfactory responses to J. Christopher's concerns about the following: analysis of test article, analysis of dosing solution using technical a.i. as the standard, appropriateness of time of dosing, statistical treatments, and presentation of fetal weight data by sex. The issue of adequacy of dosages has not been resolved. Study still not acceptable. Re-evaluation of data by C. Aldous (10/30/85).

012 963645 "Teratology Study in rabbits with Alachlor". IRDC 11/24/80. (IR-79-022) Alachlor, tech. (92.2%). Initially 16 dams/group gavaged with 0, 10, 30, or 60 mg/kg/day in corn oil. 9-14 dams pregnant at term. Insufficient information to fully evaluate, however apparent NOELs for maternal and developmental effects were the HDT = 60 mg/kg/day. UNACCEPTABLE, NOT UPGRADEABLE (too few pregnant dams at term, dosage not justified and apparently below the MTD, no pathology data presented, no clinical observations presented, unacceptable numbers of deaths and abortions in control and treated groups). J. Christopher, 4/9/85.

020 029654 (Old Record No. was 963612-1). Brief summary of 012:963645.

017 963646 Brief summary of 012:963645.

011 029622 "Summary of Toxicology Studies Conducted on Lasso Herbicide, Chronic and Delayed Effects Studies: Teratogenic Study with Lasso Technical in albino rabbits". (Rec. # 963611 given on worksheet.) The latter "Rec. #" was not applied uniquely to this study, but was used repeatedly for various types of studies within this review. This study is reported on pp. 10-11 of section C.) IBT, 8/14/72 (BTL-72-10). Summary only. Lasso, tech. An IBT study ruled invalid by EPA. 0, 10, and 30 mg/kg/day. No significant adverse effects noted. UNACCEPTABLE, NOT upgradeable. (EPA invalid, dose levels apparently too low.) J. Christopher, 4/4/85.

NEUROTOXICITY

Acute neurotoxicity, rat
Study not submitted.

90-day neurotoxicity, rat
Study not submitted.

Developmental neurotoxicity, rat
Study not submitted nor required at this time.

Delayed neurotoxicity, hen
Study not submitted nor required at this time.
IMMUNOTOXICITY
Study not submitted.

ENDOCRINE DISRUPTOR STUDIES
Study not submitted nor required at this time.

SUPPLEMENTAL STUDIES

076 017661 Monsanto, 9/17/84. N-[2-ethyl-6-(1-hydroxyethyl)phenyl]-N-(methoxymethyl)-2-methylsulfonyl)acetamide. 0, 0.01, 0.04, 0.2, 1.0, 3.0, 10 mg/plate; triplicate plates w/ & w/o S9. Test article represents a class of major alachlor metabolites. Test article mutagenic w/ & w/o S9 (to comparable degree) in TA100 strain. UNACCEPTABLE to fill alachlor GNMU data requirement, however useful data. J. Christopher, 4/8/85.

076 17657 Monsanto, 5/18/84. [N-(2,6-diethyl)phenyl-N-methoxymethyl]-2-amino-2-oxoethanesulfonic acid, sodium salt. 0, 0.01, 0.04, 0.2, 1.0, 3.0, 10 mg/plate; triplicate plates w/ & w/o S9. Test article represents a class of major alachlor metabolites. Test article occasionally elevated revertants/plate to slight extents (signif., p < 0.05) with TA100 or TA1537, but elevations were not consistent and did not appear to be biologically significant. UNACCEPTABLE, but useful data. J. Christopher, 4/8/85.

076 025283 (no Rec. # assigned when originally reviewed) Monsanto, 5/18/84. (N-[2,6-diethyl]phenyl-N-methoxymethyl)-2-(hydroxy)acetamide. 0, 0.01, 0.04, 0.2, 1.0, 3.0, 10 mg/plate; triplicate plates w/ & w/o S9. Test article represents a class of major alachlor metabolites. No evidence of mutagenicity. ACCEPTABLE study for this metabolite (does not fill data requirement for tech. a.i.). J. Christopher, 4/8/85.

076 017658 Monsanto, 5/18/84. 3-[N-[2,6-diethyl]phenyl-N-methoxymethyl)-2-amino-2-oxoethanesulfanyl]-2-hydroxypropanoic acid, sodium salt. 0, 0.01, 0.04, 0.2, 1.0, 3.0, 10 mg/plate; triplicate plates w/ & w/o S9. Test article represents a class of major alachlor metabolites. Test article not mutagenic according to significance criteria established. Study found UNACCEPTABLE due to poor response of strain TA1537 to positive control w/o S9. Acceptability is a moot issue in a supplementary test such as this: useful information was provided, and there is no apparent reason to repeat the test. J. Christopher, 4/8/85.

076 017659 Monsanto, 5/18/84. 2',6'-diethyl-N-[methoxymethyl] oxanilic acid, sodium salt. 0, 0.01, 0.04, 0.2, 1.0, 3.0, 10 mg/plate; triplicate plates w/ & w/o S9. Test article represents a class of major alachlor metabolites. Test article not mutagenic. Study found UNACCEPTABLE due to poor response of strains TA1537 and TA98 to positive control w/o S9. Acceptability is a moot issue in a supplementary test such as this: useful information was provided, and there is no apparent reason to repeat the test. J. Christopher, 4/8/85.

109 054066 Supplement to 054:006437 and the basis of the decision to upgrade the study to acceptable. "A Mechanistic Study of the Interaction of Alachlor with Blood, Part I., Distribution of Alachlor in Blood Components after Oral and Dermal Dosing in the Rat". (Monsanto, 1/29/85) Male rats were dosed with a single oral dose of 7.44 or 780 mg/kg of 14-C-labeled Alachlor. Blood samples were taken at several intervals over 48 hours and the distribution of the radioactivity in plasma and blood cells measured. Excretion in the urine was also followed. The blood level was maximal at 6 to 24 hours. This was taken as evidence that the alachlor was absorbed rapidly and the blood level was maintained over a significant period of time during which marrow cells would be exposed, in response to the deficiency noted by EPA. J. Gee, 3/13/87.
011 033209 (Rec. # 963611 given on worksheet. The latter "Rec. #" was not applied uniquely to this study, but was used repeatedly for various types of studies within this review. This study is reported on p. 17 of section C.) IBT, 7/26/72 (BTL-72-11). Dominant lethal, mouse. Summary only. Presume tech. alachlor (CP-50144, 92.6%). An IBT study ruled valid by EPA. Single ip injection of 15 or 30 mg/kg, males mated over 6-week period. No mutagenic response reported. UNACCEPTABLE, NOT UPGRADEABLE. (Summary only, no justification of dosage levels, no evidence that dosages were maximized.) J. Christopher, 4/4/85.